Squamous cell carcinoma arising in a tailgut cyst: role of radiotherapy

Diego Aldave 1, Ana Teijo 2,3, Claudia Abril 4, Laura Cerezo 1

SUMMARY
Tailgut cysts (TGCs) are rare tumours which can undergo malignant transformation. The gold standard of treatment is complete surgical excision. Multidisciplinary assessment is advisable in order to apply adjuvant treatment. Postoperative radiotherapy should be given in case of compromised surgical margins or other factors such as high histological grade or perineural and lymphovascular invasion. Here, we present a case of a squamous cell carcinoma arising from a retrorectal TGC treated with surgery and postoperative radiotherapy and review the main indications and techniques of this therapy.

BACKGROUND
Retrorectal cystic hamartomas or tailgut cysts (TGCs) are rare congenital lesions that arise from embryonic hindgut remnants when incomplete regression occurs during embryogenesis. Also, they have been related to meningotheelial multiplication and benign thyroid tissue with oncocytic transition. TGC develops in the retrorectal space, defined anteriorly by the rectum, posteriorly by the lower sacrum, superiorly by the peritoneal reflection, inferiorly by the levator ani muscle and pelvic floor, and laterally by the iliac vessels and ureters.1

These lesions are uncommon and can present diagnostic challenges as symptoms and signs are not specific. The most common complaints include pain in the buttock/lower back and constipation.2 As a result, there is a high misdiagnosis rate and delays. They are more common in women, with a woman-to-man ratio of 3:1, and the average age at diagnosis is 35 years. Patients of male gender and older age are more likely to have a malignant tumour.3

Although the majority of TGC are benign lesions, the gold standard of treatment is complete surgical excision to avoid complications such as malignant transformation, infection or perianal fistula formation. When symptomatic, these lesions tend to be associated with malignant transformation.4

There are multiple approaches to resection of retrorectal tumours that are tailored to the clinical and anatomical considerations of each patient.1 5–9 The role of radiotherapy as an adjunct to surgery is not well known, as very few cases treated with radiotherapy have been reported in the literature; therefore, it is important to publish a new case and review the indications and technical aspects of this treatment.

CASE PRESENTATION
A woman presented with pelvic and coccygeal pain of 4 years duration, which had worsened in the past 6 months. Also, in the last weeks, she noticed a lump in the upper part of her gluteal fold. No history of urinary or defaecation difficulties was reported.

On physical examination, a soft and fluctuating subcutaneous lesion was palpated without inflammatory signs. The pelvic MRI revealed a bilobed lesion surrounding the second and third coccygeal bodies of 29 mm transverse × 49 mm anteroposterior × 50 mm longitudinal diameter, hyperintense in T1 and T2, with two solid hypercaptant poles in the interior cavity, one in the left inferolateral region, measuring 6 mm × 9 mm × 20 mm, and another in the upper pole, measuring 7 mm × 7 mm × 16 mm. The mass displaces the pelvic floor muscles superiorly, without spreading towards the intrapelvic region. The rest of the intrapelvic structures were within normal limits (figure 1). A staging CT scan did not show evidence of distant metastases. Preoperative CEA (Carcinoembrionary Antigen) and CA 19.9 (Carcinoembrionary Antigen 19.9) markers were within normal limits.

The patient underwent en bloc resection of the tumour using a posterior approach (razor position) with a sacrococcygeal spindle incision. During surgery, a 5 cm polyp lobulated cystic tumour was found, with the larger component posterior to the coccyx and a 2 cm pre coccygial lobulation encompassing the last coccygeal vertebra and extending superiorly to the second coccygeal vertebra. Both parts of the lesion communicate through the anococcygeal raphe. The lesion was removed from the pars sacrococcygeal fibres of the levator, some of which were attached to the wall of the cyst and were sacrificed in order to avoid the opening of the cyst.

Figure 1 Sagittal and axial views of the diagnostic MRI showing the retrorectal cyst and their anatomical relations.
The last coccygeal vertebra was resected en bloc with the cyst to gain access to the anterior part of the cyst, located in the preoccygeal-presacral space. The resection was completed with an intact cyst. The integrity of the rectal wall was checked with methylene blue.

Total excision surgery is the gold standard, although this is not always possible since TGCs are sometimes close to important structures. These anatomical relations are shown in figure 2. Thus, the risk of the surgery would be to damage the posterior wall of the rectum, the pudendal nerves and the fibres of the levator ani muscle, but all these structures were well preserved in our case, as described above.

