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Maigne Syndrome as a Clinical Case of Nociplastic Pain

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Maigne Syndrome as a clinical case of nociplastic pain

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A handwritten signature in black ink, appearing to read "Francisco Martins". The signature is stylized with a large, looping initial 'F' and a cursive 'M'.

Assinatura do Estudante

A handwritten signature in black ink, appearing to read "João Almeida". The signature is written in a cursive style with a large initial 'J'.

Assinatura do Orientador

Maio de 2023

Dedication

To my Beloved Parents, Dearest Sister, Caring Boyfriend, and Devoted Friends,

I am deeply honoured to dedicate my master's thesis to each of you, as your unwavering support, love, and encouragement have been the driving force behind my academic journey. Your presence in my life has been an immense source of strength and inspiration, propelling me towards the successful completion of this milestone.

To my parents, Fátima Santos and Jorge Martins, your unconditional love, sacrifice, and belief in my abilities have shaped me into the person I am today. You have provided me with endless support, both emotionally and financially, enabling me to pursue my dreams. Your constant encouragement and wise guidance have instilled in me a strong work ethic and a determination to excel. This thesis is a testament to the values you have instilled in me and a reflection of the gratitude I hold in my heart for your unending support.

To my boyfriend, Gil Leite, your unwavering belief in me has been a constant source of motivation throughout this academic endeavour. Your patience, understanding, and encouragement have helped me overcome the challenges and uncertainties along the way. Your constant presence, providing a listening ear and offering valuable insights, has been invaluable. I dedicate this thesis to you as a token of my appreciation for your unwavering love and support.

To my friends, you have been my pillars of strength and my companions throughout this academic journey. Your belief in my abilities, shared experiences, and countless discussions have enriched my understanding and broadened my horizons. I am grateful for the laughter, the encouragement, and the support that you have given me. This dedication is a testament to the bond we share and a symbol of my heartfelt appreciation for your friendship.

Each of you has played an integral role in my growth and success, and I am profoundly grateful for your unwavering support, understanding, and encouragement. This thesis stands as a tribute to the love, trust, and belief you have bestowed upon me, and as a recognition of the profound impact you have had on my life.

May this dedication serve as a small token of my gratitude and a reflection of the profound impact each of you has had on my journey. Your presence in my life has made all the difference, and I am forever grateful for your unwavering support and love.

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Part 1

Resumo

Introdução:

As dores nociceptivas e neuropáticas são geralmente fáceis de diagnosticar através da anamnese, do exame físico e de outros exames diagnósticos. A dor crónica é referida como "inespecífica" quando não resulta em alterações nos exames complementares de diagnóstico ou quando as alterações descobertas não conseguem explicar a dor do doente. Isto indica que o doente não tem um diagnóstico específico.

O Dr. Robert Maigne chamou inicialmente a atenção para a Síndrome de Maigne, uma causa comum, curável de dor crónica de origem espinal, na década de 1980, bem como para aquilo a que chamou "síndrome segmentar vertebral celulotenoperiostomiálgica". A síndrome da junção toracolombar é caracterizada por dor referida com origem na junção toracolombar, que se estende da 12^a vértebra torácica à 2^a vértebra lombar e, segundo Maigne, era devida a anormalidades funcionais que, muitas vezes, não resultavam em alterações nos exames diagnósticos, caindo na classificação de dor inespecífica. As manifestações clínicas incluem dor nas áreas inervadas por esses segmentos (lombalgia, dor pseudovisceral, dor na crista ilíaca posterior, bem como sintomas de intestino irritável e dor na anca).

Muitos anos mais tarde, o Professor Andrew Fischer explicaria o processo de cronificação da dor e o acometimento do dermatomo, miótomo, esclerótomo e viscerótomo, através da sensibilização segmentar da coluna vertebral.

Objetivos:

O objetivo desta tese foi apresentar a síndrome de Maigne como uma causa subdiagnosticada de dor lombar e na anca, o seu diagnóstico e tratamento, bem como a forma como esta doença se relaciona com a sensibilização segmentar espinal e os mecanismos de cronificação que lhe estão subjacentes, para dar a conhecer a dor "inespecífica" - que foi classificada pela IASP em 2017 como "dor nociplástica".

A autora desta tese relata o seu próprio caso clínico para ilustrar a importância de uma correta avaliação e diagnóstico dos doentes com dor crónica.

Métodos:

A informação foi obtida utilizando as bases de dados médicas mais populares - PubMed, UpToDate, ClinicalKey e Google Scholar. Os termos de pesquisa incluíram "Dor crónica da anca", "Síndrome de Maigne", "Síndrome da junção toracolombar", "Dor miofascial", "Pontos gatilho miofasciais", "Hiperalgisia", "Inflamação neurogénica", "Sensibilização segmentar espinal", "Dor Nociplástica", bem como várias combinações destes termos.

Para a revisão do caso clínico, foi consultado o processo clínico da autora.

Resultados

A pesquisa inicial resultou em 157 itens. As entradas duplicadas e inúteis foram removidas após a seleção. Utilizando os artigos que sobraram e analisando as suas referências, foram selecionados 102 artigos para revisão. Muitos destes relatos de casos foram publicados em publicações de neurologia, fisioterapia, quiroprática e reabilitação. Os relatos de casos constituíam a maioria dos artigos. As revisões abrangem artigos que abordaram tópicos como anatomia, dor miofascial, sensibilização segmentar da coluna vertebral, imagiologia do nervo cluneal, tratamento do aprisionamento do nervo e pontos gatilho, e dores raquidianas relacionadas com as facetas vertebrais.

Conclusão

O conhecimento adequado das causas da dor lombar e da anca, da anatomia pertinente, dos processos de sensibilização e de cronificação da dor, bem como um exame físico orientado, permitem o diagnóstico e o tratamento de dores que, de outra forma, permaneceriam crónicas.

Palavras-chave

Síndrome de Maigne, Síndrome da Junção Toracolombar, dor na anca de origem vertebral, Sensibilização Segmentar Espinal, Sensibilização Periférica e Central, dor nociplástica, dor crónica na anca.

Abstract

Introduction:

Nociceptive and neuropathic pain are usually easy to diagnose with anamnesis, physical exam, and other diagnostic tests. Chronic pain is referred to as "non-specific" when it does not result in changes in diagnostic exams or when the changes discovered cannot explain the patient's pain. This indicates that the patient lacks a specific diagnosis.

Dr. Robert Maigne initially brought attention to the Maigne Syndrome, a common but curable cause of chronic pain of spinal origin, in the 1980s, as well as to what he called "segmental vertebral cellulotenoperiostomyalgic syndrome". According to Maigne, functional abnormalities that frequently did not change the results of diagnostic exams were the cause of thoracolumbar junction syndrome, which is characterized by referred pain that originates at the thoracolumbar junction, which runs from the second lumbar vertebra to the 12th thoracic vertebra. Pain in the regions that those segments innervate (back pain, pain on the posterior iliac crest, pseudo-visceral pain, irritable bowel symptoms and hip pain) is one of the clinical signs.

Many years later, Professor Andrew Fischer would explain the process of pain chronification and the targeting of the dermatome, myotome, sclerotome and viscerotome, through segmental spinal sensitization.

Objectives:

The aim of this thesis was to present Maigne's syndrome as an underdiagnosed cause of lumbar and hip pain, its diagnosis and management, as well as how this illness related to spinal segmental sensitization and the chronification mechanisms that underlie it, to bring awareness to the "non-specific" pain – which has been classified by the IASP in 2017 as "nociplastic pain".

The author of this thesis reports her own clinical case to illustrate the importance of a correct assessment and diagnosis of patients with chronic pain.

Methods:

Evidence was acquired using the most popular medical databases – PubMed, UpToDate, ClinicalKey and Google Scholar. The search terms included "Chronic hip pain", "Maigne's syndrome", "Thoracolumbar junction syndrome", "Myofascial pain", "Trigger points", "Hyperalgesia", "Neurogenic inflammation", "Spinal

Segmental Sensitization”, “Nociplastic Pain” as well as various combinations of these terms.

For the clinical case review, the clinical process of the author was consulted.

Results:

The initial search turned up 157 items. Duplicate and pointless entries were removed after screening. By using the leftover papers and analyzing their references, 102 articles were picked for review. Many of these case reports were published in publications for neurology, physiatric, chiropractic, and rehabilitation. Case reports made up most of the articles. The reviews cover articles that looked at topics like anatomy, myofascial pain, spinal segmental sensitization, cluneal nerve imaging, treatment of nerve entrapment and trigger points, and facet-related back pain diseases.

Conclusion:

The adequate knowledge of the physical causes of lumbar and hip pain, the pertinent anatomy, the sensitization and pain chronification processes, as well as a targeted physical exam, allows the diagnostic and treatment of pain that would, without it, remain chronic.

Keywords:

Maigne Syndrome, Thoracolumbar Junction Syndrome, hip pain of vertebral origin, Spinal Segmental Sensitization, Peripheral and Central Sensitization, chronic hip pain, nociplastic pain.

List of abbreviations

BTX-A – Botulinum Toxin A

cAMP - Cyclic Adenosine Monophosphate

CGRP - Calcitonin Gene-Related Peptide

CNS – Central Nervous System

IASP – International Association for the Study of Pain

LTR – Local Twitch Reaction

MPS – Myofascial Pain Syndrome

MTrP – Myofascial Trigger Point

NGF - Nerve Growth Factor

NRS – Numeric Rating Scale

NSAIDs – Nonsteroidal Anti-Inflammatory Drugs

PBS – Paraspinous Block

PKA - Protein Kinase A

PKC - Protein Kinase C
CCRPS – Complex Regional Pain Syndrome

PNS – Peripheral Nervous System

PPT – Pain-Pressure Threshold

QOLS – Quality of Life Scale

SSS – Spinal Segmental sensitization

TCA – Tricyclic Antidepressants

TENS – Transcutaneous Electrical Nerve Stimulation

TLJS – Thoracolumbar junction syndrome

TNF α - Tumour Necrosis Factor alfa

WDR – Wide Dynamic Range

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1. Thoracolumbar Junction Syndrome

Dr Robert Maigne was the first to describe thoracolumbar junction syndrome (TLJS), which also became known as Maigne's syndrome, a disorder which affects the thoracolumbar junction. It originates at the thoracolumbar junction (between T12 and L3), causing pain that spreads across the lateral thoracolumbar nerve branch distribution (back pain, false hip pain, pseudovisceral pain). [48] Clinical examination of the spine demonstrates pain when the facet joints or spinous processes of the thoracolumbar junction are palpated. The anterior branch of L1 innervates the groin region, its posterior segment innervates the lower lumbar side, and the lateral cutaneous segment innervates the lateral hip side, according to pain radiation and clinical findings. [49] (Figure 1).

