

Adenomyoma of the small intestine

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Abstract

Adenomyoma of the gastrointestinal tract is a rare benign tumor-like lesion. The small intestine is the second most frequent location, usually in the periampullary area, but the lesion also occurs in the jejunum and ileum. While adenomyoma of the Vaterian system is primarily diagnosed in adults, more than half of reported cases of jejunal and ileal adenomyoma have been diagnosed in pediatric patients. Adenomyoma of the periampullary area usually presents with biliary obstruction or abdominal pain, whereas jejunal and ileal adenomyoma usually presents with intussusception or is incidentally discovered during surgery or autopsy. Since endoscopic and radiological examination yields uncharacteristic findings, histopathological evaluation is important in adenomyoma diagnosis. Pathologically, adenomyoma consists of glandular structures of various sizes and interlacing smooth muscle bundles that surround the glandular elements. The pathogenesis of adenomyoma is generally considered to be either a form of hamartoma or a pancreatic heterotopia. Although limited resection is considered the most effective treatment, pancreaticoduodenectomy is often performed when the lesion occurs in the periampullary area due to preoperative misdiagnosis as a carcinoma. It is, therefore, important that clinicians and pathologists maintain current knowledge of the disease to avoid inaccurate diagnosis, which could lead to unnecessary surgery.

INTRODUCTION

Adenomyoma of the gastrointestinal (GI) tract, also referred to as a myoepithelial hamartoma, adenomyomatous hamartoma or foregut choristoma, is a benign tumor-like lesion histologically characterized by glandular structures lined by cuboidal to tall columnar epithelium and surrounded by bundles of smooth muscle. It occurs mainly in the pyloric region of the stomach^[1]. The small intestine is the second most frequent location, usually in the periampullary area, but it also occurs in the jejunum and ileum. The lesion is very rare and there have been only a few reports of case series of periampullary adenomyoma^[2,3]. Most cases of jejunal and ileal adenomyoma have been reported as single case reports and, to the best of our knowledge, there have been only 26 reported cases^[4-26].

Although the pathogenesis of adenomyoma remains unclear, it is hypothesized to be either a form of hamartoma or an incomplete heterotopic pancreas. As endoscopic and radiological examination yields uncharacteristic findings, histopathological evaluation is important in adenomyoma diagnosis. It is important that clinicians and pathologists maintain current knowledge of the disease

to avoid making inaccurate diagnoses that may lead to unnecessary surgery. To aid in the acquisition of this important knowledge, we review the clinical and pathological features of adenomyoma of the small intestine and discuss its pathogenesis.

CLINICAL FEATURES

Epidemiology

As mentioned above, adenomyoma of the small intestine is rare, especially that occurring in the small intestine distal to the duodenum. The actual incidence is unclear because very few cases have been reported. A further complicating factor in determining its true incidence is that its reportedly low incidence may be partly attributed to underreporting or nonrecognition of the condition by both surgeons and pathologists^[17]. We have diagnosed 3 cases of asymptomatic adenomyoma of the jejunum or ileum at autopsy in our institution within the past 8 years; this fact suggests that its incidence is higher than suspected.

In the investigation of 13 cases of adenomyoma of the Venterian system treated by extensive surgery, the patient age ranged from 38 to 78 years (mean 63 years) and the male-to-female ratio was 6:7^[2]. On the other hand, there have been only 26 reported cases of jejunal and ileal adenomyoma^[4-26] and the patient age ranges from 2 d to 82 years (mean 25 years), including 15 pediatric patients and 11 adult patients. The male-to-female ratio is approximately 2:1. The lesion occurs 2 to 3 times more frequently in the ileum than in the jejunum. One lesion was found in a Meckel diverticulum^[17].

Symptoms and signs

Symptoms of adenomyoma of the GI tract depend on the location of the lesion and patient age. Adenomyoma of the perampullary area usually presents with biliary obstruction (obstructive jaundice) or abdominal pain, symptoms that recur after sphincterotomy^[2]. Several cases have been incidentally detected during systemic examination for other diseases. One reported case presented with acute recurrent pancreatitis^[27].

Jejunal and ileal adenomyoma of pediatric patients usually presents with intussusception, but 1 reported case presented with intestinal obstruction^[6]. In adult patients, intussusception is an infrequent complication, with many reported cases having been incidentally detected during surgery for other diseases or during autopsy. Several cases have presented with GI bleeding (melena)^[15,25].

