Appendiceal Neuroendocrine Tumor Mimicking Acute Appendicitis

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ABSTRACT

Appendiceal carcinoids are the most frequent tumors arising from the appendix, comprising between 32 and 57% of all the appendiceal tumors. The gross appearance of the appendix showed perforation at the tip with 30 ml of periappendicular collection. On histopathological examination, carcinoid tumor on the tip of appendix was found with tumor cells arranged in tubules, acini and nests infiltrating the muscularis propria and sub serosa. Perineural and vascular invasion was not seen. Immunohistochemistry for Synaptophysin was positive with Ki-67 labelling index of 2%. We present a case of appendiceal neuroendocrine tumor with the chief complaint of acute appendicitis.

KEY WORDS

Appendectomy, Appendix, Carcinoid tumor

INTRODUCTION

Primary appendiceal neoplasm is a rare pathology accounting for 0.5-1% of all the appendectomy specimens. The term "Karzinoid" was first used by Oberndorfer in 1907 to describe a type of tumor which was benign and grew slowly in comparison to adenocarcinomas. They are derived from the sub epithelial neuroendocrine cells of the appendix, rarely causing metastasis. They occur more frequently in women than in men (2-4:1).[1] The carcinoid is located at the tip of appendix in 75% of the cases, 20% in the mid portion and 5% in the base. Here we report a case of 50 year old female who present at our surgery out-patient department with the history of right lower abdominal pain and was clinically diagnosed as acute appendicitis. On histopathological examination, tumor cells arranged in tubules, acini and nests were found infiltrating the muscularis propria and sub serosa.

CASE REPORT

A 50 year old female presented at our Surgery out-patient department with the history of right lower abdominal pain and was clinically diagnosed as acute appendicitis. Grossly, appendectomy specimen along with mesoappendix showed a perforation at the tip. The serosal surface was covered with a fibrinopurulent exudate. Cut sections showed a dilated lumen with a small circumscribed, firm, yellowish nodule measuring 0.4 cm, located 2 cm from the tip and 4 cm from the surgical resected margin. Microscopic examination revealed a carcinoid tumor arranged in tubules, acini and nests. Individual cells have uniform round nuclei, inconspicuous nucleoli, and speckled nuclear chromatin. Tumor cells were seen infiltrating the muscularis propria and sub serosa. Surgical resected margin was free of tumor deposits. Perineural and vascular invasion was not seen. An inflammatory cell infiltrates,

predominantly composed of neutrophils was extensively present within the periappendiceal tissue. Mitotic rate was less than 2 mitoses per 2 mm^2 (Fig. 1, 2a and 2b). Immunohistochemistry for Synaptophysin was positive (Fig. 3) with Ki-67 labelling index of 2% (Fig. 4). Hence, a diagnosis of Well Differentiated Neuroendocrine tumor of appendix (Grade 1) pT1NxMx (Stage I) (Given the limitation of distant metastasis and nodal involvement) was made.

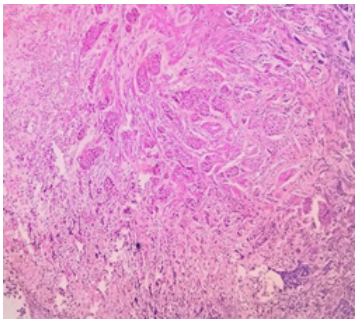

Figure 1. H & E section shows carcinoid tumor arranged in tubules, acini and nests, 10X

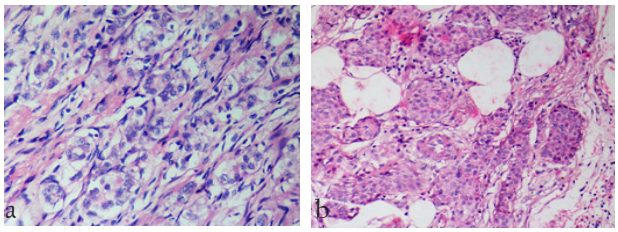

Figure 2a,b. H&E sections show tumor cells having uniform round nuclei, inconspicuous nucleoli, and speckled nuclear chromatin, 40X

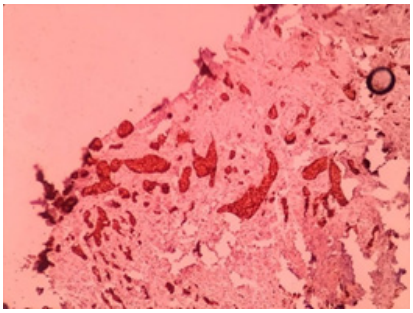

Figure 3. Synaptophysin stain demonstrates strong positive staining of tumor cells.

