Gastrointestinal stromal tumour in the anal canal: A case report with atypical location☆

Tumor del estroma gastrointestinal en canal anal: a propósito de un caso con localización atípica

Anal tumours are quite rare and account for 2% of all colorectal malignant neoplasms. Most are either epithelial tumours or melanoma.[1] Soft tissue tumours only account for 2.3% of all cases.[2]

We present the case of a gastrointestinal stromal tumour (GIST) with atypical location, which could represent a diagnostic challenge.

The case concerns a 52-year-old female patient originally from south-east Mexico, with seven prior pregnancies and bilateral tubal occlusion at the age of 35, with no other prior history of interest. The patient attended our centre with a 10 cm mass in the anal region. It was first detected by a general practitioner as a 2 cm mass one year previously and was diagnosed as probable haemorrhoids without associated symptoms. However, the mass grew rapidly with the onset of bleeding, painful bowel movements and changed stool consistency. The physical examination revealed an irregular tumour in the anal region that extended from the left ischioanal fossa to the retrorectal space with ulceration of the mucosa, with sphincter involvement and avulsion of the left levator ani.

The endoanal ultrasound (Bruel & Kjaer model 1849 [Gentofte, Denmark] with Bruel & Kjaer model 1850 7 MHz axial device and transducer) identified a 14 × 10 cm hypoechoic lesion, attached to the middle and lower rectal wall without mucosal infiltration and without apparent involvement of the anal sphincter (Fig. 1a). The CT scan revealed a well-defined lesion with irregular edges measuring 12 × 10 × 8 cm, with soft tissue density, from the distal rectal wall extending caudally to the exterior of the anus (intergluteal portion), obliterating 40% of the lumen (Fig. 1b). A transanal approach was used to resect the tumour, with the patient in the prone position and with the buttocks stretched apart. A parasacral incision was made followed by vertical dissection from the subcutaneous tissue to the gluteus muscles, and the lower edge of the tumour and the ischial tuberosity were identified. The sacrotuberous ligament was sectioned and the tumour released from the gluteus maximus (resection would have been considered in the event of muscle invasion, or resection of the lower part of the sacrum below S3 to preserve the root of the pudendal nerve, if necessary), followed by medial and cranial dissection with release of the rectum, the anal sphincter and the levator ani. As the tumour involved part of the external sphincter, this was resectioned and reconstructed. The dissection plane was located in the intersphincteric space, which allowed us to preserve the internal anal sphincter in its entirety. The wound was closed by planes. This curative approach was similar to that performed for any mesenchymal tumour in the intersphincteric space, trying to complete the resection with negative surgical margins. The patient had no faecal consistency abnormalities in the post-operative period.

Macroscopically, the lesion was a dark yellow irregular ovoid with a firm consistency, measuring 14 × 11 × 9 cm and weighing 635 g. Upon section, the surface was observed to be fasciculated, whitish-grey and with haemorrhagic areas (Fig. 1c and d). Microscopically, a neoplastic lesion composed of long and wide cell bundles was observed. The cells were tapered and polygonal with dispersed granular chromatin nuclei and the immunohistochemistry was positive for CD117 and CD34, and negative for desmin, PS-100 and smooth muscle actin (Fig. 1e–g). In addition, numerous mitoses were identified (120–140 mitoses in 50 high-power fields). A diagnosis of high-risk gastrointestinal stromal tumour was established. The patient's clinical course was favourable and she was discharged eight days after the surgery. She was offered an appointment to assess the start of adjuvant therapy with imatinib, but she withdrew from follow-up. Because there was no evidence of metastasis, abdominal–pelvic resection following histopathological diagnosis was not considered.

