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Case Report

Co-Occurrence of Submucosal Schwannoma and Low-Grade Mucinous Neoplasm in the Appendix, a Clinical Conundrum : A Case Report

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ABSTRACT

Two and more types of tumors rarely occur in the appendix, a constrained space of the human body. We experienced a rare co-occurrence of schwannoma and low-grade mucinous neoplasm (LAMN) in the appendix and obtained a lesson to scrutinize the radiological images in the follow-up period. A computer tomography (CT) performed for surveillance of bile duct stone of a 68-year-old man incidentally detected the appendiceal tumor, which characteristics were not clear at that time, 1-year before admission because of epigastric pain due to acute cholecystitis. CT showed enlargement of tumor in the appendix, and laparoscopic ileocecal resection and cholecystectomy were performed under the diagnosis of acute cholecystectomy and appendiceal tumor. Histopathological examination revealed two types of appendiceal tumors, schwannoma and low-grade appendiceal neoplasm. To the best of our knowledge, co-occurrence of schwannoma and LAMN has never been reported and this complicated our interpretation of clinical images during the course. We report a clinical lesson in handling this rare combination of tumors in the appendix with the relevant literature.

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Introduction

Appendiceal tumors including adenocarcinoma or low-grade appendiceal neoplasm (LAMN), which grow relatively fast, cause several symptoms such as appendicitis. This could be explained by the fact that the appendix has only a limited space. This feature allows us to pay attentions to the presence of tumors relatively early [1]. Slow-growing tumors in the appendix sometimes evade the early recognition even with the recent advanced modality of imaging. The discovery of these tumors in the appendix often incidentally happens during the surveillance for the other diseases.

In this communication, we report a rare case of ileocecal lesion, rare co-occurrence of schwannoma and low-grade mucinous neoplasm of the appendix, found incidentally and confirmed pathologically. A retrospective review of radiological images gave us a lesson to interpret this complicated situation. Schwannoma, especially full-blown one in the appendix, has rarely been reported probably because the limited

space of the appendix produces symptoms at an earlier stage. On the other hand, we performed a laparoscopic ileocecal resection of the appendiceal tumor that had grown during follow-up and found an appendiceal tumor composed of two different tissue types: schwannoma and LAMN. Appendiceal tumor with schwannoma and LAMN has never been reported in the literature, and there were many hurdles in determining the procedures and diagnosis in the clinical setting.

Case Presentation

A 68-year-old man was admitted to our hospital with epigastric pain. He had hypertension, hyperuricemia and nephrosclerosis. Computed tomography (CT) had shown common bile duct stones and appendiceal tumor of unknown characterization. He underwent Endoscopic Retrograde Cholangiopancreatography (ERCP) and conservative follow-up was opted for. Since the nature of the tumor was undetermined, the appendiceal tumor was followed up. At that time, the tumor on the image looked like one vague mass. Further examination

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must have been needed, but he chose only careful. One year later, he was admitted to our hospital with a chief complaint of epigastric pain again. Plain CT revealed acute cholecystitis and enlargement of the appendiceal mass. His body temperature was 37.3 °C. There was tenderness only in the upper abdomen. Laboratory analysis revealed the following: white blood cell count, 10300/mm³; C-reactive protein, 14.96 mg/dL; CEA, 1.2 ng/mL; CA, 19-9 2.8 U/mL. Abdominal ultrasonography showed gallbladder stones and inflammation around the gallbladder without significant thickening of its wall. The appendix was enlarged to a diameter of 22 mm, circumscribed by liquid or mucus density (Figure 1). Initial CT scan (1-year ago) showed wall thickening at the base of the appendix and liquid density in the periphery of the appendix, the minor axis of which was 20 mm. Preoperative CT (at the onset of acute cholecystitis) suggested findings of acute cholecystitis and appendiceal mass, the minor axis of which was 26 mm (Figure 2). Based on the above findings, we reached the diagnosis of acute cholecystitis and the suspected diagnosis of appendiceal mucinous tumor or mucinous cancer.



Figure 1: Ultrasonography. The appendix was swollen and had fluid within it. A rich blood flow was detected in the solid part and an appendiceal cancer was suspected.

