

CASE REPORT

Diagnostic conundrum of a perineal tumour: a rectal gastrointestinal stromal tumour mimic

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Abstract

Gastrointestinal stromal tumour (GIST) is a common mesenchymal tumour arising in the gastrointestinal tract, but not frequently encountered in the rectum. Herein, we describe a case of a rectal GIST which mimicked histomorphological features of a schwannoma; thus, making intraoperative frozen section evaluation challenging. Although subsequent immunohistochemistry and molecular findings readily confirmed the diagnosis of a GIST, we wish to draw attention to three clues that will help the pathologist steer clear of this potential diagnostic pitfall. One, GISTs are relatively more common than schwannomas in the rectum. Two, schwannomas usually have very little mitoses. Three, rectal GISTs commonly exhibit nuclear palisades. We also discuss the diagnostic, prognostic and therapeutic functions of immunohistochemical and molecular investigations. As the surgical intent for rectal GISTs is for en-bloc excision with wide margins, we surmise that the intraoperative consult should include GIST as a possible differential diagnosis for rectal mesenchymal tumours. In view of the potential for neoadjuvant treatment with imatinib before surgical excision to preserve sphincter function, a multidisciplinary approach is recommended for establishing most effective treatment strategy in these rare complex cases.

Keywords: rectal, gastrointestinal, schwannoma, stromal tumour, mesenchymal

INTRODUCTION

Primary mesenchymal tumours of the gastrointestinal tracts include gastrointestinal stromal tumours (GISTs), neural tumours, smooth muscle tumours, fibroblastic tumours, vascular tumours, adipocytic tumours and other rarer entities such as synovial sarcoma and perivascular epithelioid cell tumours.¹ The histomorphological features of these entities may mimic each other and make accurate diagnosis challenging. In this report, we highlight a diagnostic pitfall involving a case of rectal GIST mimicking a schwannoma.

CASE REPORT

A 57-year-old gentleman presented with a 2-month history of a perianal lesion. Magnetic resonance imaging (MRI) showed a 6.4 cm solid lobulated dumbbell-shaped enhancing lesion arising from the anorectal junction, at the 9-to-10 o'clock position, extending into the intersphincteric space (Fig. 1). The patient

then underwent an en-bloc wide excision of this perianal lesion. During the intraoperative frozen section consultation, gross examination of the tumour showed a well-circumscribed pale yellow whorled cut appearance (Fig. 1). A representative section examined microscopically showed a cellular spindle cell neoplasm with nuclear palisades (Fig. 2). As such a provisional diagnosis of schwannoma was rendered.

Subsequent formalin-fixed, paraffin-embedded, haematoxylin and eosin stained slides showed similar features of a spindle cell neoplasm arranged in interlacing bundles and fascicles. The spindled cells showed plump elongated wavy nuclei, fibrillary cytoplasm and occasional mild nuclear pleomorphism. There was prominent nuclear palisading as well as biphasic hypercellular and hypocellular areas that resembled Antoni A and B areas. In addition, the intervening gaping blood vessels showed hyalinized vessel walls. However, mitoses were not difficult to find (12 mitoses per 5 mm² equivalent area) (Fig. 2).

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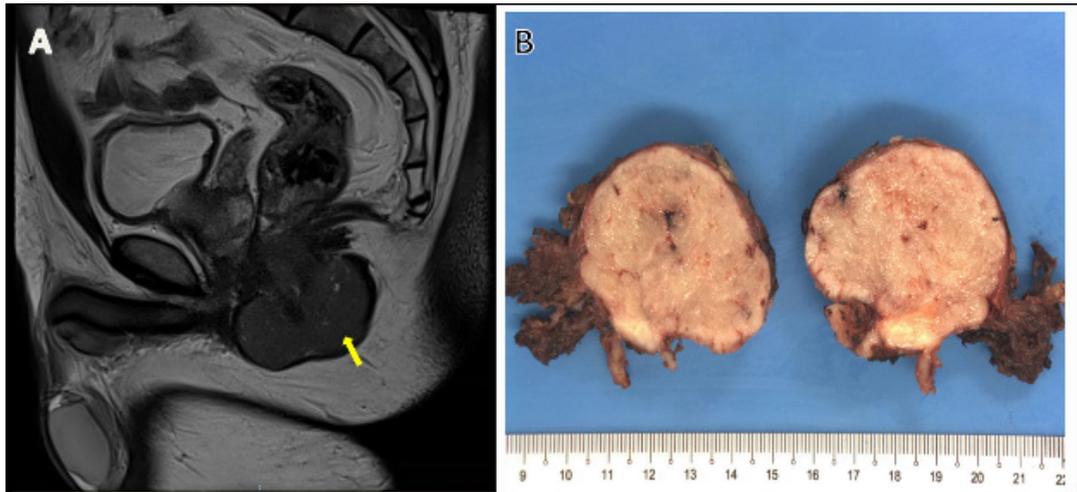


