Histology and Histopathology
From Cell Biology to Tissue Engineering

Gastrointestinal Stromal Tumor (GIST) and its relationship with germline mutations

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Background: We present the case of a 38-year-old man with a history of abdominal paraganglioma 10 years ago, who consulted for hematemesis and asthenia of 5 days' evolution. An upper gastrointestinal endoscopy was performed where a raised submucosal lesion, about 2 cm, with ulceration on its surface, was observed at the corporal-antral junction. The CT scan revealed nodular thickening of the gastric wall at the level of the lesser curvature. After the resolution of his hematemesis, it was decided to intervene on the patient, performing a partial gastrectomy.

Methods: The piece presented a tumor lesion with a maximum diameter of 1.3 cm. When cut, the tumor was whitish in color and had an elastic consistency. Histologically, it was a mesenchymal neoplasm of epithelioid cellularity that infiltrated the entire thickness of the wall, sparing the mucosa. The growth pattern was multinodular with plexiform infiltration of the muscularis propria layer. The mitotic index was > 5/50 CGA and images of vascular permeation were observed. The immunohistochemical study showed positivity for CKIT, DOG-1 and CD-34. With the diagnosis of Gastrointestinal Stromal Tumor (GIST), we proceeded to carry out the mutational study that resulted in CKIT and PDGFR Wild Type (WT).
Given the morphological characteristics and the immunohistochemical and molecular findings, we proceeded to study the presence of succinate dehydrogenase (SDH), observing a deficit of the B subunit of SDH, with the SDHA, SHCD and SDHD subunits being conserved.

Results: GISTs can be divided into two groups: type 1 (the majority) that occurs in adults, are spindle cell and are usually associated with a CKIT or PDGFR mutation; or type 2 that occur in children or young adults, with epithelioid morphology, CKIT/PDGFR WT and germline mutations in succinate dehydrogenase (SDH) subunits. Thus, type 2 GISTs are associated with a germline mutation of succinate dehydrogenase, which suggests they may be caused by defective mitochondrial oxidation; This is shown by the recent data that implicate this enzyme with this tumor as well as with others of a neuroendocrine nature. In addition, our patient had an associated history of abdominal paraganglioma, a dyad that has been identified as "Carney-Stratakis syndrome" (CCS). Carney-Stratakis syndrome occurs equally in both sexes and has autosomal dominant inheritance. It is a rare disease and is caused by germline mutations in succinate dehydrogenase B, C or D subunits, leading to tumor formation.

Conclusions: All these data should cause us to wake up, since they have clinical implications for patients with GIST that do not present the CKIT and PDGFRA (WT) mutation, since, on the one hand, these tumors are usually resistant to treatment with tyrosine inhibitors. kinase currently available, and on the other hand they and their relatives must be thoroughly studied because it may be a familial syndrome such as TC or SCC, especially if they are young patients.

Supported by……..

[1] Who Classification of Tumours Editorial Board. (2020). Gastrointestinal Tumours: Who Classification of Tumours (5th ed.). World Health Organization. 45-47.

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