A Case Report: The Incidental Finding of Neuroendocrine Tumor of Appendix Presenting as an Acute Appendicitis

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Abstract: Background: Neuroendocrine tumours (NETs) are well-differentiated epithelial neoplasms with morphological and immunohistochemical features of neuroendocrine differentiation.
Case Description: We report a 22-year-old woman with lower right abdominal pain. Patient underwent appendectomy and the specimen was sent for histopathological examination. On macroscopic examination, we received tissue originating from mass in the appendix, showed mass was brownish gray and irregular. The size was approximately 4 cm. On cut section, tumor mass appeared at apical of the appendix, 0.5 cm from the end of resection margin. On microscopic examination, tissue from the mass in appendix consist of mucosal layer to serosa layer. Mucosal layer with columnar epithelial lining partially atrophy, columnar epithelium with normal nuclear morphology. In the subepithelial, the proliferation of tumor cells appears to form nests, trabeculae, acini, and ribbon-like structures. Tumor cells are relatively uniform with round nuclei, salt & pepper chromatin, abundant and granular cytoplasm. Mitoses (<20 mitoses/10 HPF). We also found rosette like. The stroma consists of thick fibrotic connective tissue, infiltrated by tumor cells forming a single file appearance. On immunohistochemical examination in case showed synaptophysin (+), chromogranin A (+), ki67 proliferation index value is 3% and CK20 (-).
Discussion and Conclusion: NETs most typically showing organoid architecture, uniform nuclei, and coarsely granular cromatin. NETs can be low-grade (G1), intermediate-grade (G2), or high-grade (G3). For the diagnosis of NETs, expression of synaptophysin or chromogranin A must be present. Based on histopathology and immunohistochemical results, this case was diagnosed as Appendiceal neuroendocrine tumours, NOS, intermediate-grade (G2), ICD-O 8249/3, topography morphology (C18.1).

Keywords: Appendiceal, neuroendocrine tumour, neuroendocrine differentiation

I. INTRODUCTION

Tumors in the appendix are mostly found incidentally in patients who were operated on with an initial diagnosis of acute appendicitis. Only about 1% of all appendectomy specimens are reported. Neuroendocrine tumor (NET) accounts for more than 50% of neoplasms in the appendix. NET appearing in the appendix can cause carcinoid syndrome.[1]

Neuroendocrine neoplasms (NEN) are primary epithelial neoplasms that show morphological and immunophenotypic signs of neuroendocrine differentiation. NEN is classified using the scheme described in the World Health Organization (WHO) 2019, as neuroendocrine tumors (NET), neuroendocrine carcinoma (NEC) and mixed neuroendocrine non-neuroendocrine neoplasm (MiNEN).[2] NET of the appendix is the most common neuroendocrine tumor that may be found by a pathologist.[3] NET is mainly caused by enterochromaffin cells (EC-Cells) found in the gastrointestinal tract and bronchopulmonary system.[1,4] NET of the appendix is a rare tumor of the appendix, mainly reported at a young age with a good prognosis.[4] NETs of the appendix are largely curable by appendectomy alone, while NEC and MiNEN are aggressive neoplasms that require extensive surgery if possible.[3]

Most of the NETs in the appendix are detected incidentally. It is necessary to always perform a histopathological examination after appendicitis surgery. The attention of the surgeon is very important in this regard. If NEN has been diagnosed as a result of histopathological examination, it is necessary to determine whether additional treatment is required according to the histopathological features of the tumor, following current consensus-based guidelines.[1]

II. CASE DESCRIPTION

It has been reported that a 22-year-old woman came to a private hospital in Langkat with complaints of right lower abdominal pain. The patient underwent appendectomy. The resulting tissue was sent for histopathological examination.

On macroscopic examination, tissue derived from the mass in the appendix was found, the mass was brownish gray in color, irregular in shape. Tissue size is ± 4 x 2 x 1 cm with 0.5-2 cm. On cut section, a tumor mass appeared in the apical area of the appendix, 0.5 cm from the tip of the resection edge. Then a paraffin block was made with the code OP.21.10.941 (Figure 1).

