Novel treatment (new drug/intervention; established drug/procedure in new situation)

Management of a large retroperitoneal primitive neuroectodermal tumour: 'a multimodal approach'

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Summary

Retroperitoneal primitive neuroectodermal tumour (PNET) is a rare disease having poor prognosis. Treatment mainly consists of en block resection of the tumour to achieve RO resection, however multimodal approach has also been used with improved survival. The authors report a 40-year-old male with large retroperitoneal PNET adherent to aorta and compressing the inferior vena cava. He was subjected to P6 protocol chemotherapy (cyclophosphamide, adriamycin, vincristine, ifosfamide and etoposide) in view of borderline operability. Postchemotherapy contrast enhanced CT revealed significant reduction in size of the lesion. He underwent complete resection of the tumour followed by concurrent chemoradiation. He remains asymptomatic on follow-up over a period of 2 years.

BACKGROUND

Primitive neuroectodermal tumour (PNET) is a rare malignant soft tissue tumour arising from neural crest with overall incidence of 1% among all sarcoma.¹ PNET typically expresses high amounts of the MIC2 antigen (CD99) and exhibits highly characteristic chromosomal translocation t(11:22)(p13; q12).² PNET commonly arises from the soft tissue of chest wall (Askin tumour).³ PNET is a very aggressive tumour with poor prognosis, with a 5 year survival rates in the range of 45–55%.³ However, survival can be improved with multi-modal therapy (surgery, chemotherapy and radiation). Such a tumour arising from retroperitoneal space is rare with few cases been reported.⁴ We report a large retroperitoneal PNET in a adult male managed with a multi-modal approach.

CASE PRESENTATION

A 40-year-old male reported with dull aching abdominal pain predominantly in periumbilical region radiating to back. He also gave a history of decreased appetite, weight loss (8 kg over 4 months), and postprandial fullness in the epigastric region. He denied history for fever, vomiting, gastrointestinal bleeding and haematuria. He had no associated comorbidities. Clinical examination revealed a large, well defined, firm, immobile mass involving the right quadrants of the abdomen with midline extension and cross over to left quadrants.

INVESTIGATIONS AND TREATMENT

His haematological and biochemical parameters were unremarkable. Abdominal ultrasound revealed large heterogeneous lesion compressing the inferior vena cava (IVC). Contrast enhanced CT (CECT) of the abdomen and pelvis showed a 15.7×10.7×10.4 cm heterogeneously enhancing mass in the retroperitoneum with diffuse margins. Superiorly the mass was seen extending upto the head of pancreas, displacing third and fourth part of the duodenum

anteriorly and inferiorly it was extending upto the aortic bifurcation. The lesion was seen compressing the IVC and was adherent to aorta in few sections (figure 1). There was no stigma of metastatic disease. In the view of borderline operability of the lesion, staging laparoscopy and biopsy was done. Biopsy revealed malignant tumour with small round cell appearance, with positive immunohistochemistry for cytokeratin and synaptophysin. Strong positivity for Mic 2 antigen was seen, with Mib-1 staining index of 20–25%. In the view of locally advanced nature of the disease with borderline operability, he was subjected to chemotherapy. He received P6 protocol chemotherapy (cyclophosphamide, adriamycin, vincristine, etoposide and ifosfamide) along with mesna and granulocyte macrophage colony-stimulating factor. He tolerated the systemic chemotherapy well. A follow-up CECT showed significant reduction in size of the tumour with areas of decrease enhancement and well-defined margins (figure 2). He was subjected for exploration. On exploration the lesion was seen displacing the superior mesenteric artery and vein anteriorly along with the small bowel mesentery. The lesion was compressing IVC without its obvious involvement. Complete resection of the tumour was done (figure 3). Postop recovery was uneventful. Histopathology revealed PNET with clear margins. After recovery, he received concurrent chemotherapy (P6 protocol) and radiotherapy (45 Gy/25#/5 weeks).

OUTCOME AND FOLLOW-UP

He tolerated the regime well and remains to be asymptomatic on follow-up over 1 year.

DISCUSSION

PNET was first reported by Stout in 1918.⁵ Originally they were believed to be arising from the major nerves, but now considered to be from the neural crest.⁶ PNET is seen predominantly in young patients, with abdominal

Figure 1 Prechemotherapy scan reveals a large heterogeneously enhancing retroperitoneal mass with evidence of loss of fat planes between the mass and retroperitoneal vessels (aorta (short arrow) and inferior vena cava (long white arrow)).

Figure 2 Postchemotherapy scan reveals a more well-defined minimally enhancing retroperitoneal mass (white arrow) showing reduction in size compared to the prechemotherapy scan.

Figure 3 Cut section of completely excised tumour.

pain or discomfort being the commonest presentation³ as was seen in our patient. PNET is considered to be a part of 'small round blue cell tumours', which also include Ewing's sarcoma, rhabdomyosarcoma, Wilm's tumour, malignant lymphoma and desmoplastic small round cell tumours.³

PNET of the retroperitoneum has been described in few publications, it is sporadically reported in kidneys, adrenals and pelvis. To the best of our knowledge, there are 30 cases of retroperitoneal PNET reported in the literature.

The CECT appearance of PNET is non-specific, but it is the widely used diagnostic modality for identifying this tumour. CECT often shows heterogenous lobulated mass displacing the adjacent organs. Tumours often show non-enhancing necrotic areas.¹⁻⁷ In our case, CECT showed large retroperitoneal mass with heterogenous enhancement with loss of fat planes at various points, suggestive of locally advanced nature of the lesion. However, after a course of induction chemotherapy there was a reduction in size of the lesion along with decrease enhancement, suggestive of areas of necrosis.

Histopathologically, the characteristic findings are well-defined clusters of undifferentiated small round cells, surrounded by desmoplastic stroma. The tumour cells are characterised by small hyperchromatic nuclei with scanty cytoplasm. PNET typically expresses high amount of Mic 2 (CD99) antigen and exhibits highly characteristic chromosomal translocation $t(11:22)(p13;q12)$,¹ which leads to fusion of WTI and EWS genes. In our case, the diagnosis was established by typical histopathological features along with immunohistochemistry positivity (cytokeratin, synaptophysin and Mic 2 antigen).

Although the prognosis is poor, survival can be improved with multi-modal approach. Lal *et al* recommended surgical resection of >90% of the tumour burden. They used

adjuvant chemotherapy with P6 protocol along with radiation to abdominopelvic region and reported significant survival.⁸ In our case, since the tumour was seen adherent to the major abdominal vessels, we subjected the patient to induction chemotherapy. The tumour responded to it by reduction in its size and vascularity which was documented on postchemotherapy CECT. Postchemotherapy en block resection of the mass was done. Following surgery the patient received concurrent chemoradiation. The patient was kept under regular follow-up and remains asymptomatic over 2 years. There are isolated case reports highlighting the role of neoadjuvant chemotherapy in management of these lesions.⁹

Singer *et al* showed that 5 year survival for adults with Ewing's sarcoma/PNET was 49% in those having localised disease treated with combined modality.¹⁰ His results also showed favourable predictors of survival being primary origin from the bone, size <8 cm, and favourable objective response to chemotherapy.¹⁰ In our case, factors like localised disease, good response to induction chemotherapy and R0 resection, would improve survival of the patient.

To conclude a downstaging approach with induction chemotherapy of large borderline operable retroperitoneal PNETs would increase the resectability rates, translating into improved survival.

Learning points

- Induction chemotherapy in borderline resectable or locally advanced PNET would help to downstage the lesion and improve the resectability, which may translate into improvement in survival.

Competing interests None.

Patient consent Obtained.

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