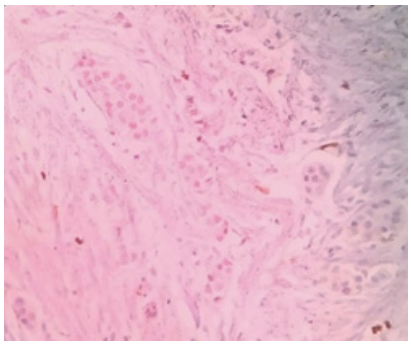

Figure 4. Assessment of Ki-67 proliferation index revealed nuclear staining in 2% of cells.

DISCUSSION

The term "Karzinoid" was first used by Oberndorfer in 1907 to describe a type of tumor which was benign and grew slowly in comparison to adenocarcinomas.[1] The relationship between the endocrine nature of carcinoid tumor and its clinical manifestations was recognized after the discovery of serotonin by Rapport et al. in 1948. In 1953, Lembeck isolated serotonin from a carcinoid tumor. Thorson and coworkers in 1954, wrote about the endocrine properties and clinical manifestations of carcinoid tumor as cutaneous flushing, diarrhea, erythema and bronchospasm.[1] Carcinoid syndrome occurs in less than 10% of patients with carcinoid tumor, (< 2% of all the appendiceal carcinoid tumor with liver metastases). This syndrome develops when the vasoactive substances produced by the carcinoid tumor enters into the systemic circulation avoiding the hepatic degradation.[2] Carcinoid tumors are of neuroectodermal origin and is classified as a part of other amine precursor uptake and decarboxylation (APUD) neoplasms.[1] They are derived from the subepithelial neuroendocrine cells of the appendix, rarely causing metastasis.[3] Carcinoid tumors are identified in various locations, as lungs (25.1%), ovaries (0.5%), biliary system (0.2%) and throughout the gastrointestinal tract (73.4%).[3] Primary appendiceal neoplasm is a rare pathology accounting for 0.5-1% of all the appendectomy specimens.[4,5] Appendiceal carcinoids are the most frequent tumors arising from the appendix, comprising between 32 and 57% of all the appendiceal tumors.[3] They occur more frequently in women than in men (2-4:1).[1] The carcinoid is located at the tip of appendix in 75% of the cases, 20% in the mid portion and 5% in the base. The median tumor diameter is 6 mm (3-17 mm). Carcinoid tumors located at the tip of appendix and measuring less than 10 mm usually presents with symptoms of acute appendicitis whereas tumors measuring more than 20 mm and located at the base may present with clinical signs of peritonitis.[6] Appendiceal carcinoid tumor carry better prognosis than that of midgut carcinoid tumor.[2] They are usually asymptomatic or presents as acute appendicitis with recurrent abdominal pain due to partial obstruction of the appendiceal lumen by the tumor and are diagnosed incidentally during surgery. Urine 5-Hydroxyindoleacetic acid (HIAA) is a good marker of endocrine activity of carcinoid tumor and the levels are high in case of patient with metastasis in comparison to those without metastasis.[3,6] Tumor size is the most reliable indicator for the assessment of the malignant potential of the appendiceal carcinoids. Most of the carcinoid tumors are less than 1 cm but rarely larger than 2 cm in diameter. For tumors measuring < 1 cm in diameter, appendectomy alone is the sufficient treatment as they rarely metastasize. For tumors measuring > 2 cm in diameter, right hemicolectomy should be done as they poses a potential risk of metastasis. For tumors measuring 1-2 cm in diameter, surgical treatment is based on the

mesoappendiceal involvement and the histological subtype of the lesion.[2-4,7] Right hemicolectomy is to be performed in individuals with histological evidence of mesoappendiceal extension, tumors located at the base of the appendix with positive margins or involvement of caecum, high grade malignant carcinoids, angioinvasion, high Ki67 levels, and younger patients with positive lymph nodes.[2-4] The five year survival rate of patients with localized disease, regional metastases and distant metastases in appendiceal carcinoid were 92%, 81% and 31% respectively.[2]

The long term prognosis of incidentally found carcinoids of the appendix is good. It is mandatory to perform histopathological examination of an appendectomy specimen to rule out neoplasm.

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