Thoracic facet joint inflammation is a common cause of pain in the lumbosacral and lower lumbar regions.[50] Between the lumbar facets in the sagittal plane and the thoracic facet in the coronal plane is the 12th thoracic vertebra, a transition section. The transitional strain during spinal motions is concentrated on the 12th thoracic vertebra. The lower lumbar and higher gluteal regions may experience unilateral radiating pain as a result of this stress, which could also be caused by injuries at the T9-L2 facet joints. [51] (Figure 2)

While the anterior part of the ramus innervates the pubic region and the anterior region of the lower abdomen, the lateral cutaneous innervates the external aspect of the hip, and the posterior branch of the superior gluteal innervates the lower lumbar subcutaneous tissues, pain propagation and clinical results are related to the T12 and L1 structural distribution of the spinal nerve root. [49].

Maigne postulated that this syndrome was mostly due to intervertebral dysfunction, including thoracolumbar disc disruption, congenital abnormalities, degenerative processes, and fibromyalgia. Intervertebral dysfunction also includes impairment of the anterior spinal nerves or posterior primary rami of thoracolumbar origin. It is crucial to exclude vertebral fractures [52] (such as burst or compression types) and/or spinal instability in patients who have experienced considerable trauma.

1.1. Clinical Symptoms

The arrangement of the associated spinal nerves matches the pattern of pain (T12, L1). After leaving the intervertebral foramen, the thoracolumbar nerve roots separate into ventral and dorsal rami. [48] The intercostal nerves T10 and T11 ventral rami terminate in the abdominal wall. Subcostal and iliohypogastric nerves are the T12 and L1 ventral rami, respectively. (Figure 3) They provide innervation to the lateral surface of the hip, the skin in the groin area, and the inferior muscles of the abdominal wall. They are responsible for groin and pseudovisceral pain. Pseudotrochanteric pain is caused by the perforating lateral cutaneous branch, which supplies the skin on the upper lateral section of the thigh [48,53, 56]. Medial and lateral branches emerge from the posterior ramus. The multifidus, as well as the interspinous muscles are innervated by the medial branch, a motor branch.

The lateral branch of the dorsal rami provides cutaneous innervation to the supraspinous and interspinous ligaments, facet joints, and subcutaneous tissues in the lumbar and buttock regions. Jean-Yves Maigne [48], contrary to the literature and the dermatome map designed by Keegan and Garrett, demonstrated the dorsal rami of T12 and L1 innervate the superior buttock region in 60% of people, and they can be compressed when they cross the iliac crest, which can explain why TLJS causes lumbar pain. (Figure 4) Sometimes these cutaneous branches penetrate through the subcutaneous tissues of the lumbar and gluteal region as distant as the greater trochanter, which explains the hip pain secondary to the TLJS. [54,56]. TLJS can mimic gastrointestinal, urological, and gynaecological issues and may lead to a false diagnosis and ineffective patient care. Testicular, buttock, and lower abdominal pain have all been linked to TLJS, which has been noted as an often-disregarded aetiology [58, 59, 60]. Trochanteric discomfort might resemble hip diseases such trochanteric bursitis and coxarthrosis. TLJS can also imitate sciatalgia, particularly in cases when the pain radiates to the leg. Motion generally makes pain worse. Painful hip flexion and adduction are common. When palpated, the trochanteric area frequently hurts. [54]

The classic symptoms include localized soreness over a specific spinous process at the thoracolumbar junction, a positive iliac-crest point test, a positive pinch-roll test, and tenderness over the implicated apophyseal joint. [54, 55]

These symptoms can be accompanied by changes to the soft tissue's sensitivity and texture, including cellulalgia on the skin, tense bands in the muscles regardless

of the presence of trigger points, and tenoperiosteal changes (in relation to a segmental spinal dysfunction), as was first described by Robert Maigne in 1968, giving it the title “segmental vertebral cellulotenoperiostomyalgic syndrome”. [62]

For a specific spinal segment, these symptoms are restricted to a fixed area. Clinically, this territory closely matches the region of the associated nerve root, although at some levels, the cellulalgia goes beyond this region and can affect multiple adjacent spinal segments at once. This syndrome's active signs, such as pseudoradicular, pseudopara-articular, or pseudovisceral pain, are frequently deceptive. [62]

These symptoms appeared to be related to the irritation of the dorsal primary ramus of the spinal nerve given their location, especially since they did not involve the lower body as in the case of isolated lumbar pain (without sciatica) originating from L4-L5 or L5-S1. [62]

2. Nociception, Neurogenic Inflammation, Peripheral and Central Sensitization

Pain, according to the 2017 IASP classification, is “An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage,” [1]. Several mechanical stimuli, such as pressure, pinching, cutting, or stretching, can trigger pain receptors in muscles. [1] Single episodes of macrotrauma or repeated microtrauma can cause acute muscular pain that lasts for less than six weeks, particularly when the muscle is overloaded biomechanically during the dynamic contraction or stretch phase. [2] While repeated overloading frequently results in delayed onset muscle pain and tension, macrotrauma typically causes muscular contusions and lacerations. Muscle pain that comes on gradually usually starts several hours following physical exertion and gets worse over the following one to three days, when it reaches its peak. [3]

Unrelieved pain can cause changes in the brain structure responsible for producing pain, and pain processes are plastic (not static), which is a crucial idea in the study of pain. [11] These modifications may take place in a way that makes pain, especially chronic pain, no longer just a symptom but rather a disease. [5,8] Chronic pain lasts longer than is often anticipated for healing and has no physiological benefit. The definition of chronic pain in the context of non-malignant illnesses suggests that, conceptually, it may last longer than 3-6 months. [8,9] Pain is considerably more than merely a linear process started by tissue injury and inflammation, even though the brain is actively involved in processing sensory input and experiencing pain. Integration of the sensory, emotional, and cognitive aspects of pain is required. [8]

According to the 2017 IASP Classification [61], nociceptive pain, previously known as inflammatory pain, is “pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors”. [1, 61] Neuropathic pain is “pain caused by a lesion or disease of the somatosensory nervous system”. [61] Nociplastic pain, previously known as functional pain, is “Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain”. [14, 61] This is the most frequent cause of musculoskeletal pain, commonly known as “non-specific pain”, and it is particularly important as it responds poorly to medication and, most of the times,

is related to normal imaging, only being diagnosable through a targeted physical exam. [1, 14, 61]

2.1. Nociception

Nociception is the neurochemical phenomenon by which nociceptors are activated by acute tissue damage and transmit pain signals to the central nervous system (CNS) via peripheral neural pathways. The process of transduction occurs in the spinal cord, where painful afferent impulses are transformed from chemical to electrical neural signals that travel cephalad to the brainstem, thalamus, and cerebral cortex. [8, 10] Nociceptive pain, which is caused when noxious stimuli activate primary afferent neurons (nociceptors), which innervate cutaneous tissues, bone, muscle, connective tissues, arteries, and viscera, can therefore be seen as an alarm system that announces the presence of a potentially harmful stimulus. [8, 10, 11, 12] Primary afferent neurons can synapse with neurons in the dorsal horn of the spinal cord and have unmyelinated (C fibres) or myelinated (A δ fibres) axons. [8] While C-fibre nociceptors with unmyelinated axons have small cell bodies and slowly conduct action potentials, A δ -fibre nociceptors with myelinated axons have medium to large cell bodies and swiftly conduct action potentials. [12, 13]

The nociceptors are sensitized by the action of chemical substances, called algiogenic, present in the tissue environment [15]: acetylcholine, bradykinin, histamine, serotonin, leukotriene, substance P, platelet-activating factor, acid radicals, potassium ions, prostaglandins, thromboxane, interleukins, tumour necrosis factor alfa (TNF α), nerve growth factor (NGF), and cyclic adenosine monophosphate (cAMP) [16, 22, 18]

2.2. Inflammation and Neurogenic Inflammation

An inflammatory process starts when the stimulus injures the tissue; this is followed by the healing phase. Leukocytes, macrophages, and inflammatory cells all generate cytokines that aid in the migration of new cells to the site of injury. [19] However, it seems that bradykinin, prostaglandin E2, NGF, and interleukins are important in peripheral nociception. Through the activation of cAMP, protein

kinases A (PKA) and C (PKC), and particular receptors (TRPV1) connected to ligand-dependent ion channels, prostaglandin and bradykinin alter the neural membrane's post-hyperpolarization period, which lowers the threshold for nerve fibre firing. [19, 20] Aggression that persists alters the PNS and sensitizes nerve fibres, leading to hyperalgesia and elevated cAMP and calcium levels in nociceptors. The action of inflammatory mediators causes neurons to spontaneously fire, increasing the response to supraliminal stimuli and lowering the threshold for nociceptors to activate. [19, 21]

When nociceptor fibres, particularly C-fibres, are activated, a variety of neuropeptides, including substance P, CGRP, and prostanoids, can be released antidromically. This is known as neurogenic inflammation. Oedema and rapid plasma extravasation follow the activation of nociceptors on a timescale that is quicker compared to immune cell infiltration. [63] Neurogenic inflammation is one of the clinical alterations that plays a significant role in migraine pain in addition to complex regional pain syndrome (CRPS). [65] After neuroinflammatory processes in the brain or spinal cord, the CNS itself may be prone to inflammation [63, 66].

