Excellent response of malignant peripheral nerve sheath tumour of retroperitoneum to radiation therapy

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SUMMARY

Malignant peripheral nerve sheath tumours are high-grade sarcomas originating from Schwann cells or nerve sheath cells. Most of these tumours are associated with major nerves of the body wall and extremities. The lower extremity and the retroperitoneum are the most common sites. Surgery is the cornerstone of treatment, however, radiation therapy is usually used as an adjuvant treatment. In this paper we present a 57-year-old Iranian woman with malignant peripheral nerve sheath tumour of retroperitoneum who was operated subtotally and then underwent radiation therapy which led to disappearance of all gross residual disease.

BACKGROUND

Malignant peripheral nerve sheath tumours (MPNSTs) account for approximately 5–10% of all soft tissue tumours.¹ Retroperitoneum is one of the common sites of disease presentation.² On the contrary, MPNST is one of the frequent tumours in retroperitoneal cavity.³ Complete surgical excision of these tumours with negative margins is the mainstay of treatment.^{1 4–8} Although there are some controversies regarding the role of radiation therapy, most specialists believe that it can improve local control,^{1 3 4 7–9} however, achieving complete radiological response after radiation therapy is not common. Now, we present a patient with subtotally resected MPNST of retroperitoneum and excellent response to radiation therapy.

CASE PRESENTATION

A 57-year-old Iranian lady was referred to our centre subsequent to subtotal resection of retroperitoneal MPNST performed 4 months earlier. The problem started 2 months before surgery when the patient herself noticed a painless mass in the left side of her belly.

She had no serious problem in medical history and no evidence of neurofibromatosis in herself or her family. Ultrasonographic examination showed an echogenic heterogenous 18.5×14.5×10 cm mass in the left side of the pelvis extending superiorly to the umbilical area. A malignant ovarian mass was at the top of the list of differential diagnosis proposed by the sonologist. Abdominopelvic CT scanning with oral and intravenous contrast (figure 1) revealed a 15×15×13 cm lobulated heterogeneous retroperitoneal soft tissue mass. Liver, pancreas and kidneys were normal and there was no evidence of peritoneal seeding or ascites. The patient was operated and multiple pieces of brownish coloured resected specimen totally measuring

21×14×5 cm were sent to the pathology department. Pathology revealed spindle-shaped neoplastic cells with large oval nuclei and prominent nucleoli arranged in fascicles with pseudorosette features. Mitotic figures, some of which were atypical were seen (figure 2A). Immunohistochemistry showed s-100 positive tumour cells (figure 2B).

INVESTIGATIONS

The patient had no complaints on referral to our centre and because of her obesity palpitation of no mass in abdominal examination was possible. The patient had an abdominopelvic CT scanning (figure 3) at referral revealing a large lobulated retroperitoneal mass adjacent to the lower pole of the left kidney causing grade I hydronephrosis.

DIFFERENTIAL DIAGNOSIS

MPNST is composed of spindle cells. Four major subtypes of MPNST are: glandular, melanocytic, rhabdomyoblastic and epithelioid.¹⁰ MPNST lesions showing rhabdomyoblastic differentiation were named as Triton tumour. Rare MPNST cases contain multiple sarcomatous tissue types, especially osteosarcoma, chondrosarcoma and angiosarcoma. Other soft tissue sarcomas such as fibrosarcoma, leiomyosarcoma and monophasic synovial sarcoma are in differential diagnosis.¹¹ It should be noted that fibrosarcoma and synovial sarcoma have a more uniform fascicular pattern, contain symmetric fusiform cells resembling fibroblasts and obviously lack features of neural differentiation. Immunostaining can be invaluable in differential diagnosis. Leiomyosarcoma can usually be distinguished from MPNST without undue difficulty. Its cells have deeply eosinophilic cytoplasm, centrally placed blunt-ended nuclei and juxta nuclear vacuoles. In a Masson trichrome stain its cytoplasm is fuchsinophilic with longitudinal striations. The cytoplasm of MPNST is usually less fuchsinophilic without longitudinal striations. An important diagnostic problem is the distinction of neurofibromas with one or more unusual features from an MPNST. This occurs typically with 'borderline' neurofibromatous lesions of von Recklinghausen's disease. A diagnosis of malignancy depends on the findings of enhanced cellularity, diffuse atypia and usually at least a low level of mitotic activity. The criterion of mitotic activity paradoxically does not apply to schwannoma. Schwannoma displaying mitotic activity pursue a benign course, and rarely has this tumour been known to undergo malignant degeneration.

