Tailgut Cysts with Malignant Transformation: Features, Diagnosis, and Treatment

EF 1 Feng Liang
E 2 Jian Li
E 3 Ke Yu
E 1 Kai Zhang
AEF 1 Tongjun Liu
AEF 1 Jiannan Li

Corresponding Authors: Tongjun Liu, e-mail: tongjunliu@163.com, Jiannan Li, e-mail: jnli@ciac.ac.cn

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A tailgut cyst is a type of benign congenital disease that mainly develops in the retro-rectal space. However, malignant transition can occur in some cases of tailgut cysts. Early and precise diagnosis, and proper treatment, are vital for patients with tailgut cysts with malignant transformation. In this review, we aim to summarize the similarities and differences in the diagnosis and treatment methods among the 3 most frequently reported types of tailgut cysts with malignant transformation. In our study, PubMed and Web of Science databases were used to search for the studies and the key words were “tailgut cysts” and “malignancy”. We found 176 articles and selected 75 articles in our survey, with 9 reviews, 35 case reports, and 31 case reports and reviews.

MeSH Keywords: Adenocarcinoma • Carcinoma, Squamous Cell • Cysts • Neuroendocrine Tumors

Abbreviations: NET – neuroendocrine tumor; CT – computed tomography; MRI – magnetic resonance imaging; GISTs – gastrointestinal stromal tumors; CK – cytokeratin; SSTR2 – somatostatin receptor subtype 2; CDX2 – caudal type homeobox 2; VMAT1 – vesicular monoamine transporter 1; TTF1 – thyroid transcription factor 1; PAP – prostate acid phosphatase; TAMIS – trans-anal minimally invasive surgery; TEM – trans-anal endoscopic micro surgery; CEA – carcinoembryonic antigen; CA19-9 – cancer antigen 19-9

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Background

Tailgut cysts are uncommon congenital lesions, most of which develop in the retro-rectal space, such as anterior to the rectum or perianal region. The posterior, anterior, superior, and inferior borders of tailgut cysts are mainly the sacrum, rectum, peritoneal reflection, and anal and coccygeus muscles, respectively [1,2]. Tailgut cysts are believed to arise from embryonic hindgut remnants. In the embryonic period, the embryo develops an appendage that is an extension of the embryonic hindgut. This caudal extension is termed the tailgut. Failure of regression of the embryonic hindgut results in the development of a tailgut cyst [3,4]. However, occasionally, tailgut cysts are related to meningotheelial multiplication and benign thyroid tissue with oncocyctic transition. Thus, there is disagreement concerning the etiology of tailgut cysts [5].

Tailgut cysts usually present with ill-defined symptoms and can occur in all age groups. However, they mainly occur in middle-aged women, and the proportion of female to male patients is 3: 1 [3,6,7]. Because of the atypical clinical symptoms and the lack of experience, tailgut cysts are easily misdiagnosed as duplication cysts and endometriotic cysts [6,7]. Patients with tailgut cysts can present with symptoms, including constipation, infertility, rectal filling, dyschezia, dysuria, lower abdominal pain, abscess, high fever, frequent micturition, and repeated urinary tract infection [8–14]. Some asymptomatic cases were identified incidentally and others were detected during physical examinations of, for example, perianal abscesses and vaginal obstructions [15]. Although the majority of tailgut cysts are benign, 30% of the reported cases in the literature were malignant [16]. When symptomatic, these lesions tend to be associated with malignant transformation [17].

Tailgut cysts can contain a variety of epithelia between cysts or in the same cyst, such as stratified squamous epithelium, and transitive, mucinous, ciliated columnar, and cubucous epithelium [18–20]. Although these cysts are usually benign, infections and fistulas may be the consequence of malignancy and not the cause [20]. Malignant transformation of tailgut cysts includes, for example, adenocarcinoma, neuroendocrine carcinoma, endometrioid carcinoma, squamous carcinoma, and sarcoma [21,22]. Hormones might also be responsible for the malignant transformation. It has been proved that ghrelin and estrogen are important in the origin and development of the malignant transition of tailgut cysts [23]. However, the clear pathogenesis of the malignant transformation of tailgut cysts remains unknown. In this review, we introduce the 3 most common types of malignant transformations in tailgut cysts (neuroendocrine tumor (NET), adenocarcinoma, and squamous carcinoma) and analyze their different diagnoses and treatments.