Both the peripheral nervous system (PNS) and the CNS can experience neuroinflammation, a localized type of inflammation [64]. Enhanced vascular permeability, leukocyte invasion, glial cell stimulation, and increased production of inflammation-related mediators including cytokines and chemokines are four characteristics of neuroinflammation [64]. The blood brain barrier becomes more permeable during a neuroinflammatory state, increasing the risk of peripheral immune cells infiltrating the CNS. In light of this, neuroinflammation is increasingly often linked to chronic pain problems, including postoperative pain following major procedures like amputation, thoracotomy, and mastectomy, as well as postoperative complications including delirium [68, 67].

Although neuroinflammation holds a significant correlation with chronic pain states and could be responsible for the mediation and continuation of pain in patients, chronic pain is typically observed as a condition that persists after the resolution of observable clinical signs and symptoms of inflammation [68]. It is noteworthy that neuroinflammation and inflammation have different relationships with chronic pain. Patients with fibromyalgia and HIV neuropathy have both been found to have chronic neuroinflammation [68, 69].

2.3. Peripheral and Central Sensitization

Peripheral sensitization, which is defined as a decreased threshold and increased sensitivity of the sensory nerve fibres in the peripheral to external stimulus. Primary hyperalgesia, an intensified stimuli-dependent pain state, is a symptom of peripheral sensitization. Peripheral sensitization frequently follows tissue damage, inflammation, and peripheral nerve injury. However, when it comes to nociplastic pain, peripheral sensitization occurs without any kind of tissue or nervous injury. Peripheral sensitization might also be the result of an old injury. Peripheral nerve damage may also cause tissue damage in some cases. Peripheral sensitization is a condition caused by the activation and sensitization of the peripheral sensory neurons by endogenous substances generated from the site of tissue injury or inflammation. [81,82,83] In other words, pain receptors which typically need a strong stimulation to be detected are changed so that a painful response can be elicited by a weak stimulus, making pain considerably more perceptible. The continued signalling from pain receptors causes the low threshold condition and, as a consequence, the painful response, to perpetuate in time, and for progressively weaker stimuli to be necessary to trigger such a response. [21,24,81,82,83]

The spinal cord is actively involved in the transmission of painful impulses. The stimuli and painful response can both be altered via intraspinal circuits. Which messages get to the cerebral cortex depends on how the intramedullary circuits interact. [23,83] Changes in peripheral impulses, either positive or negative adaptations, are implied by central sensitization. There are sustained discharges following repeated inputs, a decrease in the threshold or an increase in the responsiveness to afferent impulses, and an expansion of the receptive fields of dorsal horn neurons. [14,81,82] Sensorial signals in spinal neurons are amplified by repeated impulses in C fibres, which sends messages to the brain. Through pathways involving particular kinds of glutamate receptors, peripheral lesions cause plasticity in supraspinal regions. [16,82]

2.4. What roles do neurogenic inflammation and peripheral and central sensitization play in the chronification of pain?

Peripheral sensitization and neurogenic inflammation contribute to central sensitization by increasing the amount of nociceptive input to the CNS.

The thalamic nuclei, periaqueductal grey area, cortical regions amygdala and spinal cord were among the pain matrix structures, that underwent severe alteration, as a result of myofascial pain syndrome (MPS). The pain threshold, pain severity, and emotional impact can all be changed by this dynamic process [39]. The activation of polymodal nociceptors, which can be sensitized by chemicals produced from injured tissue and the nociceptor terminals themselves, may be the first step in the signalling process in the pain matrix structures. [39, 42, 43] Long-term alterations in gene expression, somatosensory processing, and synapse structure may result from persistent painful input. The release of neuropeptides such as substance P and calcitonin gene-related peptide (CGRP) during neurogenic inflammation can activate glial cells in the spinal cord and brain, contributing to central sensitization. [29,70,71,81] Glial cells are immune cells in the CNS that can release inflammatory mediators and modulate pain transmission. [29,81] Activation of glial cells can lead to the release of pro-inflammatory cytokines, which can increase excitability in the spinal cord and brain and contribute to central sensitization. [72,73,81]

L-glutamate and substance P are released simultaneously as a result of "afferent bombardment," a continuous unpleasant input into the dorsal horn. Wide dynamic range (WDR) neurons can become more sensitive to stimuli by opening previously inactive synaptic connections and lowering thresholds for synaptic activation. [32, 33, 34, 42, 43] This increased excitability can lead to hyperalgesia (an increased sensitivity to painful stimuli) and allodynia (pain in response to non-painful stimuli). [27,28,81-83] (Figure 5)

Sensitization increases the amount of these cell surface proteins on nociceptors and dorsal horn neurons as well as the expression of ion channel and receptor genes. Under typical conditions, the roles that pain plays in promoting and inhibiting function are dynamically balanced. [32, 33, 34] A plethora of inhibitory interneurons, which play a crucial role in avoiding the development of chronic pain, regulate the nociceptive information-transmitting neurons. [32, 33, 34, 44] These changes can also lead to persistent pain even after the initial injury or inflammation has resolved. [72,75,81]

In summary, peripheral sensitization and neurogenic inflammation contributes to the development of central sensitization, which can promote the chronification of pain by promoting long-term changes in the nervous system.

3. Spinal Segmental Sensitization

MPS is the major musculoskeletal pain and the main cause of chronic pain. [76-80] It affects people of all ages and is frequently accompanied by other primary pain conditions such as osteoarthritis, spondylosis, disc dysfunction, tendinitis, migraines, tension headaches, computer-related disorders, office syndrome, spinal dysfunction, and pelvic pain. Professors Janet G. Travell and David G. Simons were pioneers in the identification and treatment of this cause of pain and established the traditional definition of a myofascial trigger point (MTrP) as "*a hyperirritable area in skeletal muscle that is linked with a hypersensitive palpable nodule in a taut band*". They began to include palpation in all the physical examination of patients. [30] The ability to identify this kind of pain and the success of its treatment led Professor Janet Travell to treat senator Kennedy five years before he became president, becoming the official White House physician for many years. According to Gerwin et al. [31], the key findings of an MTrP, which should be present in a taut band of muscle are:

- 1) A particularly tender spot;
- 2) A local twitch reaction (LTR) and/or referred pain to distant parts of the body upon manual palpation or needling of the sore spot;
- 3) Restricted range of motion;
- 4) the ability to reproduce the patient's pain complaint through pressure on the MTrP;
 - This criterion only applies to active MTrPs because latent MTrPs do not produce spontaneous pain.
- 5) Autonomic symptoms;
- 6) Localized muscle weakness.

Professor Andrew Fischer, based on the findings of Robert Maigne, Travell and Simon, and Eric Kandel (Nobel Prize in Physiology or Medicine winner in 2000), postulates on the sensitization of spinal segments as a crucial factor in the development of chronic pain in a particular body region. Spinal segmental sensitization (SSS), as coined by Professor Andrew A. Fischer, is the name used to describe this phenomena [32,33]. This elaborates on what Robert Maigne had postulated a few years prior – while Maigne believed the dysfunction of one

segment of the spine caused the involvement of all tissues (cellulalgic, tenoperiosteal and myalgic pain of spinal origin), Fischer confirmed, with the concept of SSS, that spinal sensitization, not dysfunction, is behind the chronic pain phenomena.

As Fischer described [33]: *“SSS is a condition characterized by hyperactivity, facilitation, and hyperexcitability of a spinal segment that develops in reaction to an irritative focus, which constantly bombards the sensory ganglion by nociceptive stimuli. The irritative focus usually consists of a small area of damaged or dysfunctional tissue where peripheral sensitization or irritation of the nerve fibres generates the continuous nociceptive stimuli, causing sensitization of the CNS. The sensitization and hyperexcitability spread from sensory to motor components of the segment, inducing hypertonicity and tenderness (muscle spasm), and activate MTrPs within the myotome”*.

It is critical to distinguish between anterior horn sensitization, which causes stiffness or muscle spasm (MTrPs), and posterior horn sensitization, which causes hyperalgesia, and allodynia. [32, 33, 34] Muscle spasm and MTrPs in the myotomes that are supplied by the same sensitized spinal segment can be clinical manifestations of anterior horn sensitization, as well as hyperalgesia or allodynia of the dermatome and pressure pain sensitivity of the sclerotome are manifestations of posterior horn sensitization. 35,37

In reality, muscle pain is characterized as painful, cramping, deep, and challenging to localize. In the brainstem and spinal cord, nociceptive-specific neurons are involved in the perception of muscle pain [35, 36], and this stimulation also activates certain cortical regions associated with the affective or emotional aspects of pain [37]. Although descending pain-modulating pathways suppress muscle nociception more severely [38,39], persistent muscle nociception is more effective than cutaneous nociception at causing maladaptive neuroplastic alterations in the dorsal horn. [40]

The same sensitive spinal segment that supplies the myotomes and the sclerotome as well as the dermatome all contribute to the clinical presentation of dorsal horn sensitization. In the region of the active MTrP, there are noticeably higher concentrations of substance P, CGRP, bradykinin, TNF α and interleukin-1, serotonin, and norepinephrine. [32-40] The dorsal horn of the spinal cord is always under attack from nociceptive sensations produced in the sensitive areas. Repeated

A δ and C fibre stimulation results in a WDR sensitization within the same segment and overload, resulting in MTrPs and muscle spasm. As a result of the bombardment, the dermatome and sclerotome experience hyperalgesia, which spreads from the sensory portion of the spinal segment to the anterior horn cells, that regulate the myotome within the SSS's domain in the same segment. One of the clinical signs of SSS is the formation or increased activity of MTrPs. [32–40] SSS also contributes to the pain chronification processes previously described in chapter 3.

4. Diagnosis of thoracolumbar junction syndrome

In light of the current knowledge, the diagnosis of TLJS is based on Maigne's teachings, enriched with Fischer's knowledge of SSS.

On most cases there are no alterations on imaging, which means the diagnosis is clinical and the goal is to reproduce, during the exam, the pain the patient has been feeling.