Although gastrointestinal stromal tumours are the most common mesenchymal neoplasms of the gastrointestinal tract, they tend to occur in the stomach and are rarely reported in the anorectal region.[1–3] The originate in the cells of Cajal, which act as a pacemaker in intestinal peristalsis, and they often express CD117 (c-kit) and CD34.[2–5] GISTs of the anal region are rare, accounting for just 0.1% of all GISTs, and primarily affect men in their 50s.[2,4]

They clinically manifest as an exophytic mass in the intersphincteric space with haematochezia, pain, feeling of a mass, constipation or anaemia, although they can also be asymptomatic.[2–5] This makes it difficult to establish a suspected diagnosis as these symptoms are similar to those of other tumours that may manifest in the anal canal, such as squamous cell carcinoma, adenocarcinoma, melanoma or sarcomas.[6]

Imaging studies reveal a well-defined intramural mass with soft tissue density and exophytic growth, sometimes with central necrosis,[5] allowing them to be distinguished from carcinomas that tend to have irregular edges and may be associated with perirectal lymphadenopathy. However, no radiological criteria have been established to distinguish GISTs from other tumours of the anal region.[7] In our case, surgery was chosen based on the results of the imaging studies performed, which could act as a guide for other cases to conduct preoperative diagnosis to decide the best surgical approach.

Diagnosis is made by histopathological study; it should be differentiated from other benign and malignant soft tissue lesions and confirmed with a positive CD117 and CD34 immune profile.[2] To date, cases published in the literature of GISTs in the anal canal that express CD117 have been positive for this marker and no atypical patterns have been reported. As such, unlike the example of succinate dehydrogenase-deficient gastric GISTs, no factors have been identified on

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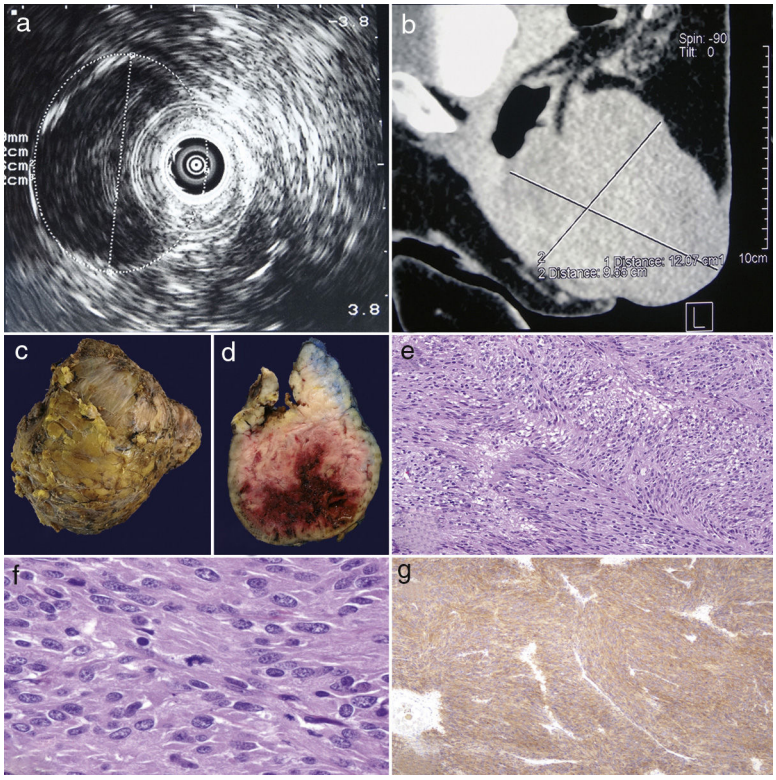

Figure 1 (a) Endoanal ultrasound with hypoechoic lesion attached to the rectal wall, (b) sagittal plane CT scan, a neoplastic lesion in the anorectal region is identified, (c) external macroscopic appearance, (d) macroscopic appearance upon section, (e) a neoplastic lesion composed of irregular and intertwined cell bundles is observed (haematoxylin and eosin, 10×), (f) the neoplastic cells are tapered with ovoid nuclei, note atypical mitoses, and (g) positive immunoreaction for CD117 in the neoplastic cells.

either a microscopic or molecular level that could be used to classify them into a separate group.[8]

Factors associated with malignancy are mitotic activity (>5 mitoses/50 HPF), tumour size (>5 cm) and necrosis[2–5]; the first two were present in our case, which is why it was considered a high-risk tumour.