Imaging Examination in the Diagnosis of Tailgut Cysts with Malignant Transformation

It is difficult to accurately diagnose tailgut cysts with malignant transition based on biopsy alone, because specimens obtained from biopsy often contain fibrous tissues only, without epithelial tissues or malignant foci. In addition, malignant tumor cells might leak into the peritoneal cavity during the process of biopsy. As a result, computed tomography (CT) and magnetic resonance imaging (MRI) are vital for the diagnosis of tailgut cysts [24,25]. Malignant and benign lesions show different characteristics on MRI examination, especially on T2-weighted images [26]. Sarkar et al. believed that radiological examination could contribute to the diagnosis of cystic lesions in the presacral space; however, a definite diagnosis can only be achieved by surgical exploration and histological examination [27].

Similarities and differences in CT and MRI diagnoses

Homogeneous retro-rectal masses range from water to soft-tissue densities in CT. Keratin fragments or inflammatory cysts might increase the density of the mass [28]. Thick walls with surrounding inflammatory changes and loss of discrete margins or continuous structures suggest that the cyst is associated with infection or malignant transformation [8,29]. The presence of calcium can benefit diagnosis of malignant transition or teratoma of tailgut cyst, because calcium is not common in cysts [30–32].

Tailgut cysts always present with hypo-intense and homogenous hyper-intense lesions on T1-weighted images and T2-weighted images, respectively. Based on previous studies, MRI may not be the best imaging method to completely distinguish malignant lesions from benign lesions [30,33–37]. This is because a high content of protein, mucinous tissues, or internal hemorrhage might lead to a high T1 signal intensity, which has been reported in cases of tailgut cyst with malignant transformation [29,38]. In addition, calcification cannot be easily detected using MRI. Fat suppression techniques are helpful for the diagnosis of lipoma and can exclude solid portions [39]. Furthermore, MRI is subtler than CT for the differential diagnosis of single and multilocular masses [35].

On MRI, NETs may be related to some cystic areas extending to the posterior margin of the rectum. The lesion appears to have a similar intensity to muscles on T1 images and a medium signal on T2 images. However, some primary NETs produce high signals on T2 images [23,33]. Mitsuyama et al. reported that a NET that extended into the retro-rectal space with some cystic components. The tumor was connected to a thickened fat terminal, which was attached to the spinal cord. The NET produced moderately high signals on T1- and T2-weighted images.
Mathew reported a middle-aged man who experienced defecation alone. Therefore, tailgut cysts can easily be misdiagnosed as cystic lesions, internal echoes can occur, making it difficult to obtain an accurate diagnosis. Although pelvic ultrasound might disclose multilocular cystic lesions, peripheral calcification and enhancement of internal components might also occur after intravenous injection of contrast media. However, the characteristics of adenocarcinoma on MRI require further research.

There are relatively few reports on tailgut cysts associated with squamous carcinoma. Moreover, there are few detailed imaging data on tailgut cysts with squamous carcinoma transformation. In one case, a subcutaneous mass with squamous carcinoma was found in the sacrum and coccyx, which was connected with the posterior rectal space. This is the reason why deep venous thrombosis in both lower extremities were found in that case. The characteristics of CT and MRI in tailgut cysts with squamous carcinoma transition require further study.

**Misdiagnosis**

Although imaging examination plays a valuable role in the diagnosis of tailgut cysts, CT or MRI alone might lead to misdiagnosis of tailgut cysts with malignant transformation.

Johnson et al. reported a case of a 16-year-old female patient who suffered from pelvic pain. There was no significant past medical history apart from constipation. During surgery, doctors found a presacral cystic mass with a well-developed bundle in the posterior midline of the anorectal ring. The probable reasons for the misdiagnosis were: CT and MRI examinations were not conducted in time or the surgeons were inexperienced with tailgut cysts.

