CASE REPORT

Malignant Peripheral Nerve Sheath Tumour of the Small Bowel Presenting with Intussusception and Perforation: a Double Jeopardy?

Ananth P. Abraham¹ · Joshua Franklyn¹ · Jagan Chandramohan² · Pranay Gaikwad¹ · John C. Muthusami¹

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Abstract Malignant peripheral nerve sheath tumours (MPNST) are rare soft tissue sarcomas which largely occur in the extremities and the head and neck region. The tumours are aggressive with a high rate of recurrence. Radical surgical resection remains the treatment of choice with adjuvant radiation therapy and chemotherapy still failing to demonstrate a clear benefit. The gastrointestinal tract is an exceedingly rare site for these tumours. We report an unusual case of a young male with an MPNST of the small bowel who presented with an ileocolic intussusception and sigmoid perforation.

Keywords Malignant peripheral nerve sheath tumour · Intussusception · Sarcoma

Introduction

Malignant peripheral nerve sheath tumours (MPNSTs) are an uncommon subgroup of soft tissue sarcomas of entomesenchymal origin. They constitute 3–12% of soft tissue sarcomas and have an overall incidence of 1/100,000 [1]. An MPNST may be defined as a malignant tumour which originates from the cells of the peripheral nerve sheath or shows differentiation towards the same. Previously used terminology such as malignant schwannoma, neurofibrosarcoma and neurogenic sarcoma are currently obsolete [2].

The usual age of presentation of MPNSTs is in the third to sixth decades [3, 4]. They predominantly involve the extremities, the trunk and the head and neck region [1, 2, 5]. Radical surgical resection is the mainstay of treatment with inadequate evidence to support the use of adjuvant radiotherapy or chemotherapy [2, 6].

MPNSTs of the gastrointestinal tract are extremely rare with very few cases having been reported till date. Most cases present non-specifically with no clinical or radiological signs that may suggest the disease prior to histopathological evaluation. The optimal treatment modality remains unclear and the role of adjuvant therapy is, at best, anecdotal. We report, to the best of our knowledge, the first case of a small bowel MPNST presenting as an ileocolic intussusception with sigmoid perforation.

Case Report

A 22-year-old male presented with complaints of loss of weight and appetite for 6 months, mucoid diarrhoea and worsening colicky abdominal pain for 2 months and low grade fever for 2 weeks. On examination, he was emaciated and pale with a pulse rate of 110 beats per minute. There was no icterus or palpable left supraclavicular lymphadenopathy. He did not have any peripheral stigmata of neurofibromatosis-1 (NF-1). Abdominal examination revealed mild asymmetric distension with a relative emptiness in the right iliac fossa and an ill-defined mass in the right upper quadrant with a restricted mobility, diffuse tenderness and guarding. Investigations revealed leukocytosis with a left-shift and low albumin. Contrast enhanced computerised tomography (CECT) of the abdomen and pelvis revealed an ileocolic intussusception reaching up to the rectum with an ill-defined lesion acting as the lead point (Fig. 1a). The surrounding omentum and mesentery showed fat stranding and increased vascularity. There

✉ Ananth P. Abraham
ananthab88@gmail.com

¹ Department of General Surgery, Christian Medical College, Vellore, Tamil Nadu, India

² Department of Pathology, Christian Medical College, Vellore, Tamil Nadu, India

Fig. 1 **a** CT of the abdomen showing the telescoped bowel and the **b** intraoperative finding of a large ileocolic intussusception with sigmoid perforation

were also a few mesenteric lymph nodes noted within the intussusceptum, and mild bilateral hydronephrosis. He was planned for an emergency laparotomy. Intraoperatively, gross bowel oedema, ileocolic intussusception with a fungating mass as the lead point and a linear sigmoid perforation were noted (Fig. 1b). Subtotal colectomy with mucus fistula of the distal end and an end ileostomy were performed.

Histopathological examination of the surgical specimen (HPE) revealed a $15 \times 15 \times 8$ cm³ proliferative mass arising from the serosa with a grey-white to light tan, soft to mucoid cut surface. Microscopically, the tumour was composed of fascicles of spindle-shaped cells with moderately pleomorphic, vesicular nuclei with coarse chromatin and inconspicuous nucleoli (Fig. 2a). Mitotic activity was ~20/10 high-power-fields. There was a surrounding desmoplasia with intervening areas of necrosis. On immunohistochemistry (IHC), the tumour cells had focal S100 positivity and were negative for CD56, CD117, DOG-1 and SMA and H-caldesmon (Fig. 2b). The distal resection margin was 15 cm away from the tumour but the proximal resection margin was involved.

Fig. 2 Photomicrographs showing **a** fascicles of atypical spindle-shaped cells with interspersed congested blood vessels (picture insert showing mitotic figure) and **b** immunohistochemical staining with S-100 protein showing patchy positivity

All mesenteric lymph nodes and the appendix were free of tumour. Postoperatively, he developed a partial wound dehiscence which was conservatively managed with daily dressings. The patient was discharged with the advice to review with the medical and radiation oncologists, but was lost to follow-up for 6 months until he returned for the reversal of the stoma and restoration of bowel continuity. A postoperative CECT of the abdomen at this time showed no evidence of residual or recurrent tumour. The case was discussed in the multidisciplinary tumour board with a decision to resect the proximal ileal margin with a frozen section biopsy ensuring a tumour-free margin prior to anastomosis and plan for adjuvant therapy based on the HPE report. He underwent a dismantling of the ileostomy and mucus fistula, resection of 5 cm of the ileum confirmed to have a tumour negative margin by frozen section biopsy, and ileosigmoid anastomosis. He made an uneventful postoperative recovery. The final HPE confirmed the absence of any residual disease and so there was no indication for adjuvant therapy. On telephonic follow up at 6 months, he was asymptomatic and was advised to follow up after another 6 months.

