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Gangliocytic Paraganglioma of the Appendix; A Rare Case Report and Review

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Abstract

Gangliocytic paraganglioma (GP) (nonchromaffin paraganglioma, paraganglioma) is a morphologically distinct tumor most commonly occurring in the second part of the duodenum in the proximity of ampulla of Vater. We herein, present a case report of appendiceal mass in a 16-year-old male who presented with recurrent right iliac fossa pain and stenosing cecal tumor on CT abdomen. He underwent right hemicolectomy and histopathological examination of appendix showed infiltration of appendiceal wall with gangliocytic paraganglioma. To our knowledge this is the first reported case of gangliocytic paraganglioma of appendix in our area.

Keywords: Gangliocytic paraganglioma; Benign appendiceal neoplasm; Immunohistochemistry

List of Abbreviations:

GP - Gangliocytic Paraganglioma
KPK - Khyber Pakhtunkhwa

Introduction

Gangliocytic paraganglioma (GP) (non-chromaffin paraganglioma, paraganglioma) is one of the rare neuroendocrine tumors with three characteristic components: epithelioid cells, spindle cells and ganglion cells.

It is generally located in duodenum. About 90% of the duodenal gangliocytic paraganglioma are located in the second part of duodenum of which about 30% of are located in the Ampulla of Vater [1]. GP have been reported in other organs i.e. respiratory system, low-level spinal cord, esophagus, pancreas, jejunum, ileum and appendix. [2] [3].

The tumor is generally classified as a benign tumor but some cases reported involvement of lymph nodes and even distant metastases. [4].

It is believed to be a nonfunctioning neuroendocrine tumor except for one case report of the corticotropin-producing GP arising in the lung [5].

The lesion was first described by Dahl et al. in 1957, and further characterized as a benign non chromaffin paraganglioma by Taylor and Helwig in 1961. [6] [7].

Case Report

We report a case of gangliocytic paraganglioma in a 16-year-old male who presented with symptoms of repeated right iliac fossa pain. CT scan report showed a stenosing cecal/appendiceal mass starting from base of appendix and reaching up to the ascending colon causing partial stenosis of cecum. Patient underwent right hemi colectomy.

A right hemi colectomy specimen was received in 10% buttered formalin at Histopathology division of Peshawar Medical College Lab. The specimen consisted of terminal ileum measuring 14x3cm, cecum measuring 10x7cm and a firm pale white enlarged elongated appendix measuring 13 x 5 x 2.5cm. Appendix was adherent to the serosal surface of cecum by loose fibrous adhesions. On sectioning the appendicular lumen was narrow and wall was thick pale, white, and firm. The cecum was partly narrowed at the level of appendix base.

Microscopically mucosa of the appendix was intact. The lamina propria was infiltrated by a triphasic lesion composed of three types of cells: epithelioid cells, spindle (Schwann cells) and ganglion type cells in varying proportions. Neither nuclear pleomorphism nor mitotic activity as well as no necrosis was seen.

Immunohistochemical analysis showed S100 positivity in ganglion cells and Synaptophysin positivity in epithelioid cells (Figure 1.E&F,1.G).