Menassa-Moussa et al. reported a 10 cm hypo-echoic left pelvic mass detected using ultrasound in a 28-year-old woman. The radiologist decided that the mass was an endometrioma. CT indicated a retro-rectal cystic mass with a calcium wall and internal septum. MRI confirmed that the tumors were located outside the ovary. T2-weighted imaging showed a high signal intensity and T1-weighted imaging showed medium signal intensity. A diagnosis of endometrioma was suggested; however, subsequent surgery revealed a retro-rectal cystic hamartoma. Although pelvic ultrasound might disclose multilocular cystic lesions, internal echoes can occur, making it difficult to determine the retro-rectal position of the mass by ultrasound alone. Therefore, tailgut cysts can easily be misdiagnosed as ovarian diseases, particularly when the ovary is invisible.

Mathew reported a middle-aged man who experienced defecation pain and rectal bleeding. Colonoscopy found a submucosal neoplasm extending from the lower rectum to the upper edge of the anal tube, squeezing the rectal wall inward. MRI showed a 7×8 cm monolocular cystic mass, the essence of which was located around the posterior rectal space and dislocated into the anterolateral rectum. On T2-weighted imaging, the peripheral solid part showed a low signal; however, there was no high signal on diffusion-weighted imaging, suggesting that the cell density of the lesion was low. Cytological examination showed normal columnar and squamous epithelial cells but no malignant cells. Thus, this posterior rectal cystic mass was considered to be a tailgut cyst. However, based on the pathological examination, spindle tumor cells had multiplied in the nuclear palisade, and c-kit was positive. The ultimate diagnosis was rectal gastrointestinal stromal tumors (GISTs).

In addition to the rare occurrence of retro-rectal cysts, the most probable reason for misdiagnosis is the insufficient experience of the physicians. An accurate diagnosis of tailgut cysts with malignant transition might be achieved by a physical examination combined with CT and MRI examinations before a definitive surgical procedure. On CT, tailgut cysts usually present as thin walled, uni- or multilocular, low density, non-enhancing lesions in the retro-rectal space. Calcification in tailgut cysts might indicate malignant transition. Blurred boundaries and encroachment on adjacent structures are also the signs of malignant transition. On MRI, tailgut cysts have low intensity on T1 images and high intensity on T2 images. Malignant changes should be considered when the cysts contain more bleeding or necrotizing, and mucous protein components.

**Histological Characteristics**

In the macroscopic view, posterior rectal cyst specimens have mucosal characteristics such as a white or pink color, smooth in appearance on one side, and irregular appearance on the other side. Microscopically, the whole intestinal wall is connected with loose fibrous tissue on one side and the cystic mass closes to the intestinal wall. In most cases, simple tailgut cysts are not evaluated using immunohistochemistry, possibly because the components of cysts are relatively simple and the clinical significance of immunohistochemistry is not obvious.

**Tailgut cysts with NETs**

NETs have been reported in the muscularis layer of cysts. The mass is soft, gray-white, solid, and cystic. Macroscopically, the boundaries of the tumors are clear. Sections appear gray-white solid with small cystic spaces around them. Histologically, cysts consist of columnar epithelial cells, some of which have clear cytoplasm or comprise keratinized squamous epithelial cells.
There is no obvious neuroendocrine cell source in the presacral space; however, many tumors may come from the glandular epithelium of tailgut cysts [49]. Microscopically, the cystic space contains mucinous material and no contiguous osseous tissue, hair, or other structures. In addition, a tumor composed of multiple epithelial cells distributed in a fibro-vascular network without necrosis has been encountered in cysts. The cells have rounded nuclei with speckled chromatin and inconspicuous nucleoli [33,49]. Occasionally, carcinoid tumors expressing immunohistochemical neuroendocrine markers can be identified in the cystic wall [50,51].

NETs can be positively stained for p53, p21, chromogranin, synaptophysin, keratin AE1-AE3, CD56, cytokeratin (CK) 7 and 19, and somatostatin receptor subtype 2 (SSTR2) [52]; however, they are negative for CK 20, caudal type homeobox 2 (CDX2), vesicular monoamine transporter 1 (VMAT1), pancreatic polypeptide, peptide YY, gastrin-releasing peptide, gastrin, glicentin, enkephalin, and glial fibrillary acidic protein [1,47,53–55].

La Rosa et al. found that the ghrelin expression detected in tailgut cyst with NETs transition could be explained by the activation of the ghrelin gene during the process of transformation. As a result, it is possible that the normal endocrine cells in the tailgut cyst are originated from ghrelin rather than expressing ghrelin. The fact that ghrelin-immunoreactive cells are not found in the tailgut cyst epithelium appears to support this assumption. However, ghrelin expression might indicate a gastric, or at least anterior intestine, phenotype of the tumors [23]. The tumor did not express other foregut markers; however, it expressed certain intestinal or more specific markers of tailgut carcinoids [23].