4.1. Examination of Mobility

The patient is first examined while at rest. As the patient stands with their legs apart, the examiner checks to see if the patient has normal, hyperaccentuated, diminished, or replaced lumbar lordosis with kyphosis. The examiner also checks for lumbar shift or scoliosis, as well as any potential pelvic imbalance brought on by an imbalance in leg length. [50,54]

The spinal mobility test should be done for flexion, extension, latero-flexion, and rotation. It should always be registered if these movements cause pain, and where [54,55]:

- Flexion – Schober's test is an exceptionally good test of spinal flexibility:
 - A mark is traced 10 cm higher and at the height of the spinous process of the first rib.
 - If the lower lumbar spine has a normal range of motion, the two markings at the conclusion of flexion should have varied an additional 4 to 5 cm. These numbers are less in the stiffness category.
- Latero-flexion – The patient should be asked to bend laterally, allowing the hand to slide along the thigh. The distance from the end of the fingers to the ground, global stiffness, a break in the latero-flexion and whether the movement provokes pain should be evaluated.
- Rotation – The physician should notice any range of motion restriction (especially when the movement produces pain in one or both directions)
- Extension – The patient is asked to lean backwards and stretch their hands above their heads. The examiner should note if the movement is possible or painful and the location of pain.

The patient should be told to sit at the tip of the table, with their legs wide, or on the table, with their legs dangling, to test passive motion. In order to identify uncomfortable or limited motions that would not have been seen with active motion testing, the examining physician will assess the spine's passive motion. We will examine rotation, latero-flexion, and extension [54,55]:

- Extension - The examiner's left forearm crosses in front of the superior region of the thorax and grabs the patient's right shoulder while they sit with their arms folded on the chest. The examiner will move the spine in extension while applying counterpressure with their right hand at the level of the superior, middle, and inferior lumbar regions.
- Latero-flexion - The examiner should maintain the patient's pelvis with one hand while applying lateral inclination with the other hand by grabbing the upper part of the patient's opposing arm and lowering the shoulder.
- Rotation: While pressing with the other hand on the patient's paraspinal area to rotate the trunk and keep the patient in an upright position, the examiner's hand moves the patient's opposing arm, which is crossed over on the chest, forward.

The manoeuvres should all be repeated on the opposite side. Examination of the neighbouring joints should also be performed.

To rule out any neurological injury that might be causing the patient's pain, the examining doctor should perform a neurological exam, which should include examination of the muscular strength, sensitivity, reflexes and specific testing according to the clinical case and patient's presentation, such as Lassegue, Braggart or inverted Lassegue. [41,46,47]

4.2. Segmental Examination

This section of the exam starts with the patient indicating the exact painful spot and the investigation of the myalgic trigger point until the patient's pain is reproduced.

Afterwards, for the segmental examination of the spine, the patient will lie prone across the table, and each spinal segment, from T10 to L5, will be evaluated

separately. The individual spinous processes are first subjected to posterior, transverse, followed by contralateral pressure. As articulations are profound at the lumbar level and will only become irritated by strong pressure applied at the facet joint, longitudinal friction should be administered over the facet joints. The interspinous ligament should also be pressed against. [32,33,34,35]

4.3. Testing hypersensitivity and allodynia

The examination should extend beyond the spinal processes affected and explore sclerotome, soreness inside the affected myotomes, as well as look for MTrPs, dermatomal allodynia (pain caused by non-painful stimuli), and hyperalgesia (increased pain by painful stimulus) of each of the affected segments.

The following criteria are used to evaluate segmental dermatomal levels [32, 33, 34, 45, 46, 47]:

- 1) Scratching the skin with a paper clip or Wartenberg pinwheel. This painful stimulus is administered across dermatomal borders, and the patient is encouraged to describe any sharpening or dulling of their discomfort at the same time. Hyperalgesia can be recognized by a painful response which is disproportional to the stimulus.
- 2) The "pinch and roll test," also known as a non-noxious stimulus delivered across dermatomal borders, involves pinching the skin between the thumb and forefinger and rolling the area beneath it. The patient is encouraged to describe any pain at the same time. (Figure 6)

The most accurate evidence for the diagnosis of sensitization is the presence of a "pinch and roll pain", which is a sign of allodynia.

The following criteria are used to evaluate segmental myotomal levels [32, 33, 34, 41, 45, 46, 47]:

- 1) Feeling for painful patches, tense bands, and MTrPs in the musculature of segmentally connected muscles that the patient is complaining about.
- 2) Using a pressure algometer to determine the myotome's local pain pressure threshold (PPT). (Figure 7)

The following criteria are used to evaluate segmental sclerotomal levels [32, 33, 34, 41, 45, 46, 47]:

- 1) Feeling the tendons, entheses, bursae, and ligaments that are connected to each other in a segment (ligament sprain).
- 2) Using a pressure algometer to objectively measure a PPT.

The segmental sensitization signs of a person's pain syndrome are identified using these examination methods. [32, 33, 34] Segmental findings on the myotome, sclerotome, and dermatome sometimes overlap, making it challenging to diagnose and treat the hypersensitive segment. [32, 33, 34, 45, 46, 47]

5. Treatment Modalities

Throughout the years, many treatments were proposed for the treatment of myalgic tension and trigger points. [32, 33, 34, 41, 45, 46, 47]

5.1. Pharmacologic Treatment Modalities

5.1.1. Nonsteroidal Anti-inflammatory Drugs (NSAID)

Nonsteroidal anti-inflammatory drugs (NSAIDs) are frequently used to treat pain, however their use in situations involving chronic pain is constrained due to adverse GI and renal effects. [84] Weak evidence supports the use of oral NSAIDs for the treatment of MPS. NSAIDs have been shown to be helpful in this regard when used topically. [85] Hsieh et al. [85] has demonstrated, in a prospective randomized control study of 153 patients, that topical diclofenac sodium, applied as a patch, offered pain alleviation and enhanced function in individuals with MPS of the upper trapezius when compared to patients who received a menthol patch.

5.1.2. Tri-cyclic Antidepressants

Tricyclic antidepressants (TCA) are prescribed to treat depression as well as a variety of pain disorders. TCAs may provide analgesia by preventing serotonin and norepinephrine reuptake along the descending spinal pain pathways. TCAs also affect sodium channels and histamine receptors [86]. Studies looking at TCAs' effectiveness in MPS have discovered a significant advantage [87, 88]. Studies examining the effectiveness of TCAs in MPS have found a sizable benefit [87, 88]. Tri-cyclic antidepressants have been shown to have positive benefits in individuals with persistent face discomfort and soreness of the local muscles by Haviv et al. [87]. Amitriptyline has been proven beneficial in treating patients with temporomandibular disorders-related persistent pain and tension-type headaches. [88]

5.1.3. Local Anaesthetics

Lidocaine has a non-specific sodium channel blocker effect that stabilizes neuronal cell membranes and prevents the initiation and conduction of nerve impulses [89]. Lidocaine injections could have adverse consequences include allergy, CNS depression, convulsions, and arrhythmias. In a prospective observational trial with 120 patients, Xie et al. [90] evaluated the effectiveness of lidocaine injections in the trapezius muscle for chronic neck discomfort related to MTrP. After 6 months of treatment, they found that lidocaine injection therapy dramatically decreased the severity and frequency of neck discomfort in patients. When 5% lidocaine patches were used instead of injections to treat neck discomfort brought on by MTrP, Firmani et al. [91] discovered that they significantly reduced pain when compared to the placebo group.

5.1.4. Botulinum Toxin

For the purpose of preventing muscle hyperactivity and spasm, botulinum toxin A (BTX-A) works by inhibiting the release of acetylcholine at the neuromuscular junction. Additionally, it stops primary sensory neurons from releasing pain neurotransmitters [89, 94]. BTX-A may cause a number of adverse reactions, including excessive or nearby undesired muscular weakening, hypersensitive response, anaphylaxis, sympathetic dysreflexia, respiratory compromise, urine retention, myasthenia gravis, and facial paralysis [95, 89]. There have been numerous studies looking into the efficacy of BTX-A in treating temporomandibular dysfunction, but the results have been mixed. Some studies have found BTX-A to be significantly more effective than manual manipulation, while others have found no benefit [89, 96, 94].

5.1.5. Opioids

Opioids are often not recommended for the treatment of MPS. Although a few small studies have shown that mild opioids can treat myofascial pain with some degree

of success [107], the majority of research contradicts the use of opioids in MPS. Additionally, it has been hypothesized that using opioids to treat acute pain may potentially hinder recovery [108].

5.2. Minimally Invasive Non-Pharmacologic Treatment Options

5.2.1. Dry Needling

A non-pharmacological strategy for treating MPS-related pain is dry needling. A thin filiform no-bore needle is inserted into MTrP during dry needling, a minimally invasive treatment method, without the use of fluids or local pharmacological drugs [97,98, 113, 114]. The needle is inserted, allowed to produce a LTR, and then it is taken out. Although the exact way that dry needling works is still up for question, it is generally accepted that the gate control hypothesis of pain is how it relieves pain. [113, 114]

In a comprehensive analysis, Liu et al. [99] looked at 11 randomized clinical trials that contrasted dry needling with other treatment modalities (such as acupuncture); the findings revealed that dry needling significantly reduced postintervention pain intensity and improved function when compared to alternative treatment.

The review conducted by Rodriguez-Mansilla et al. [98] proved more dubious, pointing to inconsistent outcomes and the higher efficacy of other treatments including injections of lidocaine and corticosteroids. By designating individuals as "responders" or "non-responders," Gerber et al. [100] tried to reduce some of the uncertainty. They discovered that many patients' MTrP changed from being active (painful at random) to dormant (painful solely through palpation) because of dry needling therapy. These participants were classified as responders, and it was discovered that they had much more analgesia than non-responders. As a result, individuals who have analgesia after the initial treatment are more likely to experience a lasting improvement, making them eligible for dry needling. [100]

5.2.2. Transcutaneous Electrical Nerve Stimulation

Applying adhesive electrodes to the skin and then electrically stimulating painful areas is known as transcutaneous electrical nerve stimulation (TENS) [101]. Electric stimulation can be applied in various combinations of frequency and intensity, but high-frequency stimulation is typically combined with low intensity and vice versa. It is considered that intensity is the most essential aspect and that the therapy should provide a strong, but not painful sensation for optimal success, despite the fact that there are no specific standards outlining the combination of these factors produces the most efficacy. Although the exact mechanism of TENS activity is unknown, it is thought that the muscle contractions it causes may normalize acetylcholine levels in the nerve's motor endplate, which may aid in relaxing tense bands of muscle [102].