The patient recovered from surgery uneventfully, except for a small dehiscence in the intergluteal surgical wound, which finally healed with local cures at the outpatient clinic. The main complications of this surgery include: asthenia (immediate), dehiscence of surgical wound (early) and fibrosis (late).

INVESTIGATIONS

Gross appearance of the surgical specimen is shown in figure 3. Microscopic analysis (figure 4) showed a multiloculated cystic lesion lined with a squamous epithelium with a smooth muscle wall with disorganised bundles and in which a gigantocellular foreign body reaction appears with expumose histiocytes, acute and chronic inflammation and calcified areas. The tumour was located at 2 mm from the most proximal radial margin. Focally, coinciding with the most solid areas, high-grade intraepithelial dysplasia and solid nests are evidenced infiltrating the thickness of the cystic wall without reaching the fat or touching the surgical margin. These nests are made up of pleomorphic cells with extensive eosinophilic cytoplasm and prominent nucleolus. Frequent figures of mitosis are evident, many of them atypical, with keratinising areas and necrosis. Occasional images of perineural invasion are identified, with no evidence of lymphovascular invasion. Surgical margins are free of dysplasia. Immunohistochemical study: p63+, CK5-6 and p53, p16 negative. Ki 67: 70%. In summary, these findings indicate the presence of squamous cell carcinoma, moderately differentiated on a retrorectal cystic hamartoma (TGC).

DIFFERENTIAL DIAGNOSIS

Combined with clinical symptoms and imaging, a histopathological diagnosis of adenocarcinoma arising in a TGC was established.

---

**Figure 2** Diagram of retrorectal cyst and their anatomical relations. This figure was entirely illustrated by D Aldave, co-author of the article.

**Figure 3** Gross appearance of the resection specimen: the lesion has been opened to show the cystic cavity and the solid indurated area in the wall.

**Figure 4** Microscopic study: H&E stain and immunohistochemical study (CK5-6 and p63).

**Figure 5** Planning target volume for radiotherapy in blue and organs to be spared: rectum (orange), bladder (yellow) and small intestine (brown).
TREATMENT
The case was discussed in the tumour board, and a final decision was made about giving postoperative radiotherapy. She was evaluated in our clinic for the adjuvant treatment.

In view of the histological findings of perineural invasion and elevated Ki 67 (70%) and the close surgical margin (2 mm in one point), we prescribed postoperative RT (Radiotherapy) to the surgical bed plus a safety margin in order to reduce the risk of local relapse. The target volume was designed on a planning CT, with an opaque marker placed on the intergluteal scar. The preoperative RM (Magnetic Resonance) diagnostic images and the description of the surgical findings were used to delimitate the target volume. The coccyx, the ischiorectal fossa and the presacral space until the level of the first sacral vertebra were included. Three-dimensional conformal radiation therapy (3DCRT) was used, with a posterior field and two lateral fields of 15 MV photons, with wedges, as shown in figure 5. The patient received a total dose of 50 Gy in 25 fractions, 5 days a week.

A cone beam CT was taken weekly, plus KV (Kilovoltage) X-rays daily to ensure accurate patient position setup, to improve the precision and accuracy of treatment delivery.

Tolerance of the treatment was good. The only complaint was increasing bowel movements of two or three times per day and slight asthenia during the last week of the treatment. Inspection of the skin showed a faint erythema in the intergluteal fold.

OUTCOME AND FOLLOW-UP
At last follow-up 12 months after treatment, the patient continues well, without evidence of disease recurrence or sequel from the treatments. The frequency of defaecation has changed from one time per day to two times per day.

DISCUSSION
TGCs are rare and relative unknown tumours that arise in the presacral space. The present case was the first TGC treated in our department in the last 30 years at least. Management of TGC is based on surgery, but radiotherapy or chemoradiotherapy (CRT) can be given to decrease the risk of recurrence in cases of malignant transformation.

Although it is not always possible, an early diagnosis is desirable for an adequate management of these cysts. CT and MRI tests are helpful. In MRI, TGCs usually have low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. MRI is more sensitive than CT for differentiation of unilocular from multilocular masses. CT and MRI can help to detect malignant transformation areas as they show suspicious features such as irregular mass contours, contrast enhancement within the cyst or nodular wall thickening as in our case. TGC should be distinguished from other lesions which may occur in the retrorectal space including teratomas, epidermal cysts, anal gland cysts and chordomas.

Biopsy is not usually recommended due to the risk of infection and tumour spreading of the mucous contain into the pelvic cavity. Biopsy should be performed only in unresectable cases. Surgical extirpation will provide an adequate specimen for definite histopathological diagnosis and will serve as definitive treatment in most cases.