In women, NETs may be hormone-associated and estrogen might be a major player in the pathogenesis of NETs [33]. Liang et al. reported that the benign epithelial cyst lining cells and tumor cells showed a strong immune response to the estrogen receptor. However, they also showed neuroendocrine differentiation. Therefore, carcinoid tumors of tailgut cysts might be hormone-associated [56]. The estrogen receptor might be a potential therapeutic target in selected patients with tailgut cysts.

Dysplasia of the cancer sequence in tailgut cysts and colonic cancer are similar, and malignant transformation is related to the transience of the tumor suppressor gene p53 [21,44,57].

**Tailgut cysts with adenocarcinoma**

Poorly differentiated adenocarcinoma is solid, glandular, and follows a papillary growth pattern [21]. The tumors can present in a somewhat random formation, and few of them are flat or nodular. One surface of the tumor tissue may show irregular lining areas of necrosis. Focal areas show extracellular mucin, with few signet-ring cells. A focused pseudo-stratified columnar appearance with severe dysplasia suggests that the cyst is lined by pseudo-stratified columnar epithelial cells and the tumor may be derived from this lining [21].

In a study performed by Krivokapic et al., irregularly shaped ovoid multilocular cysts were found. There was a large cyst on the surface of the incision and many irregular small cysts around it, all showing mucopurulent contents. Microscopically, cystic tissue had extensive epithelial coverage, which is common in the gastrointestinal tract [58].

In tumor markers, tailgut cysts with adenocarcinoma transition stain positively for carcinoembryonic antigen (CEA) and cancer antigen 19-9 (CA19-9). These markers have a valuable role in the evaluation of tumor recurrence [30,55]. In addition, there is also upregulation of the expression of Ki-67 and p53 in tailgut cysts with adenocarcinoma transition. Upregulation of p53 expression is a result of a mutation in the p53 gene, which is associated with the dysregulation in cell proliferation [59].

**Tailgut cysts with squamous carcinoma**

Tailgut cysts with squamous carcinoma transition may be lined by a squamous epithelium with dysplasia. The tumor consists of atypical and normal squamous cells and shows keratinization in solid masses. Furthermore, the tumor can also invade subcutaneous adipose tissue and skeletal muscle tissue [60]. Histopathological findings of tailgut cysts with squamous carcinoma transition comprise stratified squamous epithelium and columnar epithelium. In addition, there is extensive proliferation of smooth muscle bundles and linear deposition of calcium salts in dense fibrous connective tissues [34]. Currently, there is a lack of definite immunohistochemical reports of squamous carcinoma in tailgut cysts.

**Differences in Treatment**

Proper clinical examination not only establishes an accurate diagnosis, but also helps determine the best surgical approach for patients with tailgut cysts [61]. Although successful ultrasound-guided fine needle aspiration has been reported, the risk of malignant cell bleeding, infection, and spread to the abdominal cavity remains high, which increases the difficulty of subsequent surgical resection [24,62]. Therefore, complete histological examination after surgery is recommended [63,64]. In the treatment of posterior rectal space tumors, complete removal of the epithelial lining and clear margin of excision are still the most basic options. However, when cystic lesions are associated with fistulas or abscesses, particularly when neighboring structures are involved or the disease is not properly diagnosed, treatment can be very difficult [62,65]. Whether or not colectomy is performed for benign congenital presacral...
The possibility of recurrence, bleeding, chronic infection, and carcinoma are still a matter of debate. The current trend is to retain the coccyx, unless the malignant tumors require whole excision or the cysts adhere closely to the coccyx [66]. The surgical approach is based on the anatomical site [60]. There are 4 accepted methods of surgical approach, including the sacrococcygeal approach, the single abdominal approach, the combined sacrococcygeal approach, and the anal approach. The first method applies to tumors of grade S3 or below. In addition, the sacrococcygeal approach is preferred when bone involvement is suspected. The sacrococcygeal approach allows direct uncovering of the lesions, increasing the possibility of coccygectomy [67]. The advantage of the second method is that it can provide a good view of almost all pelvic structures and can be regarded as a treatment for high lesions without sacral involvement (higher than S3). The third method is the anterior-posterior approach, which combines the 2 techniques, including posterior sacral opening and abdominal anatomy. This method can better display all the involved structures and provides a wider resection range in restricted areas such as the posterior rectal space. In addition, when the mass is attached to the coccyx, it is not necessary to remove the coccyx in most cases [1,34]. The fourth approach is mainly used for rectal adenoma and tumors in the retro-rectal space [68].