The treatment of choice is surgery and the approach depends on each individual case; either local excision with transanal approach or radical resection (abdominal–pelvic resection).[2,3] Adjuvant therapy with imatinib (tyrosine kinase inhibitor) has been shown to improve survival[2] and tends to be used to treat recurrence, unresectable tumour or metastasis.[4] As recurrence can be as high as 62% in the first three years, close follow-up is important.[2] Incomplete resection is an independent risk factor that has a negative impact on disease-free survival.[9] As such, every effort must be made during surgery to achieve resection with negative margins for neoplastic cells.

Because anal GISTs are rare, there is a lack of consensus over which treatment is most effective. The reporting of these cases, their management and the clinical outcomes is therefore extremely important. A pathological study is vital to rule out other causes of malignancy, and long-term follow-up is essential due to the high rate of recurrence.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Autoimmune hepatitis and coeliac disease. Simultaneous onset of both diseases☆

Hepatitis autoinmune y enfermedad celiaca. Aparición simultánea de las 2 enfermedades

We present a patient who developed autoimmune hepatitis (AIH) and coeliac disease simultaneously, requiring both immunosuppressant therapy and a gluten-free diet to achieve remission of both diseases.

The case concerns a 50-year-old male patient, non-smoker and occasional consumer of alcohol, with no medical or surgical prior history of interest who, after a Mediterranean cruise, developed diarrhoea without blood, mucous or pus. A complete blood count was performed that revealed hypertransaminasaemia (GPT 352 U/l, GOT 318 U/l, GGT 64 U/l), with negative serology (HAV, HCV, Epstein–Barr virus, CMV), negative stool cultures and faecal parasites, as well as normal thyroid function and iron profile. Liver enzymes were normal in a prior blood panel. The abdominal ultrasound was also normal. The patient also had dyspepsia with persistent diarrhoea. More precise lab tests were performed, which were positive for ANA (1/80) and anti-transglutaminase (248 U/ml), and revealed elevated IgG and IgA levels (18.63 g/l and 5.19 g/l, respectively). The genetic testing was positive for HLA-DR 3 and HLA-DQ 2. A gastroscopy was performed with biopsies of the second portion of the duodenum (AP: finding of intraepithelial lymphocytes and subtotal/total villous atrophy in assessed fragments of the distal duodenum) and liver biopsy (AP: periportal hepatitis with intense inflammatory activity, with moderate interface hepatitis, moderate lobular inflammatory activity with focal necrosis and fibrosis forming septa and focal architectural distortion. No steatosis or iron deposit). The pre-treatment score for AIH was 17.

After confirming the two diagnoses, treatment was started with prednisone 30 mg, azathioprine 50 mg and a gluten-free diet. The prednisone dose was gradually reduced, with normal hepatic enzyme and anti-tissue transglutaminase antibody levels four months after the introduction of treatment. IgG levels normalised at two months. After completing eight months of a tapering regimen of corticosteroids and experiencing side effects such as the onset of moon face, corticosteroid treatment was suspended, while azathioprine and the gluten-free diet were maintained. Five years after the initial onset of symptoms and following a liver biopsy that confirmed histological remission of AIH, azathioprine was finally suspended, maintaining a gluten-free diet as the only treatment. Since then, all ultrasound scans, blood tests and pathology studies have been normal. The patient is currently asymptomatic and undergoes regular check-ups for both AIH and gluten-sensitive enteropathy (coeliac disease).

It is not uncommon for a single person to have several different autoimmune diseases.[1] It has been shown that genetic predisposition can give rise to various autoimmune diseases, as they often share the same genetic loci. This is true of coeliac disease and AIH, as both conditions express similar gene combinations that encode HLA class II molecules in chromosome 6.[2] The prevalence of coeliac disease in adult patients with AIH is 10% higher than in the general population.[3] Coeliac disease has been associated with autoimmune liver diseases (AIH, primary sclerosing cholangitis, primary biliary cholangitis) as well as hepatitis B and C, non-alcoholic steatohepatitis, Wilson's disease, cirrhosis and portal hypertension and hypertransaminasaemia associated with coeliac disease.[2]

However, the unusual feature of this case is that both diseases manifested simultaneously, rather than one preceding the other (which is more common). This raises the question of whether the same trigger may have been responsible

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