Thus, when material from a small biopsy specimen is evaluated, it is hazardous to attempt to

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Figure 1 CT scanning shows a large retroperitoneal tumour.

distinguish a cellular schwannoma from an MPNST solely on the basis of mitotic activity. In this situation, a larger sample of the mass is necessary to determine if the tumour in question has an Antoni A and B pattern, perivascular hyalinisation, encapsulation or other typical features of a schwannoma.¹²

TREATMENT

Since three-dimensional (3D) conformal therapy is not available in our centre yet, a two-dimensional treatment with two parallel apposed fields according to preoperative tumour volume and 2 cm margins in each side was performed with a daily dose of 180cGY and was continued to 3600cGY. Then, the margins were decreased to 1 cm and the treatment continued to 4500cGY. At last, 1500cGy radiation dose was delivered to the postoperative residual tumour with anterior and posterior oblique fields. The patient tolerated the treatment well without any serious problem. Six weeks later, CT scanning was repeated and showed partial response (figure 4). We proposed that the patient refer to the surgeon for reoperation; however she refused to do so. She planned to travel from which she returned 6 weeks later and this time she accepted visiting the surgeon. CT scanning was repeated for re-evaluation and fortunately and surprisingly there was no evidence of tumour (figure 5).

Figure 3 CT scanning shows a gross residual after surgery.

OUTCOME AND FOLLOW-UP

Now 4-month postradiation therapy the patient's condition is fairly well.

DISCUSSION

Sarcomas account for one-third of retroperitoneal tumours and 15% of soft tissue sarcomas arise in the retroperitoneum.^{13 14} The most common histological subtypes of retroperitoneal sarcomas are liposarcoma (41%), leiomyosarcoma (28%), malignant fibrous histiocytoma (7%), fibrosarcoma (6%) and MPNST (3%), respectively.¹³ MPNSTs, also reported as 'malignant schwannoma', 'neurogenic sarcoma' and 'neurofibrosarcoma', are rare tumours of the neural sheath.¹¹ MPNSTs account for approximately 5–10% of all soft tissue tumours and they have a known association with neurofibromatosis type 1 (NF-1).¹ About 40–50% of MPNSTs are associated with a family history of NF-1¹¹ and 2–29% of patients with NF-1 develop MPNST.¹ Radiation therapy may be a risk factor.^{4 7–9 11} Most MPNSTs occur in conjunction with large peripheral nerves such as the sciatic nerve, the brachial plexus and the sacral plexus.⁴ Ducatman *et al*⁹ evaluated 120 cases and showed that 46% of tumours arose from the trunk. In another study by Ghosh *et al*,⁶ from 115 patients tumours in 17(15%) cases originated from retroperitoneum. Usual clinical presentation is an enlarging mass with or without pain and dysesthesia. Motor weakness might occur.^{4 5} In our patient it presented as a painless mass.

Figure 2 (A) Malignant peripheral nerve sheath tumour (MPNST) consisting exclusively of dense fascicles of spindled cells (H&E×40). (B) S-100 protein immunostain shows focal staining of cells in an MPNST (×40).

Figure 4 CT scanning 6 weeks after radiation therapy shows more than 50% decreasing tumour size.