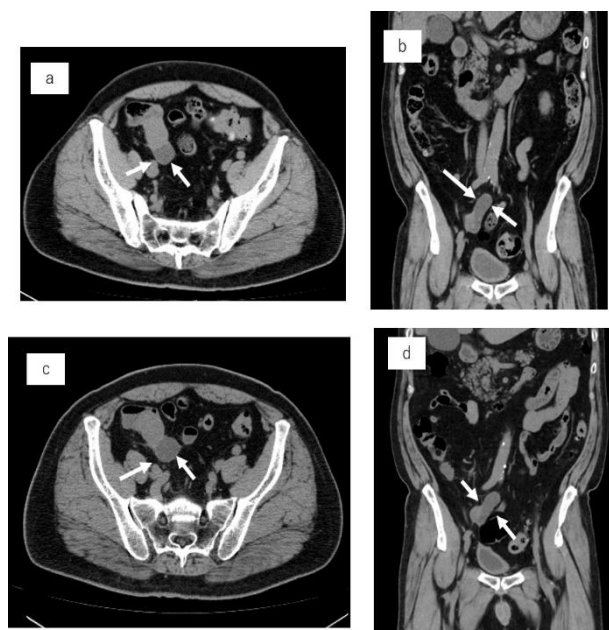


Figure 2: CT. **a), b)** At the first visit. The appendiceal wall was thickened and enlarged. A fluid was detected inside the appendix, and its minor axis was 20 mm (arrow). **c), d)** At the operation. The appendix was being enlarged and its minor axis was 26mm. No apparent lymph node swelling was noted.

The laparoscopic cholecystectomy and ileocecal resection were performed simultaneously. In the operation, the appendix and a part of the cecum were swollen and adhered firmly to the abdominal wall. Intraoperative macroscopic diagnosis was infiltration of appendiceal tumor into the abdominal wall. Intraoperative pathological diagnosis was not requested. Ileocecal resection with combined resection of the abdominal wall and dissection of the D2 lymph nodes was performed (Figure 3).

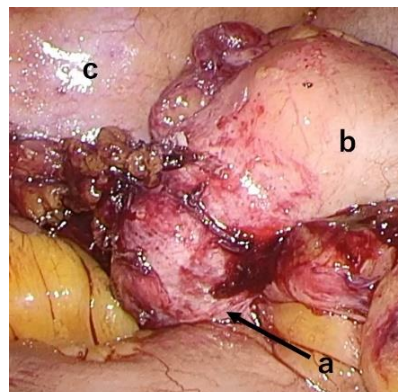


Figure 3: Operative findings. **a)** The appendix was swollen and firmly adhered to surrounding tissues. We suspected a malignant disease and performed ileocecal resection with lymph node dissection. **b)** Ileocecum. **c)** Abdominal wall.

The resected specimens showed that the tumor was an appendiceal tumor that had spread to the cecum and had a white color, the size of which was 6.0×4.0×3.0 mm. It was a solid mass with clear borders. Macroscopically, the tumor seemed to be one enlarged mass (Figure 4).



Figure 4: Gross pathological findings. A well-defined solid tumor was found in the appendix (arrowhead).

Histopathological examinations revealed two components growing independently in the appendix. One was a spindle cell tumor with lymphoid cuffing-like lymphocytes in the submucosa of appendix in whole circumference. Immunostaining revealed S-100 (++) , CD34 (-), SMA (-), CD31 (-), CD117 (-), and DOG1 (-), verified the diagnosis of schwannoma. There was another proliferative component containing papillary growth of high columnar epithelium. This lesion was connected to the normal columnar epithelium of the appendix. Though some of these columnar cell epithelia got stratified and protruded into cystic space, the basement membrane was intact. Multiple sections were searched for, but there was no clear invasion, indicating the diagnosis of LAMN was best (Figure 5). He had an uneventful postoperative course during his hospital stay and had no recurrence after the operation.

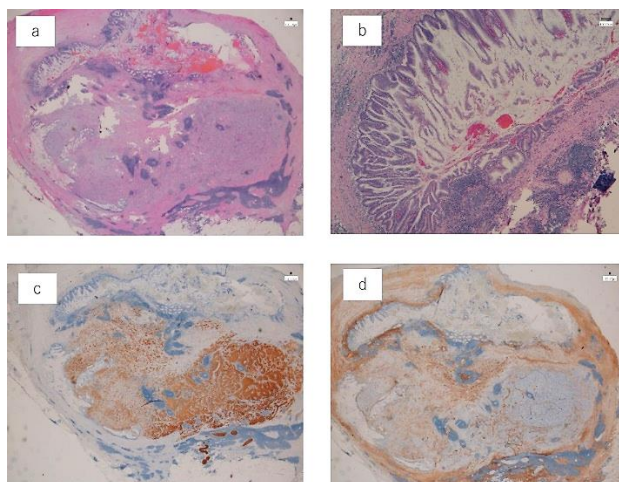


Figure 5: Pathological findings. **a)** HE: The tumor main body was a spindle cell tumor with lymphoid cuffing-like lymphocyte aggregates under the appendix mucosa. **b)** HE: A tumor including papillary enlargement of columnar epithelium was found in the main appendiceal tumor. There was no clear infiltration and it was considered LAMN. **c)** S-100 strongly positive. **d)** SMA negative.