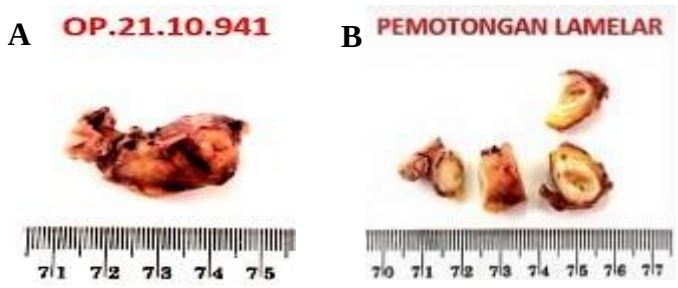

Figure 1. Appendix macroscopic. A. Tissue originating from the mass in the appendix. B. On cut section, a tumor mass appears in the apical area of the appendix, 0.5 cm from the edge of the resection.

On microscopic examination, tissue from the mass in appendix consist of mucosal layer to serosa layer. Mucosal layer with columnar epithelial lining partially atrophy, columnar epithelium with normal nuclear morphology. In the subepithelial, the proliferation of tumor cells appears to form nests, trabeculae, acini, and ribbon-like structures. Tumor cells are relatively uniform with round nuclei, salt & pepper chromatin, abundant and granular cytoplasm. Mitosis (<20 mitoses/10 HPF). We also found rosette like. The stroma consists of thick fibrotic connective tissue, infiltrated by tumor cells forming a single file appearance. On immunohistochemical examination in case showed synaptophysin (+), chromogranin A (+), ki67 proliferation index value is 3% and CK20 (-).

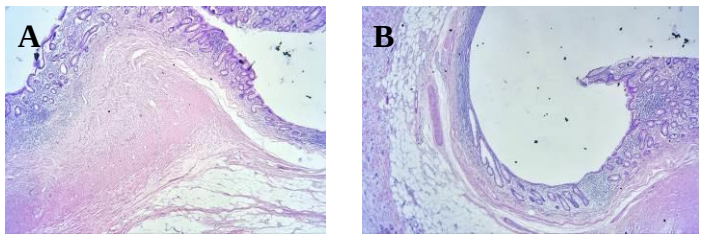

Figure 2. A. The tissue originating from the mass in the appendix ranged from a mucosal layer to a serosa layer (H&E, x40). B. Mucosal layer with partially atrophic columnar epithelial lining, columnar epithelium with core morphology within normal limits (H&E, x40).

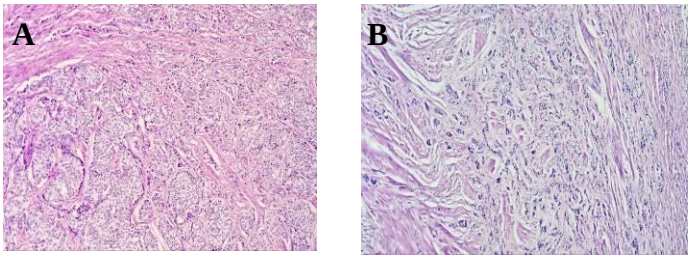

Figure 3. A.B. The subepithelial cells showed proliferation of tumor cells forming nests, trabeculae, acini, and ribbon-like structures (H&E, x100).

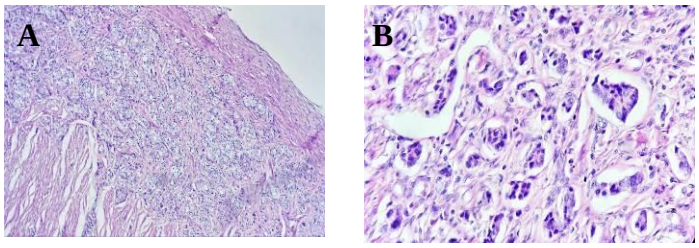

Figure 4. A. Tumor cells were relatively uniform (H&E, x100). B. Round nucleus, salt & pepper chromatin, abundant and granular cytoplasm. Mitosis was found (< 20 mitoses/10 LPB). (H&E, x400).