Discussion

MPNSTs are biologically aggressive tumours with high rates of local recurrence and haematogenous metastasis. Review of literature suggests that 5–42% of patients with MPNSTs have associated neurofibromatosis type I (NF-1) and conversely, individuals with NF-1 have a 9–13% risk of developing an MPNST during their lifetime [7–9]. The incidence of sporadic tumours is extremely rare—less than 0.001% of the reported tumours, and they usually present in the third to sixth decades of life [10]. This is in contradistinction of those affected by NF-1, who have an earlier mean age of diagnosis [11]. Although patients with NF-1 are more prone to present with larger tumours, individual large studies have failed to demonstrate any significant difference in the long-term survival [2, 3, 6]. However, a recent meta-analysis has shown a significantly lower overall and disease-specific survival amongst the patients with NF-1. MPNSTs show no gender predilection although separate studies have shown both male and female preponderance [1, 12].

Pathologic diagnosis of MPNSTs is often difficult since they are a diverse group of heterogeneous neoplasms, often with multiple histological origins and varying differentiation patterns [13]. Fascicles of spindle cells woven into a herring bone pattern, displaying varying degrees of mitosis and necrosis are consistent findings [1]. The presence of palisading arrangement, nuclear atypia and bizarre giant cells facilitate diagnosis [14]. There are no specific IHC markers of MPNSTs. The S-100 protein is present in all cells derived from the neural crest. The S-100 immunoreactivity is detected in 100 % of schwannomas and neurofibromas but only in 50–60% of the MPNSTs (weak or focal positivity) possibly due to its dedifferentiation [15]. The CD56 and Protein Gene Product 9.5 (PGP 9.5) are also sensitive but non-specific markers of MPNSTs [13]. The presence of P53 and Ki67 can also help in diagnosing malignant peripheral nerve sheath tumour [4]. However, the markers like DOG-1, CD34 and CD117 seen in gastrointestinal stromal tumours and Desmin, H-caldesmone and SMA found in the smooth muscle tumours help exclude other spindle cell tumours.

On imaging, the greatest challenge is to differentiate an MPNST from its benign counterparts, the schwannoma and neurofibroma. In general, the larger lesions with irregular borders and peri-lesional oedema are more likely to be malignant. On MRI, a heterogeneous T1 signal may differentiate an MPNST from the usually iso-intense neurofibroma while the presence of an intra-tumoral cystic lesion is most suggestive of a schwannoma [16, 17].

Primary malignancies of the intestine commonly present with abdominal pain (63%), vomiting (48%), weight loss (44%) or gastrointestinal bleeding (23%) [18]. Although very few case reports have described benign schwannomas of the

bowel presenting with intussusception, only one other report of an intussusception caused by an MPNST was found in the English literature [7, 14, 19–21]. Another report by Mohtaram et al. describes a case of small bowel MPNST discovered after intestinal perforation, resulting in a fatal outcome [22].

Owing to its rarity, there are no established management protocols for gastrointestinal MPNSTs. Management has been extrapolated from the treatment recommendations for MPNSTs located elsewhere in the body. The mainstay of treatment remains aggressive surgical resection. Routine nodal clearance is not indicated [1].

The role of adjuvant radiotherapy and chemotherapy is controversial. Most large studies have failed to demonstrate proven improvement in overall survival with adjuvant radiotherapy, although a few stated that there was a trend towards statistical significance [2, 4, 6, 23, 24]. The use of adjuvant radiotherapy is especially advocated when clear surgical resection margins are not possible [6, 24]. Sarcomas are traditionally resistant to chemotherapy and very few studies have investigated the role of chemotherapy in the treatment of MPNSTs. However, a recent meta-analysis of the pooled data of 12 trials examining the efficacy of first-line chemotherapy in the treatment of MPNSTs compared to other soft tissue sarcomas found promising results with the combination of doxorubicin and ifosfamide [25].

The MPNSTs have the highest recurrence rates amongst sarcomas [26]. Anghileri et al. reported one of the largest case series of MPNSTs with the 10-year local recurrence, distant metastasis and disease-specific mortality rates of 29, 29 and 43%, respectively. The significant adverse prognostic factors are the tumours located in the trunk and head and neck region, recurrent disease, positive surgical resection margins, larger tumour size and tumour grade [2, 6].

The present case was diagnosed to have ileocolic intussusception with a soft tissue tumour forming the lead point. The diagnosis of MPNST was clinched on histopathological examination of the surgical specimen along with IHC. The present case is reported to highlight the importance of a high index of suspicion in patients with unusual presentations of abdominal pain, the role of imaging in diagnosing intussusception and finally, the role of IHC in diagnosing MPNST of the gut.

In conclusion, MPNSTs are amongst the most aggressive soft tissue sarcomas. MPNSTs of the gastrointestinal tract are extremely rare and their ideal management is yet to be formulated. However, from the literature as well as in our case, it appears that attainment of clear resection margins is of paramount importance. Radiotherapy, notwithstanding, the long-term morbidity to the bowel and chemotherapy may have a significant role to play in recurrent disease and in cases where wide local excision cannot be achieved. Through the experience with this case, we suggest that when the wide local excision of MPNSTs of the gastrointestinal tract is feasible,

careful postoperative follow-up with periodic imaging may be a preferable management option.

Compliance with Ethical Standards

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Conflict of Interest The authors declare that they have no conflict of interest.

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