FIG. 1: (A) MRI image of solid lobulated dumbbell-shaped lesion arising from anorectal junction and extending into intersphincteric space. (B) Macroscopic appearance of tumour showing circumscription and a pale yellow whorled cut surface

Ancillary immunohistochemical stains revealed negative expression for S100, SOX10 and desmin. Instead there was diffuse strong expression of CD117 (c-kit), DOG-1 and CD34 (Fig. 3). Molecular analysis for mutations in KIT exons 9 and 11 was undertaken and two foci of substitution-type mutations were detected in exon 11. Both the immunohistochemical and molecular evidence points towards a diagnosis of GIST rather than schwannoma. The tumour was also deemed to have a high risk of progressive disease, as per Miettinen and Lasota's guidelines for risk assessment of GISTs.²

As the tumour abuts against the sphincteric muscles, clear margins were difficult to achieve without compromising continence, which was a function the patient wished to preserve. In view of the positive surgical resection margin, Imatinib, a tyrosine kinase inhibitor approved for treatment of GISTs, was started postoperatively. Patient was tolerating treatment well at the third month follow-up.

DISCUSSION

Schwannomas are benign biphasic nerve sheath tumours derived from Schwann cells. Within the gastrointestinal tract, they have been reported in the stomach, colon and rectum. However primary schwannomas of the colon and rectum, not associated with systemic neurofibromatosis (von Recklinghausen disease), are extremely rare with an incidence of approximately 3% reported in a large scale study.³

GISTs, derived from interstitial cells of

Cajal, have been described throughout the gastrointestinal tract and are mostly found in the stomach (50%-60%), followed by the small intestine (30%-40%), with only about 5% of all GISTs occurring in the rectum.^{1,4,5} In contrast, GISTs are not all benign and occupies a spectrum from almost negligible to high risk of progressive disease.² Common forms of disease progression include local recurrence and hepatic metastases.²

In our case report, we have shown how a rectal GIST can morphologically mimic a schwannoma. The classical and typical features of a schwannoma such as nuclear palisades (Verocay bodies), a biphasic pattern incorporating hypercellular (Antoni A) and hypocellular (Antoni B) areas and hyalinized thickened blood vessel walls were all demonstrated. In an intraoperative frozen section consultation setting that does not have the luxury of immunohistochemical and molecular tools, recognition of this diagnostic pitfall is even more important.

From our literature search, we found three clues that will help avoid this diagnostic pitfall. One, in the anorectal region, GISTs are relatively more common than schwannomas. The latter manifests only as case reports in the literature. A study of 600 mesenchymal tumours by Miettinen only revealed a single case of rectal schwannoma.² Two, schwannomas usually have very little mitoses (less than 5 mitoses per 50 HPFs).^{1,3} Three, rectal GISTs tend to show nuclear palisades.⁶ Hence the finding of Verocay-like bodies on histology should not equate to a diagnosis of schwannoma. With these clues,