5.2.3. Trigger Point Injections

The most popular form of treatment for controlling resistant MPS is trigger point injections [103, 104]. Since many years ago, trigger point injections are used to alleviate musculoskeletal discomfort. Having a tender point in a taut band accompanying a recognized or anticipated pain referral, trigger points remain the physical examination's go-to indicator of myofascial pain [105]. Contractures, nerve damage, abscess formation gangrene, and both systemic and local reactions have all been listed as adverse effects [103, 104, 106]. Additionally, the use of ultrasonography has been suggested to considerably lower complication rates while improving results. [103, 104, 106]

Kumbhare et al.'s thorough review [103] went into great detail into the sonoanatomy of trigger points and the relationship between physical attributes and ultrasound testing. Only two studies, out of the 31 references found by their evidence synthesis, used ultrasound to identify MTrP. The other experiments almost certainly employed a "blind technique." According to the review of these studies, the blind technique improved pain scores on the visual analog scale in a variable manner; however, the two ultrasound studies showed marked improvements in pain scores, increased LTR, and significantly decreased the number of MTrP needles inserted as well as the amount of treatment sessions [115, 116]. Out of the 2 studies, the larger one by Bubnov and Wang [116] with 133 patients used ultrasound guidance for pterygopalatine muscle trigger point

injections, and a significant improvement was seen in a large number of patients. They also looked at 44 patients [115] who had shoulder muscular soreness, and they found that ultrasound-guided injections also produced notable benefits.

5.2.4. Paraspinous Block

Paraspinous lidocaine injections, or paraspinous block, were first introduced by Professor Andrew Fischer and are still considered one of the most effective techniques for treatment of peripheral sensitization and irritative foci. [109] The paraspinous block (PSB) procedure involves applying local anaesthetic (1% lidocaine) along the spinous processes and their connection in the form of the supraspinous/interspinous ligaments. In order to precisely desensitize (return to baseline sensitivity) the hypersensitive segment and hence relieve segmental pain, PSBs are effective. This is demonstrated by normalizing of the hyperalgesic dermatome (scratch test) and allodynia (pinch and roll). [109] On motor testing, the MTrPs become less painful, and the spasm in the corresponding myotome is eased. These results can be measured through evaluation of pain pressure threshold (PPT) with an algometer. [124] The tense muscular cord is thought to temporarily relax as a result of PSBs, allowing for better oxygen supply, ATP replenishment to liberate the actin-myosin chains and stretch the muscle fibre, as well as the clearance of metabolite waste. These elements support ending the cycle of tension and suffering. [117][120]

Dry needling and local lidocaine injection both produce comparable results, although it has been demonstrated that local anaesthetic administration causes less post-needling discomfort. [118,119] When ultrasonography is available, it may be thought about using it to guide injections while confirming the required structure and depth and avoiding neurovascular structures. [120, 122]

Imamura et al. [124] reviewed the use of trigger point injections of lidocaine for the treatment of nonspecific chronic back pain for the first time, in a randomized trial including 381 patients divided into 3 categories – those who received paraspinous lidocaine injections and standard treatment (group 1), those who received sham lidocaine injections and standard treatment (group 2), and those who received standard treatment only (group 3). In group 1, 71.4% (90 of 126) responded positively to the treatment, significantly more than subjects in the group

2 (54.4%, 68 of 125), and group 3 (53.5%, 68 of 127). Therefore, it was concluded that the changes in pain threshold were significant immediately after treatment, with effects lasting up to 3 months after treatment completion. [124]

5.2.5. Ergonomics and Patient Re-education

In the therapeutic period, exercise is prescribed to prevent recurrences. It should integrate postural correction, flexibility of postural muscles and muscle strengthening, according to individual deficits, but always including the core muscles.

Ergonomics is the scientific study of how humans interact with systems and the profession that applies theory, principles, data, and methods to design work systems that optimize human well-being and overall system performance [92]. The best method for lasting prevention of musculoskeletal problems and enhancing quality of life is to adhere to the ergonomics process while creating and evaluating work systems.[92]

Posture refers to the position of the body and its parts. A good working posture involves aligning the head, shoulders, arms, forearms, wrist, and spine to minimize stress on the musculoskeletal system [93, 111]. This means keeping the head neutral, shoulders straight and low, arms close to the body, supporting the forearms, and avoiding ulnar or radial deviations and wrist flexion. The spine should always be aligned, and unnecessary torsion and bending should be avoided [93, 111].

After the therapeutic period, regular exercise such as yoga or pilates is essential for reducing musculoskeletal disorders, improving flexibility, endurance, and conditioning [110, 111].

6. Clinical Case

Chronic musculoskeletal pain with innocent imaging often poses diagnostic challenges. It is particularly important for doctors to be familiar with myalgic tension, the most common cause of chronic pain, and with one of the lesser-known syndromes that can cause it: Maigne's syndrome or the thoracolumbar transition syndrome. The goal of this paper is to raise awareness about Maigne's syndrome as a cause of chronic nociplastic pain and to draw attention to the need for clinical diagnosis and directed treatment.

6.1. Patient Information

On May 7, 2021, a 22-year-old Caucasian Portuguese female medical student presented with a 4-year history of localized left hip pain. Since August 2017 she reports numerous emergency room visits, specialist appointments (in orthopaedics, rheumatology and physiatrics) and physical therapy sessions, as well as traditional Chinese medicine treatments (specifically, acupuncture and Tui Na), and many different medications, including opioids as needed, with no improvement to her symptomology. The subsidiary exams performed – lumbar and hip x-Ray, hip ultrasound, lumbar and pelvic MRI – were all unremarkable.

Past medical history was relevant for mononucleosis at the age of 8 and a complete tear of the calcaneofibular ligament at 14, with complete resolution of all complaints at the time with physical therapy. She did not smoke, drink, or take any medication. She played basketball at a semi-professional level for 8 years, but she now found herself unable to walk for longer than 10 minutes at a time. No additional past, family, or social history was deemed pertinent.

6.2. Timeline

The pain first presented as a sudden onset of stabbing pain over at the side of the left hip after a roughly 5km walk on the beach. The pain onset, over the trochanteric area, radiated up to the spine and down the lateral of the leg, affecting the first two toes on the left foot, lasted a few seconds, and caused loss of strength on the left lower limb, and a consequent fall. After the pain subsided,

it was replaced with paraesthesia over the side of the thigh, which lasted for 2 hours, followed by pain over the trochanteric area.

The pain over the trochanteric area persisted for the next 4 years, constant, sharp and deep, 7/10 in intensity with periods of 10/10 pain with various activities (using a 10-point numeric rating scale (NRS), with 0 being no pain at all and 10 being the worst pain imaginable) – bending, sitting, lifting, walking and standing for more than 10 minutes exacerbated her symptoms. Sleeping was intolerable without the use of a pillow between her legs, and she had taken to sleeping on her back, awaking whenever she changed position. No alleviating factors. The patient reports medication as needed with Paracetamol 500 mg + Tramadol 34.5mg, but refers barely taking the medication, as it did not seem to help the pain.

6.3.Clinical Findings

Imaging performed prior to the patient's presentation demonstrated no acute osseous pathology, structural lesions, dislocation, fracture, or mass. Echography of the gluteus muscles revealed a tendinosis of the gluteus medius tendon, which was resolved with physical therapy, and no changes in the pain pattern or intensity. Long spine X-ray revealed no deviation or lower limb dysmetria. Magnetic resonance imaging of the pelvis showed no abnormalities of the hips.

6.4.Diagnostic Assessment and Interpretation

There was no weakness associated with a specific myotomal distribution. Her balance was not impaired. Neurologic exam was normal. Gait testing, which analyses how a patient walks and identifies any abnormal walking patterns, was normal.

Modified Trendelenburg test, which assesses weakness of the hip abductors, was normal. Passive and active motion amplitudes for abduction, adduction, flexion, extension, internal and external rotation of the hip were full and pain-free. The FABER test, which inspects for lesions in the sacroiliac or coxofemoral joints, was negative. Lasègue test for lumbar radiculopathy and Braggart test for lumbosacral radiculopathy were also negative bilaterally.

Severe pain during the palpating manoeuvre over the upper third of the tensor fasciae latae muscle, over the trochanter in the left trochanteric area, replicated the initial pain. There was no concomitant hypersensitivity or allodynia . The initial diagnosis of tensor fasciae latae myofascial pain was made, as a single trigger point was identified, being very well localized and isolated.

The Flanagan Quality of Life Scale (QOLS) [120] score at presentation was of 61/112, with the patient giving less points to social life related questions and health related questions.

6.5.Intervention

After two sessions of trigger point injections of lidocaine over the tensor fasciae latae, the patient reported an improvement in pain, 5/10 on the NRS. Tenderness over the left trochanter-disappeared the day after the procedures.

Two days before the third and final session of localized trigger point injections, the patient started reporting pain on her left inguinal fold while walking, which she described as electrical shocks with an intensity of 8/10, as well as persistent pain over the left posterior articular T12-L1 level, which she rated a 6/10.

Inspection for segmental dysfunctional and its corresponding referred pain was performed. The pain was reproduced by lateral pressure on the T12 spinous process, pressure at the left posterior articular T12-L1 level and on the T12-L1 interspinous ligament. Based on these findings, the final diagnosis of thoracolumbar junction syndrome was made.

One more session of localized trigger point injection was performed, as well as two sessions of paraspinous lidocaine injection at the T12-L1 level. The patient was taught to maintain postural correction, in her daily activities, flexibility training and advised to maintain physical activity.

6.6.Follow-up and Outcome

After the treatment she was able to resume normal day life and physical activity. QOLS score was consistently high (96/112). The patient reported complete resolution of the pain, and no further complaints over the following 2 years.

7. Discussion

Maigne [53,54,55], in the 1980s, was the first to describe TLJS, which causes referred pain originating in the thoracolumbar junction, and clinical manifestations included pain in the areas innervated by segments of the thoracolumbar junction (back pain, pseudo-visceral pain, pain on the posterior iliac crest, irritable bowel symptoms and hip pain). Maigne postulated that TLJS could be caused by “segmental vertebral cellulotenoperiostomyalgic syndrome”, which comprised of functional abnormalities that did not result in changes in diagnostic exams.