Malignant transformation of a TGC is not very common, ranging from 2% to 13% of the cases. In a recent series of 52 retrorectal tumours, 56% were TGCs, and only four were malignant (Carpelan-Holmström 2020). Histologies of malignant transformation of TGC include adenocarcinoma, neuroendocrine carcinoma, endometrioid carcinoma, squamous carcinoma and sarcoma. Squamous cell carcinoma was reported previously in only two cases, so this would be the third case published in literature. One of the previously reported cases was synchronous with a rectal adenocarcinoma.

It has been suggested that hormones, like ghrelin and oestrogen, might be important in the development of malignant transformation of TGCS. In fact, TGC is more frequent in women than in men. However, the clear pathogenesis of the malignant transformation of TGC remains unknown.

Treatment of TGC is based on surgery guided by preoperative imaging. Limited reports exist on recurrence rates after TGC resection. Some reported a range of 0%–16%, usually related to incomplete excision or poor histological prognostic factors.

The publications about the use of radiotherapy before or after surgical intervention are sparse. We carry out a search in PubMed with the keywords: ‘retrorectal cystic hamartomas OR tailgut cysts AND malignant transformation AND radiotherapy’. Most of them were adenocarcinomas (44%) and in most cases surgery was the only treatment (86%). In only 6 of the 40 patients with malignant transformation and adjuvant treatment was administered, being CRT in 3, post-operative radiotherapy in 1 and chemotherapy in 2 patients (table 1).

In table 1, we summarise the published cases of malignant transformation TC, their histology and the treatment applied.

| Table 1 Published cases of TC (Computed Tomography) treated with RT |
|------------------------|----------------------|-----------------|--------------------------|
| Author, year          | Histology            | Indications for RT                              | Dose, fractionation and volume treatment |
| Baxt et al 2021       | Adenocarcinoma       | Invasion of anal sphincters and perianal skin. | Neoadjuvant. 50 Gy in 25 fractions + oral capecitabine. |
| Wang et al 2020       | Adenocarcinoma       | Uterus and rectum compressed.                   | – |
| Tay and Azhari 2020   | Squamous cell carcinoma | Invasion of skin surface and bowel.            | – |
| Martins et al 2019    | Adenocarcinoma       | Vascular and perineural invasion.               | Adjuvant. 54 Gy in 30 fractions to the pelvis (including sacrum), IMRT + oral capecitabine. |
| Nuno André Almeida Costa et al 2018 | Adenocarcinoma     | Focal invasion of the removed sacrum (S4 and S5) and perineal and vascular permeation. | Adjuvant radiotherapy and chemotherapy. |
| Demirel et al 2018    | Squamous cell carcinoma | Invasion of rectum, bladder, right ischiorectal and ischiocalanal fossa. | Adjuvant. 66 Gy in 30 fractions to the operative and residual sites of the tumour, IMRT. |
| Mitsuyma et al 2015   | Neuroendocrine       | Invasion of the lymph nodes.                   | Adjuvant. 59.4 Gy in 37 fractions to the presacral lymph nodes. |
| Jarboui et al 2008    | Adenocarcinoma       | Focus of adenocarcinoma in the wall.           | Adjuvant. 45 Gy in 25 fractions + intravenous 5-fluorouracil and folinic acid. |

IMRT, intensity modulated radiation therapy.
Learning points

► Retrorrectal cystic hamartomas or tailgut cysts are rare congenital tumours which can undergo malignant transformation.

► The gold standard of treatment is complete surgical excision.

► Postoperative radiotherapy should be given in case of compromised surgical margins or other factors such as high histological grade, the proliferation index (Ki 67) or perineural/lymphovascular invasion in order to reduce the local recurrence rate.

Contributors DA performed the literature search, made the table, has entirely illustrated figure 2 and wrote parts of the manuscript. AT performed the pathology study and made the pictures of the pathological specimen. CA helped with the manuscript redaction and did the interpretation of the pathological findings. LC treated the patient and supervised the elaboration of the case report.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

ORCID iDs
Diego Aldave http://orcid.org/0000-0002-9596-3081
Ana Tejo http://orcid.org/0000-0002-8280-8446