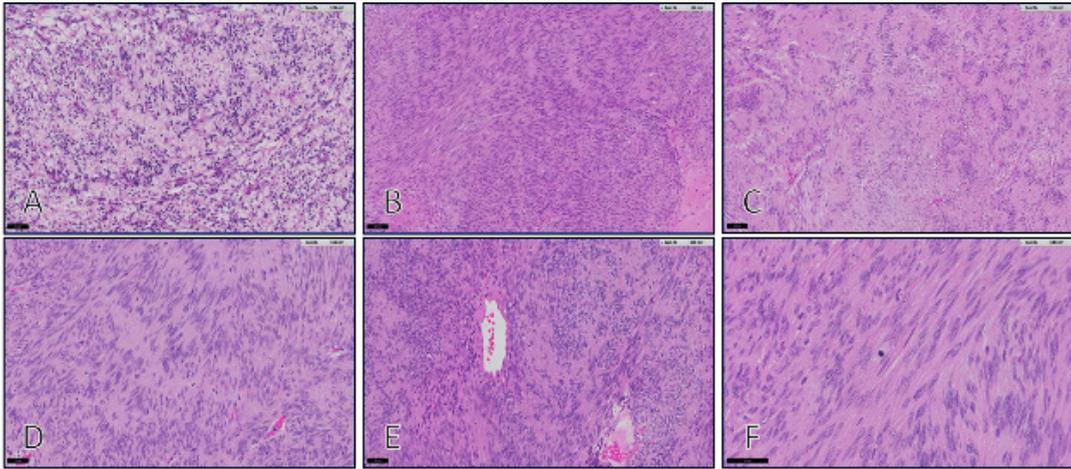


FIG. 2: (A) Intraoperative frozen section showing areas of nuclear palisading that mimics Verocay bodies in a schwannoma (H&E, 200x). Subsequent formalin-fixed paraffin-embedded sections that show (B) hypercellular Antoni A areas, (C) hypocellular Antoni B areas, (D) nuclear palisades and (E) mural hyalinization of blood vessels (H&E, 100x). (F) Mitoses are present (H&E, 400x)

the frozen section report should include GIST as a possible differential as the management of GIST and schwannomas is different.

Whenever GIST is on the list of differential diagnoses, we believe that the diagnostic workup should include immunohistochemistry for CD117 and DOG-1. The use of molecular techniques as a diagnostic modality has its own perils, as a significant but smaller subset of GISTs harbour PDGFRA, BRAF V600 or succinate dehydrogenase (SDH) complex mutations instead of KIT mutations.¹ As such, guidelines have mainly labeled the use of molecular techniques as a therapeutic and prognostication

tool, rather than as a diagnostic modality.⁷ The use of molecular techniques as a diagnostic tool has however been noted to be helpful in certain instances such as endoscopic ultrasound guided fine needle aspiration.⁸ Furthermore, combined use of CD117 and DOG-1 immunohistochemistry has reported sensitivities and specificities of over 95%, making it even harder for molecular techniques to supersede.⁹

The surgical management for rectal GISTs typically involves *en-bloc* resection with wide margins. However in the anorectal region and in the context of sphincter preservation, neoadjuvant treatment with imatinib to shrink the tumour

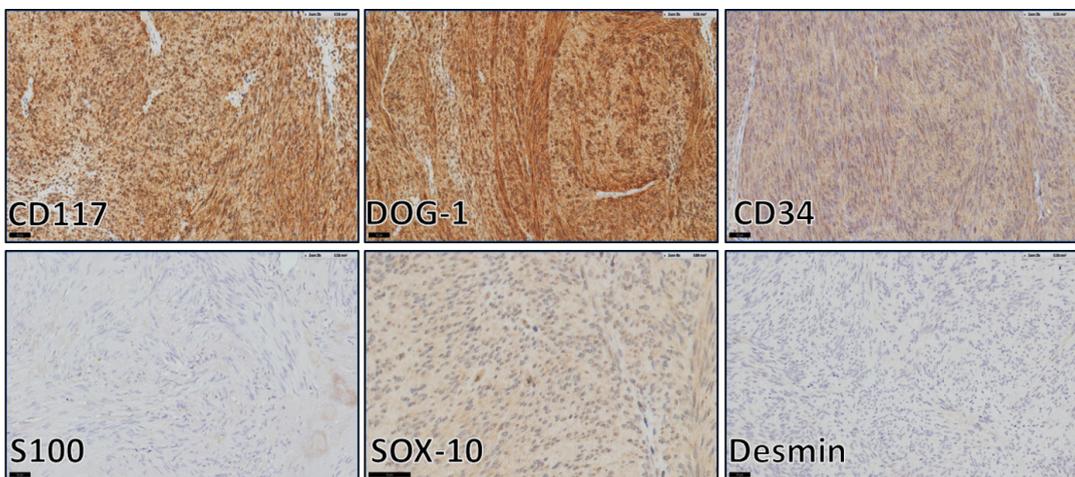


FIG. 3: Spindled tumour cells showing diffuse and strong immunopositivity to CD117 (200x), DOG-1 (200x) and CD34 (200x), while being immunonegative for S100 (200x), SOX-10 (400x) and Desmin (200x)

before local excision has been associated with improved disease-free survival rate.^{5,10} However as such cases are rare and complex, a multidisciplinary approach is recommended.^{5,10}

Conclusion

We highlight a diagnostic pitfall with morphological features of a rectal gastrointestinal stromal tumour (GIST) mimicking a schwannoma. As the management of these two entities is different, we suggested clues that will aid in the consideration of GIST in the differential diagnoses. We believe that immunohistochemistry and molecular techniques can help avoid a misdiagnosis. Due to the rarity and complexity of such cases, a multidisciplinary approach is recommended.

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