Years later, Professor Andrew Fischer, based on the findings of Robert Maigne, Travell and Simon, and Eric Kandel, postulates on the sensitization of spinal segments being a crucial factor in the development of chronic pain. While Maigne believed the dysfunction of one segment of the spine caused the involvement of all tissues (cellulalgic, tenoperiosteal and myalgic pain of spinal origin), Fischer confirmed that sensitization, and not dysfunction, is behind the chronic pain phenomena. SSS happens when sensory neurons in certain areas of the body release neuropeptides, causing inflammation (neurogenic inflammation), which activate the nociceptive neurons.

The inflammatory mediators will cause the nociceptive neurons to spontaneously fire, increasing their response to stimuli (peripheral sensitization) and cause the CNS to become hypersensitive to pain and other non-noxious stimuli, resulting in an amplified response to noxious stimuli and the perception of pain in response to normally non-painful stimuli (central sensitization). The sensitization and hyperexcitability spread from sensory to motor components of the affected segment, inducing tenderness.

In other words, pain receptors, which typically need a strong stimulation to be detected, change due to endogenous chemicals released from the site of inflammation, causing a painful response to be elicited by a weaker stimulus, thus making the pain more perceptible. As the signalling from pain receptors continues, the low threshold condition perpetuates in time. This causes for the painful response to extend over time and for progressively weaker stimuli to be necessary to trigger such a response.

Since the sensitized spinal segment that supplies the myotome also supplies the sclerotome and dermatome, the changes spread to the other components of the

affected segment, causing muscle spasms, MTrPs (myotomal presentation), hyperalgesia or allodynia (dermatomal presentation) and pressure pain sensitivity (sclerotomal presentation).

Fischer's explanation revolutionized the diagnosis and treatment of TLJS. Since, in most cases, there are no alterations on imaging, the diagnosis is clinical, and the goal is to reproduce the pain the patient has been feeling, first identifying the myalgic trigger point(s) and then identifying the irritated spinal segment. After identification, both the trigger points and irritated spinal segment should be treated, one of the most effective treatments being the trigger point injections and a paravertebral block in the case of chronic sensitization.

While this condition is easy to treat once identified, since it is not well known, doctors typically inform patients that their pain is only "referred pain" or the "consequence of stress" in the absence of confirmatory tests that could otherwise help us understand regional and chronic musculoskeletal pain of metameric distribution (that encompasses a section of the spine with radiation to the limbs or trunk). Worse still, due to the seemingly excessively painful behaviour in comparison to the results of the auxiliary tests, medical professionals may start to assume a psychiatric condition or malingering.

8. Conclusion

Medical professionals can fail to recognize the thoracolumbar junction as a potential cause of hip and pelvic nociceptive pain. If practitioners are better equipped to identify the chance that TLJS can result in hip complaints and take appropriate action, extensive medical testing and perhaps surgery may be avoided. The treatment targeted at the thoracolumbar junction for individuals with hip and groin pain is only briefly discussed in the literature. Despite being mentioned in various reviews, no research has specifically examined the use of local anaesthetic injection for medium to long term pain relief for individuals with hip pain at the thoracolumbar junction.

To evaluate the efficacy of the various therapeutic techniques mentioned in the literature, there needs to be more awareness of this cause of chronic pain and longer-term investigations.

Annex

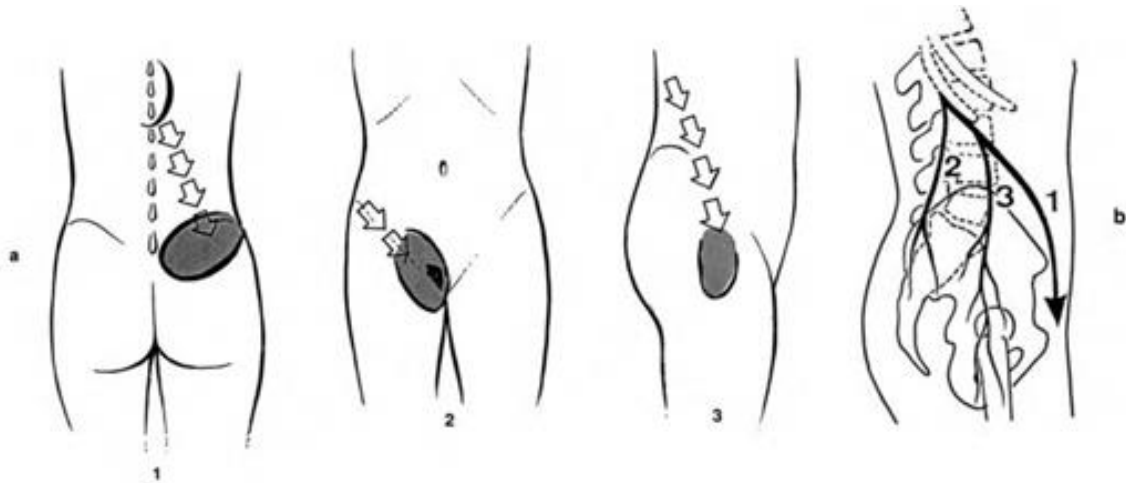


Figure 1 TLJS pain referral patterns: 1, posteriorly — pseudovisceral pain, low back pain; 2, anteriorly — pseudovisceral pain, pubic discomfort; 3, laterally — pseudotrochanteric pain, false meralgia paresthetica. The thoracolumbar junction is typically not where patients with these illnesses report feeling pain. b. The anterior ramus (1), posterior ramus (2), and lateral perforating branch (3) are the three divisions of the T12 and L1 spinal nerves.

Maigne, Robert, and Walter L. Nieves. *Diagnosis and Treatment of Pain of Vertebral Origin*. 2nd ed, CRC/Taylor & Francis, 2006, p. 383

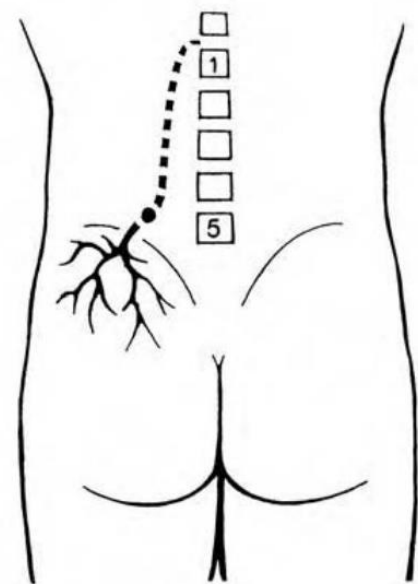
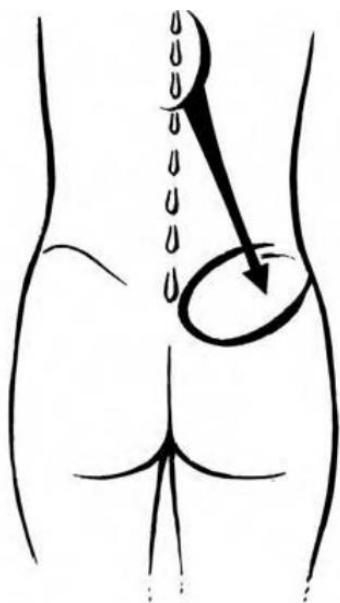


Figure 2 Low back pain might have a thoracolumbar junctional origin – the cutaneous branch of the posterior ramus of the thoracolumbar junction can cause pain in the lower lumbar and upper gluteal regions.

Maigne, Robert, and Walter L. Nieves. *Diagnosis and Treatment of Pain of Vertebral Origin*. 2nd ed, CRC/Taylor & Francis, 2006, p. 289

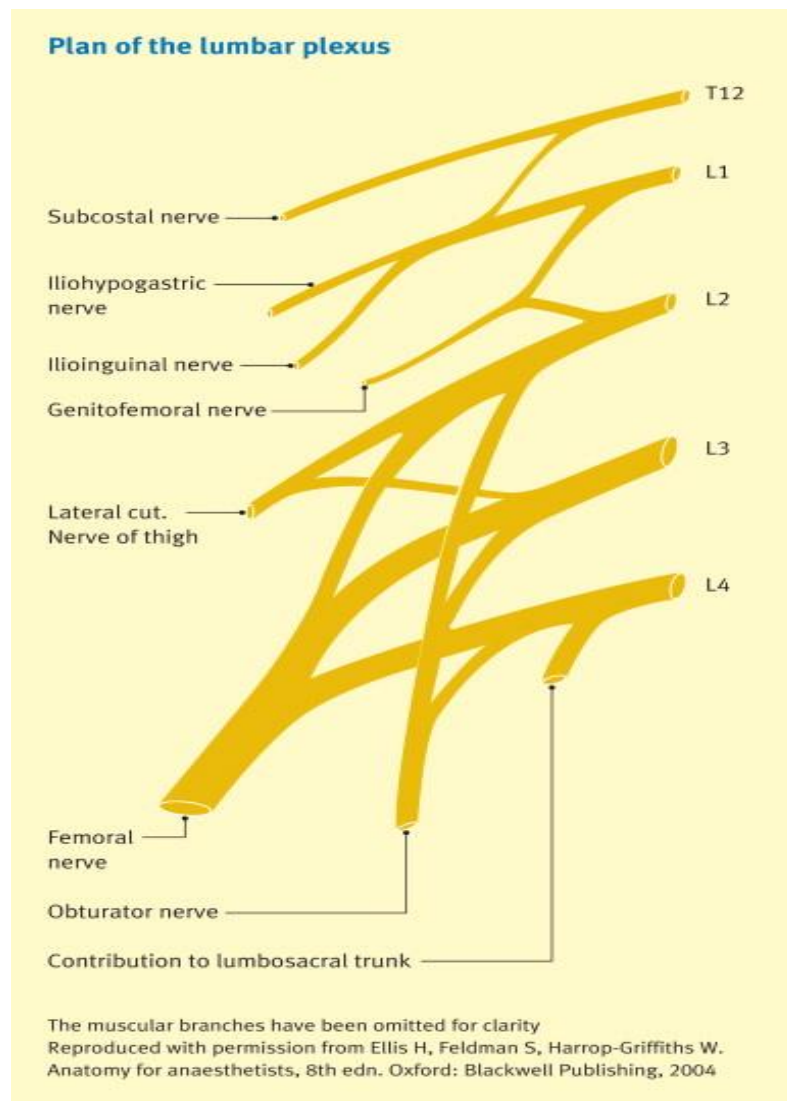


Figure 3 The lumbar plexus

Ellis, Harold. 'The Lumbar and Sacral Plexuses'. *Anaesthesia & Intensive Care Medicine*, vol. 8, no. 4, Apr. 2007, pp. 142–43. DOI.org (Crossref), <https://doi.org/10.1016/j.mpaic.2007.01.008>.