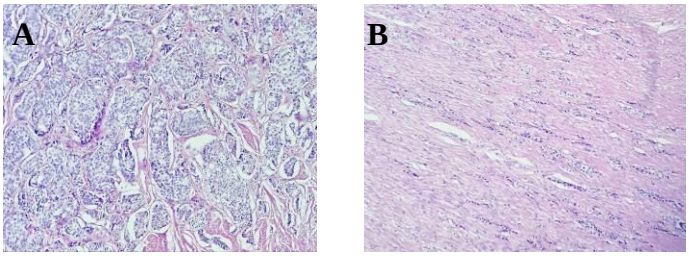

Figure 5. A. “rosette like” view (H&E, x100) and B. The stroma is composed of thick fibrotic connective tissue, infiltrated by tumor cells forming a “single file” image (H&E, x100).

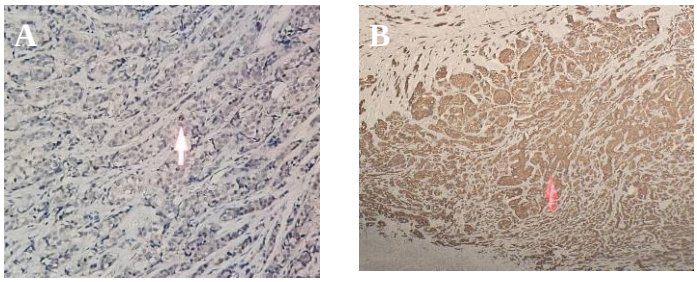

Figure 6. Immunohistochemical examination. A. Ki67 3%. B. Synaptophysin (+) (H&E, x40).

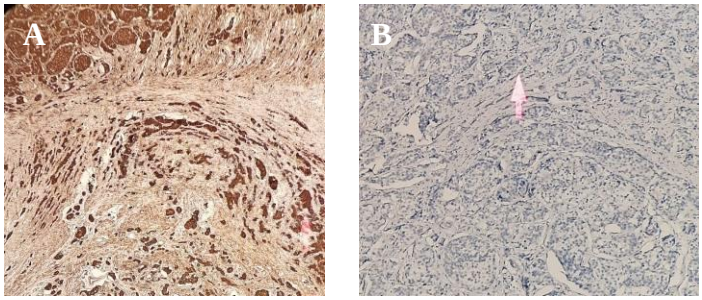

Figure 7. Immunohistochemical examination. A. Chromogranin

A (+). B. CK20 (-) (H&E, x40)

Based on histopathology and immunohistochemical results, this case was diagnosed as Appendiceal neuroendocrine tumours, NOS, intermediate-grade (G2), ICD-O 8249/3, topography morphology (C18.1).

III. DISCUSSION

Appendix NEN is an epithelial neoplasm of the appendix with neuroendocrine differentiation, including well differentiated NET and poorly differentiated NEC. MiNEN is an epithelial neoplasm, consisting of a mixture of neuroendocrine components with non-neuroendocrine components, which is morphologically and immunohistochemically recognizable and at least each component is found in 30% of neoplasms.[2]

The incidence of NET in the appendix is about 0.2–0.7% of all appendectomy cases performed.[4] Based on data analysis, it was reported that NET in the appendix was the fifth most common gastrointestinal NET, after the small intestine, rectum, pancreas, and stomach. The incidence of NET is about 0.15-0.6 cases per 100,000 persons in one year, with a slightly female predominance with the highest incidence at the age of 30 years to 40 years, which is much younger than the median age for primary malignant neoplasms of other appendixes. NET of the appendix is common in children, with a better prognosis. Preoperative diagnosis is usually very rare.[2,6,7]