**Tailgut cysts with NETs**

The differentiation of the NETs determines the prognosis and therapeutic approach [69]. However, because of the small number of reported cases, accurate clinical and follow-up investigations of all cases are not possible; therefore, it is impossible to classify presacral carcinoid tumors into well-differentiated neuroendocrine tumors subgroups according to the WHO criteria [23]. Some malignant NETs can be eliminated by routine radiotherapy and chemotherapy. The tyrosine kinase inhibitor, sunitinib, and an oral target of rapamycin inhibitor have been found to increase the progression-free survival in patients with advanced pancreatic NETs [70].

For grade 2–3 NETs, the administration of postoperative somatostatin might improve the patients’ prognosis [23]. Mitsuyama et al. reported that grade 2 and 3 NETs had malignant risk and could resist treatment and develop further. If the specimens were positive for somatostatin receptor 2, somatostatin therapy was recommended after complete resection of the tumors. Additional surgery is required for local recurrence and metastasis. If the lesion cannot be removed, additional radiotherapy or chemotherapy is needed [40].

**Tailgut cysts with adenocarcinoma and squamous carcinoma**

The possibility of recurrence, bleeding, chronic infection, and malignant transformation of adenocarcinoma or squamous cell carcinoma is always present [71]. Surgical resection followed by chemotherapy is the mainstream treatment method for tailgut cysts with adenocarcinoma and squamous carcinoma transition. The type of surgical approach depends on the level of the lesion. When the tumors are below the S3 level, surgical resection should be performed through the perineum. For lesions that are above the S3 level, the abdominal approach or a combined anteroposterior approach are preferred [26].

**Other surgical methods**

Recently, some new surgical approaches have been reported to treat tailgut cysts. Trans-anal minimally invasive surgery (TAMIS) allows minimally invasive excision of tailgut cysts and is an alternative to the posterior para-sacrococcygeal approach [17]. There are 5 potential benefits of TAMIS, such as mild discomfort, reduced risk of sacral nerve injury, fully exposure and visualization, and no visible scars [17]. Trans-anal endoscopic microsurgery (TEM) for posterior rectal submucosal lesions is safe and viable. It has merits such as low incidence and less surgical injury [72]. Occasionally, a trans-vaginal approach can be used for small lesions in female patients.

Laparoscopic surgery is also a viable method. It provides a useful tool to display the deep structure of the presacral space allowing reduced blood vessel and nerve damage [73–75]. It is also an effective choice for low retro-rectal tumorsable and provides the merit of an amplification effect in the pelvic contraction [70]. However, because of the seeding effects of tumor cells, the laparoscopic approach should not be performed if there is any suspicion of malignancy [33,34].

**Conclusions**

The symptoms and signs of tailgut cysts are not specific, and their rarity means that clinical experience is not widespread. As a result, there is a high misdiagnosis rate. There are many types of malignant transitions in tailgut cysts. Currently, tailgut cysts with NETs, adenocarcinoma, and squamous carcinoma transition are the most common types. Cytological biopsy is still not recommended before surgery because of the risk of false positives or tumor implantation and spread. CT and MRI play an important role in preoperative diagnosis, which can determine the shape, size, margin, infiltration degree, cyst contents, and malignant transformations. Complete resection is the main treatment method for tailgut cysts. Then, according to the pathological examination, which is performed to determine the type of malignant transformation, supplemental treatment, such as hormone inhibition, radiotherapy, and chemotherapy, can be administered. We believe that this review provides basic principles for the diagnosis and treatment of tailgut cysts with malignant transition.
Despite the rarity of tailgut cyst, this pathology may lead to severe morbidity. It is important to be familiar with this issue and to recognize tailgut malignancy features.

We believe that this review provides basic principles for the diagnosis and treatment of tailgut cysts with malignant transition.

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Conflict of interest

None.

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