Abstract

Oncocytic tumours are composed by large epithelial cells with a granular cytoplasm which is filled with a large number of morphological and functionally abnormal mitochondria (oncocytic cells, oxyphilic cells or, whenever in the thyroid, Hürthle cells). These tumours occur in parenchymas and organs with low proliferative index, like the thyroid and the salivary glands. The mitochondria accumulation in the cytoplasm of cells may be the result of a primary alteration in mitochondrial DNA (mtDNA), or it can be a consequence of mutations in nuclear DNA (nDNA) that encodes for mitochondrial proteins.

Alterations in the mtDNA, with significant differences between oncocytic and non-oncocytic thyroid tumours have been reported. In a previous study performed in thyroid tumours, the presence of a deletion, designated as common deletion (CD) of the mtDNA, was detected in all oncocytic cell tumours included in the series. In the same study, an association between the existence of polymorphisms in mitochondrial genes encoding complex V of the mitochondrial respiratory chain and the occurrence of oncocytic tumours was also detected. Finally, a higher frequency of alterations in displacement-loop (D-loop) was found in the oncocytic tumours.

Warthin tumours of the salivary glands consist in two components: an oncocytic epithelial component and a lymphoid component, being both polyclonal. The histogenesis of Warthin tumour remains controversial, and two theories are on the table: the so-called heterotopic theory and the theory that emphasizes the role played by immunological mechanisms.

Besides the study on record that describes the presence of the CD in Warthin tumours, there are no other publications, as far as we know, describing the occurrence/absence of alterations in mtDNA in Warthin tumours.

In an attempt to progress in the understanding of the relationship between alterations in mtDNA in oncocytic cell tumours in general, and Warthin tumours in particular, we studied 19 Warthin tumours of the parotid gland, and the respective non neoplastic parenchyma in 13 cases, regarding some mtDNA alterations. We performed a revision of the clinical information, macroscopic and microscopic characteristics from all the cases; DNA extraction was performed from samples obtained using microdissection. We searched for the following mtDNA alterations: CD, mutations in the
D-loop and in the subunits 6 and 8 of the complex V (ATPase) of the mitochondrial respiratory chain.

We detected the presence of instability in the D-loop region in 63.2% of the Warthin tumours and in one case in the adjacent normal tissue. We detected somatic mutations in ATPase 6 in 5.3% of the cases. Mutations in the 8 subunit were not found. We were not able to detect the presence/absence of the CD in the studied tissues because of technical problems.

Mutations in ATPase 6 show some preference by tumours with an oncocytic phenotype. We did not obtain evidence favouring the existence of a determinant role for the instability of the non-codifying D-loop region in the process of oncocytic transformation of Warthin tumours.

In conclusion, we observed that the alterations that we found in mtDNA of Warthin tumours do not differ substantially from those previously obtained in Hürthle cells tumours of the thyroid, both with respect to the type of alterations and to their frequency.