NET in the appendix, especially in the area of the tip of the appendix, is about 67% of adult patients and 73% of pediatric patients.[2] NET of the appendix shows a non-specific clinical picture. Most are asymptomatic. Approximately 80% of cases are discovered incidentally after surgery for acute appendicitis. Association with carcinoid syndrome is very rare and is indicative of metastases. NEC often presents with advanced disease, similar to other carcinomas of the appendix.[2,8]

Most patients with appendicitis NET do not require further procedures or examinations after appendectomy. However, in patients with high grade NEN, additional screening is required, even if it is smaller than 1 cm, patients with tumors between 1 cm and 2 cm or larger than 2 cm, and patients with incomplete resection and metastatic disease. Plasma chromogranin A is the most accurate blood marker currently available, with levels elevated in 80%-100% of NET patients. Other tests including levels of 5-hydroxy indole acetic acid (5-HIAA), which is a serotonin metabolite, shown in 24-hour urine, computed tomography-scan (CT-scan), and octreotide scintigraphy may be performed to support the diagnosis in patients with suspected NET.[9,10]

Macroscopically, NET in the appendix after formalin fixation appears as a well-defined yellowish nodule. Many NETs are diagnosed incidentally and are not seen macroscopically, so cut section of the entire end of the appendix in two longitudinal sections is recommended. Most appendiceal tissue is < 2 cm in diameter (52-62% < 1 cm, 28-30% 1-2 cm, and 8-19% > 2 cm).[2]

Well differentiated NET is a well-differentiated epithelial neoplasm with morphological and immunohistochemical features representing neuroendocrine differentiation, most commonly exhibiting organoid architecture, uniform nuclei, and coarse and granular chromatin. NET can be low grade (G1), intermediate grade (G2), or high grade (G3). The well differentiated nature of NETs means that, neoplastic cells bear a strong resemblance to non-neoplastic neuroendocrine cells, typically including strong immunoexpression of common neuroendocrine markers such as chromogranin A and synaptophysin. NET generally displays architectural patterns in the form of nests, cords, and ribbons. The formation of glands by neoplastic cells is common, especially in the ileum and pancreas, as well as in the appendix and duodenum. Nucleus with coarse, clumped chromatin, with a classic salt and pepper appearance, but some NETs show more diffuse granular chromatin and others have prominent nucleoli. The cytoplasm may show intense granularity. Most of the NETs had a low proliferation rate, with a mitotic rate < 20 mitoses/2 mm2 and a Ki-67 proliferation index <20%.[5]

Follow-up for NET in the appendix is still a matter of debate for several reasons, mostly registry-based data, as well as limited long-term survival data. The majority of patients with appendiceal NET have an excellent outcome, most of them recover with appendectomy.[2] Postoperative follow-up, in appendiceal NET which is limited to the appendix with a size of about 2 cm, can only be done in the form of appendectomy, and follow-up is not possible. needed. For more extensive NET or tumors with lymph node metastases, treatment with a right hemicolectomy is recommended, with history, physical examination, chromogranin testing, and CT scan of the patient between 3 and 12 months after resection. One year after resection, history taking, physical examination, chromogranin test and CT scan are recommended every 6 to 12 months.[11]

IV. CONCLUSION

After conducted this case report, we conclude some points in the following:

1. Most of the NETs in the appendix are detected incidentally. It is necessary to always perform a histopathological examination after appendicitis surgery. The attention of the surgeon is very important in this regard.
2. We report a 22-year-old woman with right lower abdominal pain. The patient underwent appendectomy and the resulting tissue was sent for histopathological examination. Based on histopathological and immunohistochemical features, this case was diagnosed as Appendiceal neuroendocrine tumours, NOS, intermediate-grade (G2), ICD-O 8249/3, topographic morphology (C18.1).

VI. COMPETING INTERESTS

The author has no financial interests relevant to the product or company described in this article.

V. ACKNOWLEDGMENT

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VI. ETHICAL APPROVAL

Health Research Ethical Committee, Universitas Sumatera Utara, Medan, Indonesia approved this study.

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