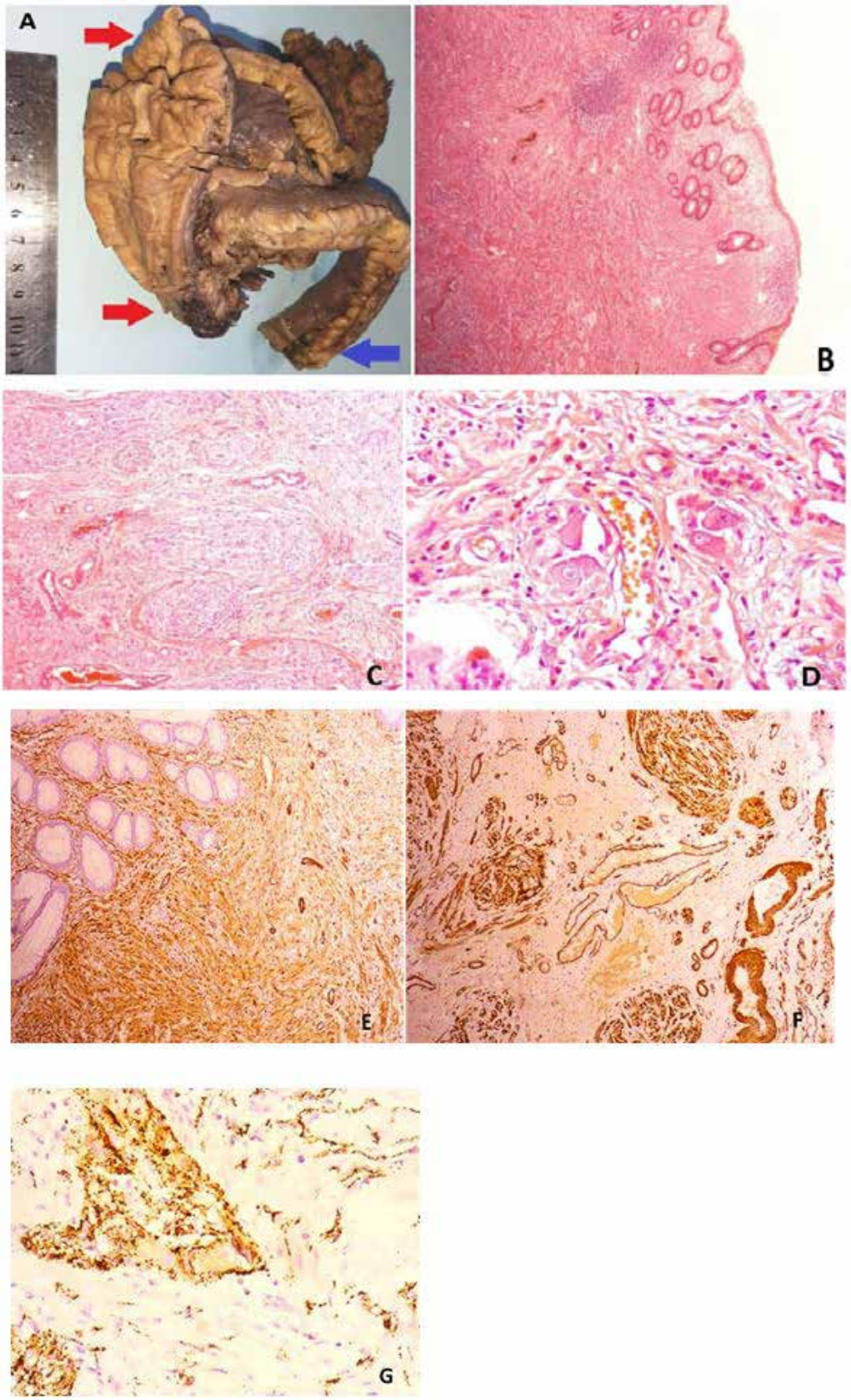

Figure: A. Right Hemi colectomy specimen- Gross appearance: Red arrows points towards an appendiceal mass and blue arrow points towards ileum. **B.** Appendicular epithelium with lamina propria diffusely infiltrated by the lesion. (H&E Stain; 10x). **C.** Collection of spindle cells showing elongated spiral nuclei with tapering ends (H&E Stain; 40x). **D.** Multiple clusters of ganglion cells in the lamina propria (H&E stain). **E&F.** S100 immunostaining highlights the spindle cells and ganglion cells among the epithelioid nests [40x].**G.** Synaptophysin immunostaining highlights the ganglion cells (40x).