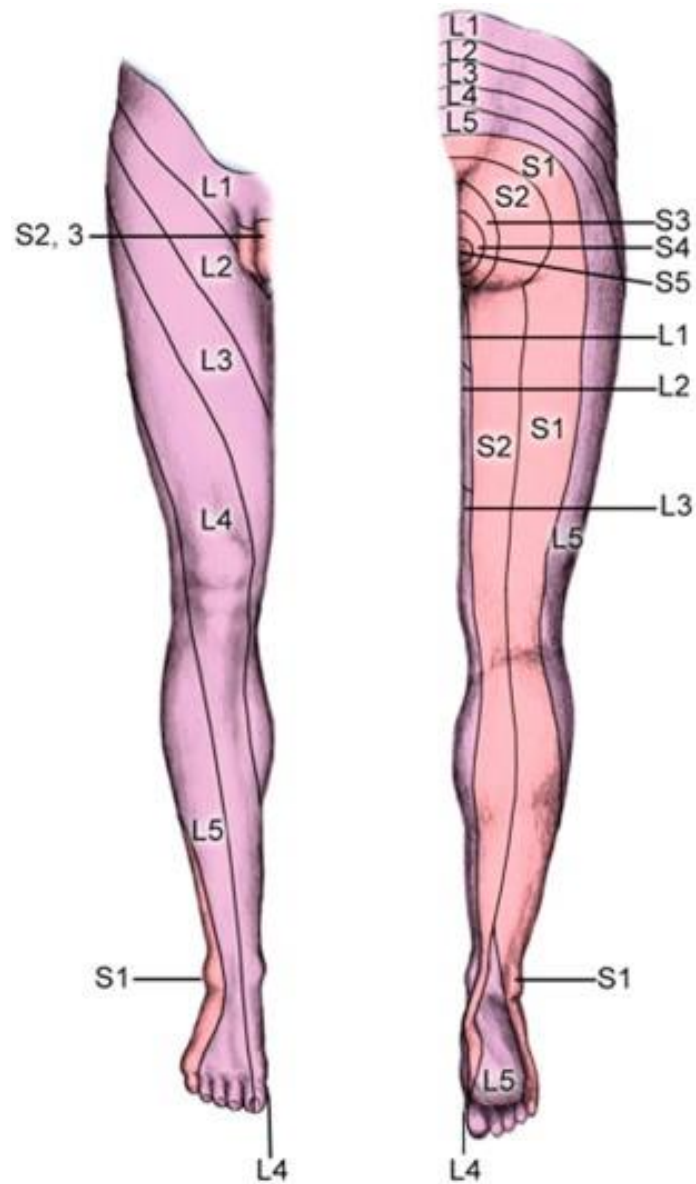


Figure 4 Dermatomal innervation map of the lower limb, according to Keegan and Garrett (1948)

Dermatomes Anatomy: Overview, Gross Anatomy, Natural Variants. June 2020. eMedicine, <https://emedicine.medscape.com/article/1878388-overview>.

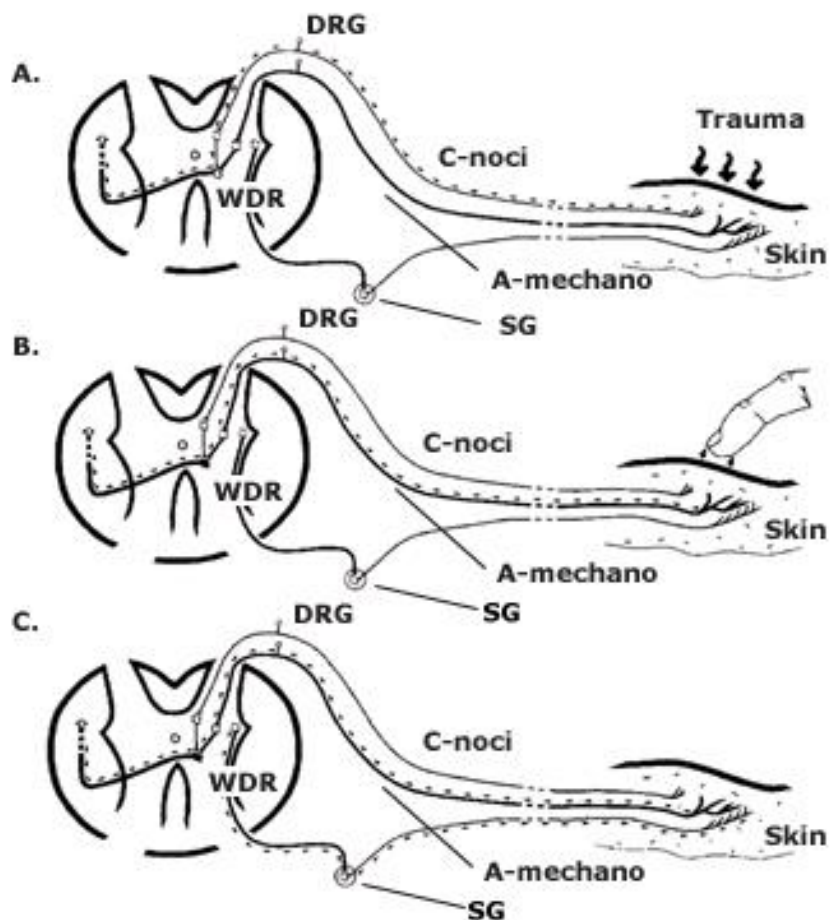


Figure 5 The instantaneous response to cutaneous trauma is shown. The dorsal root ganglion, where the spinal cord is located, is the pathway via which C-nociceptors' action potentials travel. There, they stimulate and sensitize wide-dynamic-range (WDR) neurons, whose axons climb to higher locations. The WDR neurons in B are still sensitive and are now responsive to light touch-activated activity in the large diameter A-mechanoreceptors. There is allodynia in this condition. The same sensitized WDR neurons respond to activity from A-mechanoreceptors in C, but this time, sympathetic efferent actions on the sensory receptor are used to begin the activity instead of cutaneous stimulation. This stage is the ongoing pain that is sympathetically maintained. Although it has been demonstrated that spinal interneurons are positioned along the "pain" pathway, there are many more conceivable configurations.

Roberts, WJ. A hypothesis on the physiological basis for causalgia and related pains. *PAIN* 1986; 24:297



Figure 6 The pinch and roll test.

Aktas, Ilknur, et al. 'Testicular Pain Due to Thoracolumbar Junction Syndrome: A Case Report'. *Revista Internacional de Andrología*, vol. 14, no. 4, Oct. 2016, pp. 148–52. DOI.org (Crossref), <https://doi.org/10.1016/j.androl.2016.04.004>



Figure 7 Using a digital pressure algometer to measure the PPT at the trapezius muscle.

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Part 2

Maigne Syndrome as a Clinical Case of Nociplastic Pain

Key Words: Maigne Syndrome; Thoracolumbar Junction Syndrome; hip pain of vertebral origin; Spinal Segmental Sensitization; Peripheral and Central Sensitization; chronic nociplastic hip pain.

Abstract

Chronic pain affects 30% of the world's population, which makes it one of the major public health issues. It is also well established that myofascial pain syndrome (MPS) is the primary contributor to both musculoskeletal pain and chronic pain, with a significant personal and financial impact. On contrary of nociceptive and neuropathic pain, typically straightforward to diagnose with anamnesis, physical exam, and complementary diagnostic tests, chronic unspecific pain typically doesn't result in alterations in diagnostic tests, meaning it goes undiagnosed and, as a result, inaccurately treated.

The purpose of this article is to create awareness about how nociplastic pain can be diagnosed and treated, giving as an example Maigne's syndrome as an underdiagnosed cause of chronic lumbar and hip pain.

To highlight the significance of a proper assessment and treatment of patients with chronic unspecific pain, the author presents her own clinical situation of hip pain, showcasing how she went 4 years without a diagnosis, while being submitted to several diagnostic tests which showed no alterations and led to multiple ineffective treatments.

Introduction

Chronic pain affects 30% of the world's population [1], which makes it one of the major public health issues nowadays.

Chronic musculoskeletal pain with innocent imaging often poses diagnostic challenges. It is very important for doctors to be familiar with myalgic tension, the most common cause of chronic pain, and with one of the lesser-known syndromes that can cause it: Maigne's syndrome, also known as thoracolumbar junction syndrome.

Doctor Robert Maigne was the first to describe thoracolumbar junction syndrome (TLJS), which also became known as Maigne's syndrome, a disorder which affects the thoracolumbar junction. It originates at the thoracolumbar junction (between T12 and L3), causing pain that spreads across the lateral thoracolumbar nerve branch distribution (back pain, false hip pain, pseudovisceral pain). [7] Clinical examination of the spine demonstrates pain when the facet joints or spinous processes of the thoracolumbar junction are palpated. [8] Maigne postulated that this syndrome was mostly due to intervertebral dysfunction, including thoracolumbar disc disruption, congenital abnormalities, degenerative processes, and fibromyalgia.

Professor Andrew Fischer, based on the findings of Robert Maigne, Travell and Simon, and Eric Kandel (Nobel Prize in Physiology or Medicine winner in 2000), postulates on the sensitization of spinal segments as a crucial factor in the development of chronic pain in a particular body region. Spinal segmental sensitization (SSS), as coined by Professor Andrew A. Fischer, is the name used to describe this phenomena [9,10].

