Erdheim-Chester Disease and Neuroendocrine Gastrointestinal Neoplasms

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Erdheim-Chester Disease and Neuroendocrine Gastrointestinal Neoplasms

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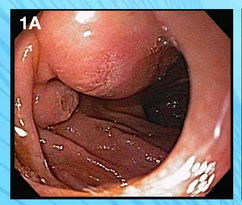
BACKGROUND

Erdheim-Chester disease (ECD) is a rare, non-Langerhans histocytosis, mainly affecting adults ages 40 - 70. This clonal disorder is marked by recurrent BRAFV600E mutations in over 68% of patients and presents as uncontrolled inflammation of multiple organ systems. This pattern of cytokine expression and protein kinase signaling results in pro-inflammatory recruitment of histiocytes. Only 500 cases have been described in the literature with longstanding uncertainty about etiology and classification. While data supporting treatment is limited, IFN-α and pegylated IFN-α are considered first-line options with Kinase inhibitors demonstrating dramatic improvement in a small number of cases.

CASE

A 65 year-old female presented with new onset, transient neurologic symptoms of ataxia, headaches, right-sided weakness, and dysarthria. A brain MRI demonstrated multiple enhancing supratentorial and infratentorial lesions with calvarium involvement. Right temporal lobe and dural masses were also noted and biopsied. Pathology described foamy histiocytes with tissue demonstrating a BRAFV600E mutation, which is consistent with ECD. Having predominantly progressive CNS and osseous involvement rendered the patient eligible for a phase II study of Vemurafenib therapy. She tolerated the treatment with clinical improvement over one year. She then presented with melena, was found to have a clean-based antral ulceration on EGD, and was treated conservatively. Several months later, a PET scan revealed a new subepithelial duodenal mass with FDG avidity. Patient underwent an endoscopic ultrasound guided fine needle aspiration (Figure 1). Pathology revealed a low grade neuroendocrine neoplasm and is currently pending endoscopic removal (Figure 2).



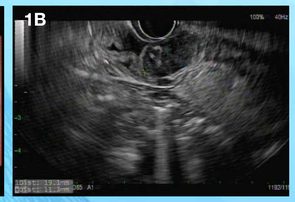
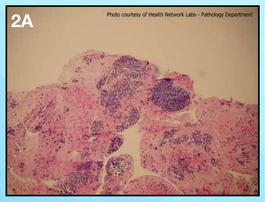
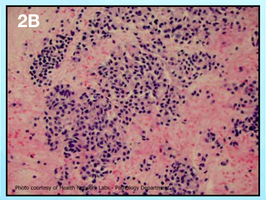


Figure 1:

A - Subepithelial lesion in the second portion of the duodenum adjacent to the papilla.

B - Lesion visualized with linear Echoendoscope showing a hypoechoic mass measuring 19.1 x 11.3 mm. It involves superficial layers 1 and 2, but spares the muscularis propria.





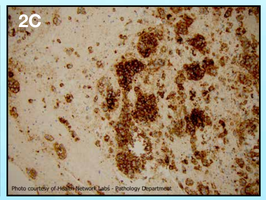


Figure 2:

A - Nests of epithelial neoplasm (low power).

B - Nests of low grade tumor (high power) showing homogeneous population of cells.

C - Positive immunohistochemistry staining for Synaptophysin (a marker for neuroendocrine differentiation).

DISCUSSION

The most recent multidisciplinary meta-analysis and literature review proposes that ECD can have a neuroendocrine predominance in addition to Osseous, CNS, Cardiac, Retroperitoneal, Orbital-craniofacial, and Pulmonary manifestations. Of the endocrinopathies described in literature, diabetes insipidus, hyperprolactinemia, gonadotropin insufficiency, and hypotestosteronism were most observed. The pituitary gland and stalk along with the hypothalamus have been known to display radiographic abnormalities with such findings. Gastrointestinal malignancies with neuroendocrine features are not typically associated with ECD and have not been noted to date. It is of great importance to keep in mind that the patient described here is one of the very few cases to receive “off-label” treatment with a Kinase inhibitor such as Vemurafenib. A common and well documented toxicity of this agent is cutaneous squamous cell carcinomas. BRAF inhibition is potentially unsafe with known risks of accelerating pre-malignant lesions through compensatory overexpression of the proto-oncogene. With no clinical trials to assess the long-term effects of Vemurafenib, the critical question becomes whether or not the medication can be responsible for the development of neuroendocrine neoplasms. This case provides the opportunity to review and add to the current literature available on Erdheim-Chester disease while highlighting the importance of pursuing clinical trials to guide treatment.

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