Discussion

Gangliocytic paraganglioma is a rare entity with uncertain histogenesis. It is generally located in duodenum. About 90% of the duodenal gangliocytic paraganglioma are located in the second part of duodenum of which about 30% of are located in the Ampulla of Vater [1].

GP have also been reported in other organs i.e., respiratory system, low-level spinal cord, esophagus, pancreas, jejunum, ileum, and appendix. [2, 3].

About 200 cases have been reported since the documentation of first case in 1957 [8] further characterized as a benign nonchromaffin paraganglioma by Taylor and Helwig in 1961 [6]. In 1971 the term gangliocytic paraganglioma was established by Kepes and Zacharias as they recognized the common features between paraganglioma and ganglioneuroma [7]. In the modern literature we identified the reports of gangliocytic paraganglioma of appendix [9, 10]

The tumor usually affects the middle-aged people with slight predominance in males. There is no specific symptoms related to the tumor, patients maybe asymptomatic or incidentally discover it during imaging for other purposes, or it may cause mass effect and presents with abdominal pain, gastrointestinal bleeding due to ulceration over the lesion, features of intestinal obstruction and bile duct obstruction [4]. Most of the cases are hormonally inactive however; some cases have been reported to release somatostatin or pancreatic polypeptide secretion [11, 12]

This tumor has a variety of differential diagnosis which makes the diagnosis difficult in some cases. The differential diagnosis is Carcinoid tumor, Ganglio-neuroma, Pigmented Paraganglioma and Gastrointestinal stromal tumor [GIST], Hamartoma, Lymphoma, Hemangioma and Duodenal cancer and Sarcomas. This differentiation is usually done by imaging, biopsy and immunohistochemical analyses detecting the expression of various markers and proteins [11-16]

The pathological origin of GP is unclear. A few authors suggest that the lesion originates from the ectopic pancreatic tissue [17], from pluripotent stem cells located at the base of intestinal glands[18], or from endodermally derived epithelial cells in the ventral primordium of the pancreas [19].

The three pathognomonic features of this tumor are [1] Epithelioid cells containing dense- core granules ultra-structurally and exhibiting immunoreactivity for a variety of markers, particularly pancreatic polypeptide [PP], synaptophysin, chromogranin and progesterone [2] Ganglion cells immunoreactive for S100, neuron-specific enolase, synaptophysin and other neural markers; [3] Spindle-shaped Schwann cells immunoreactive for S-100 protein.

Phenotypical analysis by immunohistochemical examination is considered crucial step in the diagnosis of GP and immunohistochemically these tumors stain positive for a variety of markers as shown in the current case e.g. neuron-specific enolase, pancreatic polypeptide, somatostatin, and myelin basic protein and neurofilament proteins. [20, 21]

Mostly these tumors have a benign clinical course, although rarely they may recur or metastasize to regional lymph nodes. [4, 22, 23] The following therapeutic approaches for GP were suggested by Barret et al.

1. Tumor measuring <2cm in diameter without evidence of peritumoral lymph node involvement on abdominal CT scan should be treated with endoscopic mucosal resection, if the tumor is involving the ampulla than surgical resection with ampullectomy or laproscopic transduodenal tumorectomy combined with preoperative duodenoscopy should be done.

2. Large tumors with lymph node metastasis or histopathological features such as infiltrative borders on local resection, nuclear pleomorphism and high mitotic activity should be treated with pancreaticoduodenectomy with lymph node dissection [24].
Until now the histological features of predicting malignant potential of GP have not been reported. It has been suggested that nuclear pleomorphism, mitosis and infiltrative margins raises the concern in the behavior of this lesion. [25]

Conclusion

Appendiceal gangliocytic paraganglioma is a rare entity. Mostly it arises in second part of duodenum and appendix is a rare site. Gangliocytic paraganglioma has a generally benign clinical course. [22, 23]. However, follow up of the patient is recommended. Up to the best of our knowledge we report first case of gangliocytic paraganglioma from KPK province, Pakistan.

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