Endoscopy

On endoscopic examination, adenomyoma of the duodenum is detected as a submucosal tumor-like nodule covered by normal mucosa. Although it is generally difficult to detect jejunal or ileal lesion by endoscopy, 1 reported case of adenomyoma of the proximal jejunum was identified by push enteroscopy^[25].

Radiographic findings

Adenomyoma of the GI tract may be detected as an enhancing polypoid lesion by abdominal computed tomography (CT)^[21]. Perampullary adenomyoma may be detected as an abnormal shadow on endoscopic retrograde cholangiopancreatography (ERCP)^[28]. When ampullary adenomyoma causes stenosis or obstruction of the biliary tract, bile duct dilatation can be detected by abdominal ultrasonography, abdominal CT, ERCP and magnetic resonance cholangiopancreatography; bile duct obstruction can be confirmed by percutaneous transhepatic cholangiography.

PATHOLOGICAL FEATURES

Gross appearance

Grossly, adenomyoma of the GI tract is an intramural nodule covered by mucosa and it protrudes into the lumen (Figure 1A and B). The diameter of adenomyoma in reported cases ranges from 0.6 cm to 4.5 cm.

Microscopic findings

Histologically, adenomyoma of the small intestine mainly occupies the submucosa (Figure 2) and often extends into the muscularis propria. The lesion consists of glandular structures of various sizes and interlacing smooth muscle bundles surrounding the glandular elements (Figure 3). Cystically dilated glands are usually observed. The glandular structures are lined by cuboidal to tall columnar epithelium with basally oriented nuclei. Goblet cells are occasionally interspersed (Figure 4A) and we previously reported a case in which Paneth cells were also observed (Figure 4B)^[23]. Those glands are surrounded by interlacing smooth muscle bundles. Myofibroblasts and fibroblasts may also proliferate^[2,3]. Both the epithelial and smooth muscle cells lack nuclear atypia. Pancreatic acini and islet tissue are not present. Pathological diagnosis by biopsy specimen is usually difficult, partly because the lesion mainly occupies the submucosa.

Immunohistochemical staining

Immunohistochemically, the glandular element of adenomyoma of the small intestine is positive for cytokeratin (CK) 7 (Figure 5A) and negative for CK 20 (Figure 5B)^[23,26], while normal intestinal epithelial cells around the lesion are negative for CK 7 and positive for CK 20. The glandular epithelial cells of the lesion do not express CDX-2, a marker of intestinal mucosal epithelium^[26]. The smooth muscle cells surrounding the glandular elements are positive for α -smooth muscle actin and desmin (Figure 6)^[20,23].

Differential diagnosis

Differential diagnoses of adenomyoma of the small intestine include enteritis cystica profunda, pneumatosis cystoides intestinalis, adenocarcinoma and hamartomatous polyp in Peutz-Jeghers syndrome. Cysts of enteritis

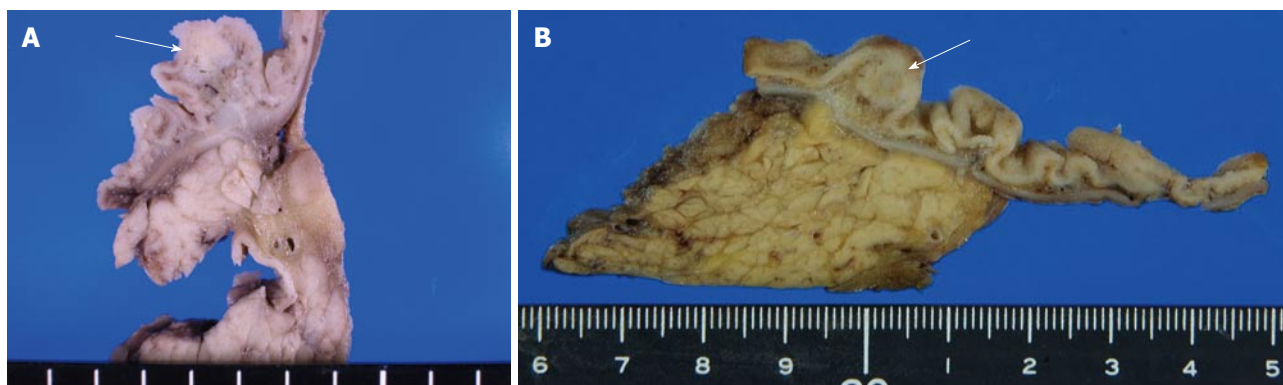


Figure 1 Gross appearance of adenomyoma of the periampullary region. The lesions are observed as intramural nodules covered by mucosa and they protrude into the lumen (A, B, arrows).