REFERENCES
1. Sakr A, Kim HS, Han YD, et al. Single-center experience of 24 cases of tailgut cyst. Ann Coloproctool 2019;35:268–74.
2. Cody HS, Marcove RC, Quan SH. Malignant retrorectal tumors: 28 years’ experience at Memorial Sloan-Kettering cancer center. Dis Colon Rectum 1981;24:501–6.
3. Baek SK, Hwang GS, Vinci A, et al. Retrorectal tumors: a comprehensive literature review. World J Surg 2016;40:2001–15.
4. McCarroll RH, Moore LJ. Transanal minimally invasive surgery for resection of retrorectal cyst. J Surg Case Rep 2018;2018:rjy021.
5. Gutierrez O, Haj-Imam H, Griffiths E, et al. Presacral mass in the setting of an ovarian cyst and abdominal pain. BMI Case Rep. 2017;2017:bcr201719803.
6. Li WJ, Li J, Yu K, et al. Retrorectal adenosarcoma arising from tailgut cyst: a rare case report. BMC Surg 2019;19:180.
7. Vinciuggera GLR, Mercantini P, La Torre M, et al. Transitional cell carcinoma of the retrorectal space arisen in tailgut cyst: a case report and review of the literature. Int J Surg Pathol 2014;22:280–5.
8. La Rosa S, Bonti L, Finzi G, et al. GheIn-producing well-differentiated neuroendocrine tumor (carcinoid) of tailgut cyst. morphological, immunohistochemical, and RT-PCR study of a case and review of the literature. Endocr Pathol 2010;21:190–8.
9. Patsouras D, Pawa N, Osmani H, et al. Management of tailgut cyst in tertiary referral centre: a 10-year experience. Colorectal Dis 2015;17:724–9.
10. Yang DM, Park CH, Jin W, et al. Tailgut cyst: MRI evaluation. AJR Am J Roentgenol 2005;184:1519–23.
11. Almeida Costa NA, Rio G. Adenocarcinoma within a tailgut cyst. BMI Case Rep 2018;184:brv2018-226107.
12. Abukulut S. Unusual cause of defecation disturbance: a presacral tailgut cyst. Eur Rev Med Pharmacol Sci 2013;17:1688–99.
13. Kodera K, Eto S, Fukusawa N, et al. Laparoscopic resection of a neuroendocrine tumor that almost fully replaced tailgut cysts: a case report. Surg Case Rep 2020;6:269.
14. Marano A, Giuffrida MC, Peluso C, et al. Robotic approach to large tailgut cyst with malignant transformation: a case report. Int J Surg Case Rep 2020;77:S57–60.
15. Lee A, Suhardja TS, Nguyen TC, et al. Neuroendocrine tumour developing within a long-standing tailgut cyst: case report and review of the literature. Clin J Gastroenterol 2019;12:539–51.
16. Mathis KL, Dozois EJ, Grewal MS, et al. Malignant risk and surgical outcomes of presacral tailgut cysts. Br J Surg 2010;97:575–9.
17. Gaud UJ, Goyal T, Shukla M, et al. Synchronous occurrence of adenocarcinoma of the rectum with squamous cell carcinoma of a retrorectal cyst: report of a case and review of the literature. BMJ Case Rep 2009;2009:brd12.2008.1398.
18. Bawerz M, Thibaudneau E, Libois V, et al. Retrorectal mucinous adenosarcoma arising from a tailgut cyst: a case report. Case Rep Oncol 2021;14:147–51.
19. Tay SK, Ashar R. Metastatic squamous cell carcinoma arising from a retrorectal cystic hamartoma (tailgut cyst), Human Pathology. In: Case reports., 2020 :20, 200382. ISBN: 2217-3300.
20. Jarboui S, Jaraya H, Mihoub MB, et al. Retrorectal cystic hamartoma associated with malignant disease. Can J Surg 2008;51:115–6.
21. Spada F, Pelosi G, Squadrone M, et al. Neuroendocrine tumour arising inside a Retro-rectal tailgut cyst: report of two cases and a review of the literature. Endocrmedialsience 2011;5:201.
22. Wang M, Liu G, Wu Y, et al. Tailgut cyst with adenocarcinoma transition: a rare case report. Medicine 2020;99:e20941.
23. Martins P, Canotilho R, Peyroteo M, et al. Tailgut cyst adenocarcinoma. Autops. Case Rep. 2019;10:e2019115.
24. Demirel AH, Cetin E, Temiz A. Squamous cell carcinoma arising in a sacrococcygeal tailgut cyst. An Bras Dermatol 2018;93:733–5.
25. Mitsuayama T, Kubota M, Nakamura Y, et al. Neuroendocrine tumor arising from tailgut cyst with spinal cord tethering: case report and literature review. Spine J 2015;15:e1–8.