This elaborates on what Robert Maigne had postulated a few years prior – while Maigne believed the dysfunction of one segment of the spine caused the involvement of all tissues (cellulalgic, tenoperiosteal and myalgic pain of spinal origin), Fischer confirmed, with the concept of SSS, that spinal segmental sensitization, not dysfunction, is behind the chronic pain phenomena, which fits what the IASP defined as “nociplastic pain”.

This case report has been reported in line with the CARE guidelines.

Patient Information

On May 7, 2021, a 22-year-old Caucasian Portuguese female medical student presented with a 4-year history of localized left hip pain. Since August 2017 she reports numerous emergency room visits, specialist appointments (in orthopaedics, rheumatology and psychiatrics) and physical therapy sessions, as well as traditional Chinese medicine treatments (specifically, acupuncture and Tui Na), and many different medications, including opioids as needed, with no improvement to her symptomology. The subsidiary exams performed – lumbar and hip x-Ray, hip ultrasound, lumbar and pelvic MRI – were all unremarkable.

Past medical history was relevant for mononucleosis at the age of 8 and a complete tear of the calcaneofibular ligament at 14, with complete resolution of all complaints at the time with physical therapy. She did not smoke, drink, or take any medication. She played basketball at a semi-professional level for 8 years, but she now found herself unable to walk for longer than 10 minutes at a time. No additional past, family, or social history was deemed pertinent.

Timeline

The pain first presented as a sudden onset of stabbing pain over at the side of the left hip after a roughly 5km walk on the beach. The pain onset, over the trochanteric area, radiated up to the spine and down the lateral of the leg, affecting the first two toes on the left foot, lasted a few seconds, and caused loss of strength on the left lower limb, and a consequent fall. After the pain subsided, it was replaced with paraesthesia over the side of the thigh, which lasted for 2 hours, followed by pain over the trochanteric area.

The pain over the trochanteric area persisted for the next 4 years, constant, sharp and deep, 7/10 in intensity with periods of 10/10 pain with various activities (using a 10-point numeric rating scale (NRS), with 0 being no pain at all and 10 being the worst pain imaginable) – bending, sitting, lifting, walking

and standing for more than 10 minutes exacerbated her symptoms. Sleeping was intolerable without the use of a pillow between her legs, and she had taken to sleeping on her back, awaking whenever she changed position. No alleviating factors. The patient reports medication as needed with Paracetamol 500 mg + Tramadol 34.5mg, but refers barely taking the medication, as it did not seem to help the pain.

Clinical Findings

Imaging performed prior to the patient's presentation demonstrated no acute osseous pathology, structural lesions, dislocation, fracture, or mass. Echography of the gluteus muscles revealed a tendinosis of the gluteus medius tendon, which was resolved with physical therapy, and no changes in the pain pattern or intensity. Long spine X-ray revealed no deviation or lower limb dysmetria. Magnetic resonance imaging of the pelvis showed no abnormalities of the hips.

Diagnostic Assessment and Interpretation

There was no weakness associated with a specific myotomal distribution. Her balance was not impaired. Neurologic exam was normal. Gait testing, which analyses how a patient walks and identifies any abnormal walking patterns, was normal.

Modified Trendelenburg test, which assesses weakness of the hip abductors, was normal. Passive and active motion amplitudes for abduction, adduction, flexion, extension, internal and external rotation of the hip were full and pain-free. The FABER test, which inspects for lesions in the sacroiliac or coxofemoral joints, was negative. Lasègue test for lumbar radiculopathy and Braggart test for lumbosacral radiculopathy were also negative bilaterally.

Severe pain during the palpating manoeuvre over the upper third of the tensor fasciae latae muscle, over the trochanter in the left trochanteric area, replicated the initial pain. There was no concomitant hypersensitivity or allodynia. The initial diagnosis of tensor fasciae latae myofascial pain was made, as a single trigger point was identified, being very well localized and isolated.

The Flanagan Quality of Life Scale (QOLS) [11] score at presentation was of 61/112, with the patient giving less points to social life related questions and health related questions.

Intervention

After two sessions of trigger point injections of lidocaine over the tensor fasciae latae, the patient reported an improvement in pain, 5/10 on the NRS. Tenderness over the left trochanter disappeared the day after the procedures.

Two days before the third and final session of localized trigger point injections, the patient started reporting pain on her left inguinal fold while walking, which

she described as electrical shocks with an intensity of 8/10, as well as persistent pain over the left posterior articular T12-L1 level, which she rated a 6/10.

Inspection for segmental dysfunctional and its corresponding referred pain was performed. The pain was reproduced by lateral pressure on the T12 spinous process, pressure at the left posterior articular T12-L1 level and on the T12-L1 interspinous ligament. Based on these findings, the final diagnosis of thoracolumbar junction syndrome was made.

One more session of localized trigger point injection was performed, as well as two sessions of paraspinous lidocaine injection at the T12-L1 level. The patient was taught to maintain postural correction, in her daily activities, flexibility training and advised to maintain physical activity.

Follow-up and Outcome

After the treatment she was able to resume normal day life and physical activity. QOLS score was consistently high (96/112). The patient reported complete resolution of the pain, and no further complaints over the following 2 years.

Discussion

Maigne [12,13,14], in the 1980s, was the first to describe thoracolumbar junction syndrome, which causes referred pain originating in the thoracolumbar junction, and clinical manifestations included pain in the areas innervated by segments of the thoracolumbar junction (back pain, pseudo-visceral pain, pain on the posterior iliac crest, irritable bowel symptoms and hip pain). Maigne postulated that thoracolumbar junction syndrome could result in “segmental vertebral cellulotenoperiostomyalgic syndrome”, which comprised of functional abnormalities that did not result in changes in diagnostic exams.

Years later, Professor Andrew Fischer [9,10], based on the findings of Robert Maigne, Travell and Simon, and Eric Kandel [2-8, 12-14], postulates on the sensitization of spinal segments being a crucial factor in the development of chronic pain. While Maigne believed the dysfunction of one segment of the spine caused the involvement of all tissues (cellulalgic, tenoperiosteal and myalgic pain of spinal origin), Fischer confirmed that sensitization, and not dysfunction, is behind the chronic pain phenomena. Spinal segmental sensitization happens when sensory neurons in certain areas of the body release neuropeptides, causing inflammation (neurogenic inflammation), which activate the nociceptive neurons.

The inflammatory mediators will cause the nociceptive neurons to spontaneously fire, increasing their response to stimuli (peripheral sensitization) and cause the central nervous system to become hypersensitive to pain and other non-noxious stimuli, resulting in an amplified response to

noxious stimuli and the perception of pain in response to normally non-painful stimuli (central sensitization). The sensitization and hyperexcitability spread from sensory to motor components of the affected segment, inducing tenderness.

In other words, pain receptors, which typically need a strong stimulation to be detected, change due to endogenous chemicals released from the site of inflammation, causing a painful response to be elicited by a weaker stimulus, thus making the pain more perceptible. As the signalling from pain receptors continues, the low threshold condition perpetuates in time. This causes for the painful response to extend over time and for progressively weaker stimuli to be necessary to trigger such a response.

Professor Fischer refers that this central sensitization, on the spinal level, occurs in segments and, since the sensitized spinal segment that supplies the myotome also supplies the sclerotome and dermatome, the changes spread to the other components of the affected segment, causing muscle spasms, myofascial trigger points (myotomal presentation), hyperalgesia or allodynia (dermatomal presentation) and pressure pain sensitivity (sclerotomal presentation).

Fischer's explanation revolutionized the diagnosis and treatment of thoracolumbar junction syndrome. Since, in most cases, there are no alterations on imaging, the diagnosis is clinical, and the goal is to reproduce the pain the patient has been feeling, first identifying the myalgic trigger point(s) and then identifying the irritated spinal segment. After identification, both the trigger points and irritated spinal segment should be treated, one of the most effective treatments being the trigger point injections and a paravertebral block in the case of chronic sensitization.

Despite, in this case, the trigger point location corresponding to the L5 dermatome, we know that, according to the studies performed by Jean-Yves Maigne [15], (which are contrary to the literature of the time, as well as the dermatome map designed by Keegan and Garrett) - the dorsal rami of T12 and L1, penetrate through the subcutaneous tissues of the lumbar and gluteal region as distant as the greater trochanter. This explains that the pain felt over the trochanteric region originated in the thoracolumbar junction (T12-L1). [13,16]

While this condition is easy to treat once identified, since it is not well known, doctors typically inform patients that their pain is only "referred pain" or the "consequence of stress" in the absence of confirmatory tests. Worse still, due to the seemingly excessively painful behaviour in comparison to the results of the auxiliary tests, medical professionals may start to assume a psychiatric condition or malingering.

The lack of medical knowledge and the high incidence of nociplastic pain make it essential to disseminate the awareness on spinal sensitization.

Any kind of analgesic has a modest efficacy in treating chronic pain [18], and nociplastic pain may be made worse by opioid use, which makes them useless in treating chronic pain. [17, 18, 19] Non-pharmacological approaches should be prioritized for treating nociplastic pain because most drugs have only

modest benefits and frequently induce side effects, which are more common in nociplastic disorders. [20]

Conclusion

In the past five years, the term "nociplastic pain" has entered the medical lexicon to characterize pain syndromes that are not neuropathic nor nociceptive but are still frequently experienced by people all over the world. In the coming decades, as new disorders are acknowledged to have nociplastic components and as distinct pathophysiological mechanisms and biomarkers are discovered, the structure of nociplastic conditions is going to evolve. With the exception of discomfort, the clinical symptoms of these many pain syndromes are highly overlapping and virtually entirely subjective. Creating efficient treatment plans requires a deeper comprehension of the underlying mechanisms.

Medical professionals can fail to recognize the thoracolumbar junction as a potential cause of nociplastic pain. If practitioners are better equipped to identify the chance that TLJS can result in hip complaints and take appropriate action, extensive medical testing and perhaps surgery may be avoided. The treatment targeted at the thoracolumbar junction for individuals with hip and groin pain is only briefly discussed in the literature. Despite being mentioned in various reviews, no research has specifically examined the use of local anaesthetic injection for medium to long term pain relief for individuals with hip pain originating at the thoracolumbar junction. To evaluate the efficacy of the various therapeutic techniques mentioned in the literature, there needs to be more awareness of this cause of chronic pain and longer-term investigations.

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