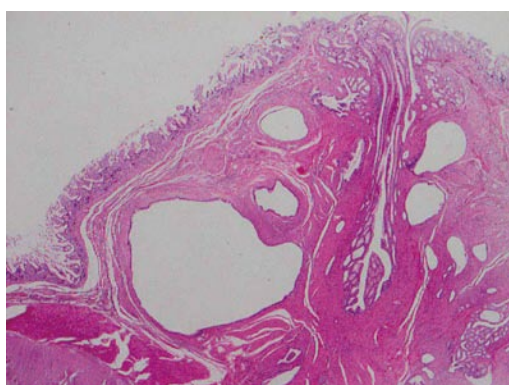


Figure 2 Low-power view of adenomyoma of the small intestine. A nodular lesion mainly occupies the submucosa (hematoxylin and eosin stain, $\times 10$).

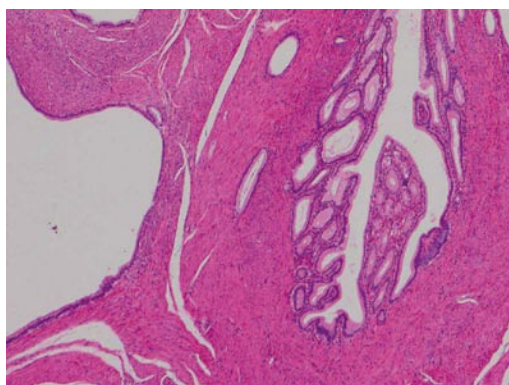


Figure 3 High-power view of adenomyoma of the small intestine. The lesion consists of glandular structures of various sizes and interlacing smooth muscle bundles (hematoxylin and eosin stain, $\times 40$).

cystica profunda are not surrounded by smooth muscle bundles. In pneumatosis cystoides intestinalis, the cysts contain gas and are lined by multinucleated giant cells, while the glands and cysts of the adenomyoma are lined by epithelial cells. The characteristics of adenomyoma that differentiate it from adenocarcinoma include the absence of cellular atypia and desmoplastic stroma and the presence of smooth muscle bundles surrounding the glands and cysts. In Peutz-Jeghers syndrome, the essen-

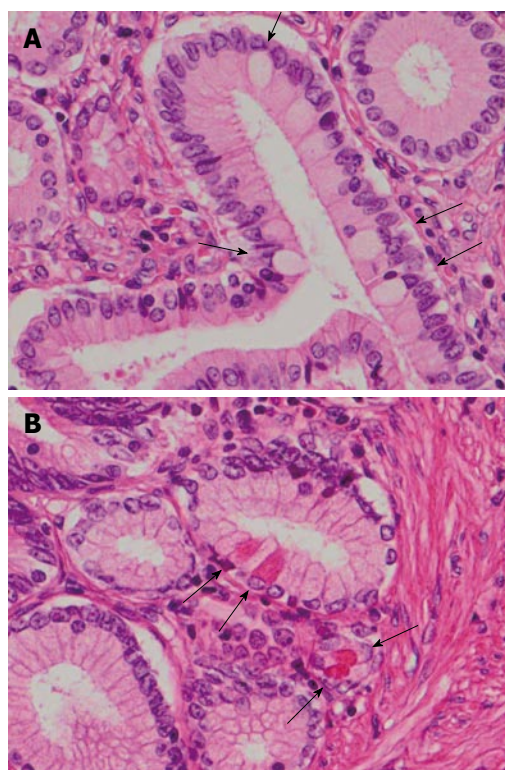


Figure 4 Appearance of goblet cells (A, arrows) and Paneth cells (B, arrows) in the intestinal adenomyoma (hematoxylin and eosin stain, $\times 400$).

tial feature is branching cores of muscular fibers derived from the muscularis mucosae and covered by normal mucosa, while adenomyoma is located in submucosa and/or muscularis propria.

TREATMENT AND PROGNOSIS

Endoscopic or surgical limited resection of the lesion is considered the most effective treatment for adenomyoma of the periampullary region. However, pancreaticoduodenectomy is often performed because the lesion is frequently preoperatively misdiagnosed as a carcinoma. Intraoperative frozen section diagnosis is useful to avoid excessive surgery.