Tumour size is usually greater than 5 cm especially in patients with NF-1.⁶⁻⁹ Our patient had a very large mass of about 15×15×13 cm. CT scanning is the most useful tool in the evaluation of retroperitoneal tumours.¹³⁻¹⁴ Modern multidetector computed CT scanners provide an excellent information of the relationship between nearby structures and are critical to preoperative planning. Besides, it can identify metastatic lesions in the liver or peritoneal cavity. In addition, characterisation of fatty tumours and detection of intra-abdominal metastasis are possible with CT scanning. For the pelvis, CT scanning is an excellent modality for detecting bone invasion.¹³ Although MRI is the imaging modality of choice for evaluation of MPNSTs of extremity and head and neck,⁴⁻¹¹ motion artefacts decrease its sensitivity for evaluation of retroperitoneal tumours.¹³ According to these facts we used CT scanning. Whenever a suspected sarcoma exists in retroperitoneal cavity and it is resectable, surgery and resection of tumour with negative margin would be the choice. However, whenever diagnosis changes the preoperative therapy, a percutaneous biopsy is performed.¹³⁻¹⁴ Most of the MPNSTs are high grade.⁴⁻⁷ They are highly cellular, pleomorphic and mitotically active, with areas of necrosis and frequent vascular proliferation.⁷ There are many controversies regarding the role of radiation therapy in management of MPNST.¹⁻⁴⁻⁵⁻⁹ According to some of these studies radiation

Figure 5 CT scanning 12 weeks after radiation therapy shows an excellent tumour response.

therapy decreases the risk of local recurrence and improves local control, however, it does not make for better survival. Most specialists recommend radiation therapy in high-risk patients: large tumour size (more than 5 cm or more than 10 cm in different centres), high grade tumours and margin positive tumours. There is also some disagreement about optimal timing of radiation therapy: preoperatively versus postoperatively. Each one has some advantages and disadvantages. In a preoperative setting, tumour volume and its relation to adjacent organs is accurately seen in CT scanning and therefore radiation planning is more reliable. On the other hand, a large tumour pushes the critical organs such as small intestine, liver and kidneys and acts as a natural shield and therefore using larger amounts of radiation dose usually necessary for treating sarcomas could be possible. Lower doses and smaller treating area could be acceptable. Theoretically, tumour with intact blood supply shows a better response to radiation therapy, tumour shrinkage increases resectability and the chance of tumour spillage decreases. However, postsurgical complications, most often wound infections or dehiscence increase, and precise staging is impossible in such settings. There are even more controversies about the role of chemotherapy in MPNSTs.⁴⁻⁵⁻⁷⁻⁹⁻¹⁵⁻¹⁹ Chemotherapy used in unresectable tumours and local or systemic relapse may produce some degrees of response. In adjuvant settings it may be helpful in young patients with large high grade tumours.

There are several imaging criteria for assessment of tumour response to radiation therapy and/or chemotherapy. Two of the most famous are the WHO criteria and Response Evaluation Criteria in Solid Tumours in both of which responses must be confirmed at 4 weeks. However, at what time after termination of treatment, for example, must preoperative radiation and/or chemotherapy imaging be repeated for assessment? This is not mentioned in any of those two criteria. There are some controversies over the optimal time for reassessment and then operation in various tumours such that part of their treatment was done preoperatively. It takes a period of time for maximal tumour response to radiation and/or chemotherapy to happen. It is approximately 4–8 weeks for various tumour types such as rectal adenocarcinoma, oesophageal cancer, head and neck tumours and according to limited studies soft tissue sarcomas. On the other hand, most surgeons believe that radiation induced fibrosis increases beyond this time and operation becomes technically difficult and the risk of surgical complications and locoregional recurrence increases. There are some reports indicating that longer time intervals may cause better tumour response. In our patient, although CT scanning 6 weeks post-treatment showed a partial response mass however, reassessment at 6 weeks later (12 weeks) post-treatment showed incredible complete response.

Learning points

- In spite of controversies surrounding the effectiveness of radiation therapy in management of malignant peripheral nerve sheath tumours (MPNSTs) this modality, at least in some cases like ours can be useful.
- It seems that radiation therapy might eradicate a large gross residue.
- Longer time interval between radiation therapy and tumour reassessment (about 12 weeks) may be necessary to obtain maximal response in case of MPNST treatment.

Competing interests None.

Patient consent Obtained.

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