Discussion

Schwannoma is a benign tumor originated from Schwann cells and can arise at any neural tissue. As for the gastrointestinal tract, schwannoma originates from the Auerbach plexus and is most likely to arise at the stomach. Those that develop in the colon are rare and those of appendix appear to be fairly rare [1, 2, 3]. According to Ozawa *et al.*, of 59 schwannoma cases arising at the large intestine, the most common site was rectum (28 cases, 48%), only 7 cases (12%) were appendices and cecum [4]. Schwannoma is a benign disease that grows very slowly. It causes nonspecific symptoms such as abdominal pain, abdominal mass, and gastrointestinal bleeding when it arises at the gastrointestinal tract [5]. Immunostaining is useful for differential diagnosis. Schwannoma is characterized by positive staining with S-100 protein and NSE, which are nervous system markers, and not with desmin, α -SMA, c-kit, and CD34, which are myogenic markers [6, 7].

LAMN was first reported in 1866 by Rokitsky [8]. Like many tumors composing columnar and mucinous neoplasms in other organs such as pancreas and ovary, the biological behavior of these type are sometimes unpredictable, thus though general histological and morphological characteristics lack overt evidence of malignant nature such as invasiveness and vessel involvement, these tumors should be handled with care and classified as a potentially malignant tumor in 2019 according to the WHO classification [9]. In the latest Japanese classification system and guidelines, they put LAMN as a new category (in the 8th edition of the Colorectal Cancer Agreement) [10]. LAMN is a tumor characterized by abundant extracellular mucus, developing frequently in middle-aged and elderly people. Histopathologically, it is a well-differentiated mucinous cancer with poor cellular components accompanied by abundant mucus. Preoperative diagnosis of LAMN is not easy, but CT, MRI, and abdominal ultrasonography are sometimes helpful for diagnosis. Papillary protuberances or localized nodules inside the cyst prefer malignant counterpart, cystadenocarcinoma, but there are

many cases in which preoperative definitive diagnosis was difficult especially in clinical settings with limited resources [11].

Surgical resection is the principle for both schwannoma and LAMN, but no clear criteria have been established for the procedure. With regard to appendiceal schwannoma, which is a benign and mesenchymal tumor, local resection without lymph node dissection is sufficient. The long-term prognosis actually remains unknown because of few cases reports [12]. Although mucinous cystadenoma was previously considered to be sufficient for appendectomy or partial cecal resection, recent reports, indicating that difficulties of predicting the recurrence of these potentially malignant cases, have prompted surgeons more careful procedures for the recurrence. Actually, the number of reports of LAMN in which ileocecal resection with lymph node dissections was done has been increasing in recent years [13-15]. In this case, we think the ileocecal resection with lymph node dissection was retrospectively appropriate. Intraoperative assumption of malignancy invading to adjacent tissue urged the attending surgeons to decide D2 dissection.

There are few reports of appendiceal tumors composed of different tissue types. With the keywords “appendiceal schwannoma”, “low-profile appendix mucinous tumor”, “appendiceal schwannoma”, and “low-grade appendiceal mucinous neoplasm (LAMN)”, searching by PubMed (1950-2018), only one case similar to this case was found in an English paper [16]. In that report, ileocecal resection was performed for cecal cancer. The appendix of the resected specimen was associated with neurohamartoma and neuroendocrine tumor. The report of an appendiceal schwannoma and an appendiceal tumor with LAMN was not limited to our search, including English papers, and this case was considered to be the first case.

In general, external factors that cause a common carcinogenic mechanism, genetic predisposition of individuals, can explain why tumors of different tissue types coexist. However, the mechanism of development common to both schwannoma and LAMN remains unknown. In this case, schwannoma occupied the majority of the tumor, indicating that LAMN may have occurred for some reason while the schwannoma was slowly growing. Two types of tumors are rarely observed in the appendix because the appendix has only a limited space. A fast-growing tumor arising at the appendix may lead to symptoms such as occlusion early. In this case, a benign schwannoma that progressed slowly appeared at first, and LAMN, which had an increasing tendency, developed later. This allowed two types of tumors to develop independently. Considering the fact that an appendiceal tumor was discovered accidentally because of another disease, this case was a rare situation, leading us to find an appendiceal tumor composed of two types of tumors.

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