Figure 5 Results of immunohistochemical staining for cytokeratin 7 and cytokeratin 20. The glandular element of the lesion is positive for cytokeratin 7 (A) and negative for cytokeratin 20 (B) ($\times 200$).

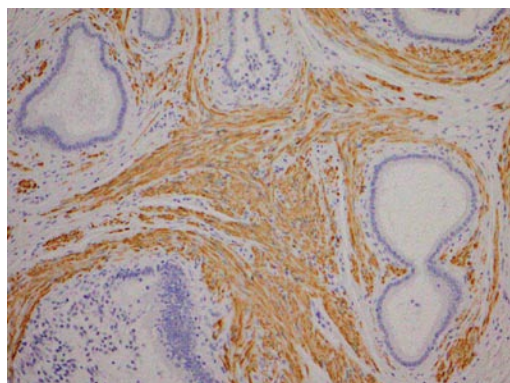


Figure 6 Results of immunohistochemical staining for desmin. Smooth muscle cells surrounding the glandular elements are positive for desmin ($\times 100$).

A partial enterectomy or simple resection of the lesion is performed for a jejunal or ileal adenomyoma complicated by intussusception. When it is not complicated by intussusception, simple resection of the lesion is sufficient treatment. Intraoperative frozen section diagnosis is also useful when the lesion exists in this location. As adenomyoma of the GI tract is a benign lesion, the prognosis for its treatment is very good.

Follow-up is considered to be a potential option for avoiding unnecessary surgery for benign adenomyoma, particularly in the jejunum and ileum, if the size of the lesion is small. Follow-up study may elucidate the natural course of the lesion.

PATHOGENESIS

As mentioned above, the pathogenesis of adenomyoma of the GI tract is generally considered either a form of a hamartoma or a pancreatic heterotopia, although this is not fully understood. The term “hamartoma” refers to an excessive but focal overgrowth of cells or tissues native to the organ in which it occurs, while the term “heterotopia” refers to a growth of microscopically normal cells or tissues in an abnormal location.

Gal *et al.*^[9] reported 3 cases of adenomyoma of the small intestine and suggested that “adenomyomas should be regarded as hamartomas of the GI tract” based on the fact that those cases contained goblet cells, argentaffin cells and smooth muscle stroma. Several authors reported cases with the transitional area between the epithelial component of the adenomyoma and epithelium of the overlying mucosa and considered it to be evidence that the epithelial component of the lesion originated from the epithelium of the small intestine^[21,26].

In general, CK 7 is distributed in the pancreatic duct epithelium but is essentially absent in GI epithelium. On the other hand, CK 20 is distributed in the GI epithelium but is absent in pancreatic duct epithelium^[29]. Accordingly, the pattern of cytokeratin expression [CK 7 (+), CK 20 (-)] of the glandular element of adenomyoma coincides with that of the pancreatic duct epithelium but not with that of the intestinal epithelium, thus supporting the heterotopic pancreas theory. This theory was further supported by Babál *et al.*^[30]'s detection of histochemical reactivities of the duodenal adenomyoma similar to the reactivities of duct epithelium in the neighboring pancreas, as well as Yao *et al.*^[17]'s reporting of a case of adenomyoma occurring in a Meckel diverticulum. In their examination of a case series of adenomyoma of the Vaterian system, Handra-Luca *et al.*^[2] identified that 3 of 13 cases were characterized by pancreatic heterotopias with both exocrine and endocrine pancreatic tissue being present in continuity with the adenomyoma.

In our opinion, the heterotopic pancreas theory regarding the lesion's pathogenesis might be more convincing than the hamartoma theory. The appearance of goblet cells and argentaffin cells might be explained by a metaplastic mechanism, while the presence of hyperplastic smooth muscle tissue might be explained by secondary muscle proliferation caused by a stimulus emanating from misplaced epithelium. We acknowledge that whether transition between the epithelial component of the lesion and the epithelium of the overlying mucosa is truly evidence of hamartomatous pathogenesis remains open to question. However, of course, further examinations are necessary to determine the pathogenesis of the lesion.

CONCLUSION

Adenomyoma of the GI tract is a rare benign tumor-like lesion whose pathogenesis remains not fully understood. When adenomyoma occurs in the Vaterian system, its

clinical differentiation from a carcinoma is difficult, often leading to a needless pancreaticoduodenectomy. To avoid unnecessary radical surgery, clinicians and pathologists should maintain current knowledge of the lesion and the most effective means of treatment.

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