Short Communication

Desmoplastic small-round-cell tumor presenting as a Sister Joseph nodule

Abstract

We document a rare presentation of desmoplastic small-round-cell tumor (DSRCT) in a 25-year-old male. He presented with a nodular swelling in the umbilical region that was clinically suggestive of Sister Joseph nodule. Imaging studies showed multiple nodules over the peritoneum and the gastrointestinal endoscopies showed no lesions. An excision biopsy of the umbilical lesion showed small round cells with dense desmoplasia and immunohistotyping confirmed the diagnosis of DSRCT. Desmoplastic small-round-cell tumor is notable for its poor prognosis.

Key words:
Desmoplastic small-round-cell tumor, nodule, umbilicus

Introduction

Desmoplastic small-round-cell tumor (DSRCT) is a rare malignancy of adolescence and young adults. With a characteristic histology, specific immunohistochemistry, and a poor prognosis, it is typified by a very short survival after diagnosis.

Case summary

A 25-year-old man presented to the surgical department with complaints of pain and swelling in the lower abdomen. Examination revealed abdominal distension with a few dilated veins over the abdomen and a nodule over the umbilicus [Figure 1]. A clinical diagnosis of Sister Joseph nodule was made. Ultrasound revealed multiple nodules in the peritoneum. Computerized tomography revealed the presence of diffuse peritoneal, mesenteric nodules lymph nodes, and hepatomegaly [Figure 2]. Although we suspected a disseminated malignancy, the upper and lower gastro intestinal scopy was negative. Patient underwent an excision biopsy of the Sister Joseph nodule.

Histolopathological examination showed small round cells with an intense desmoplastic reaction arranged in islands, trabecular pattern, and as a single-file fashion [Figure 3]. Tumor cells were small-to-medium sized, with round to oval darkly stained basophilic nuclei having very scanty cytoplasm. Many mitotic figures were noted. In view of the numerous differentials to be considered for a small round cell tumor, an immunohistochemistry panel was ordered. The tumor was found to be positive for epithelial (cytokeratin) [Figure 4], mesenchymal (vimentin, desmin) [Figure 5], smooth muscle actin (myogenic), neural markers (S100), and negative for CD45 and CD99. This clinched the diagnosis of DSRCT.

Discussion

Desmoplastic small-round-cell tumor, an uncommon tumor usually seen in young adult males was first described by Gerald and Rosai.[1] The lesion presents with an abdominopelvic mass and ascites.[2,3] Imaging studies show large confluent masses over the parietal peritoneum, nodules over the mesentery, and ascites, usually with no organ involvement. Pressure effects on neighboring structures (intestines, ureters) have been described. Desmoplastic small-round-cell tumors have been described on other mesothelial surfaces such as pleura and tunica

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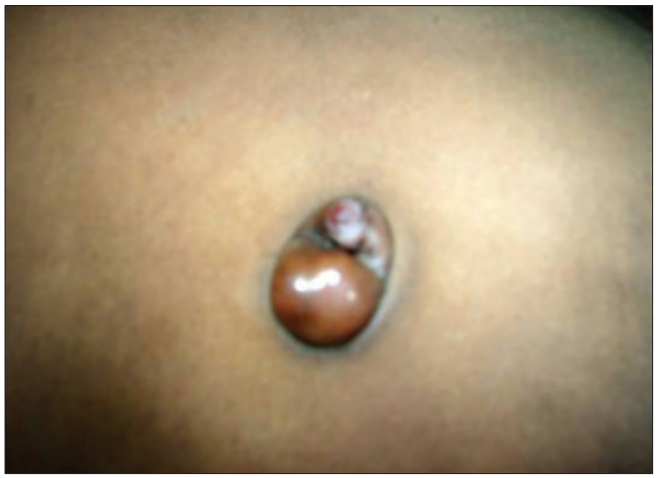

Figure 1: Shows a nodule over the umbilicus, suggestive of Sister Joseph nodule

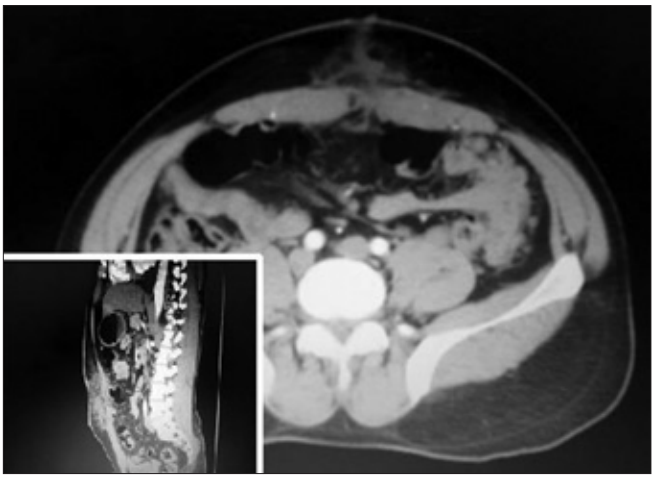

Figure 2: Computed tomography image shows multiple nodules and the Sister Joseph nodule

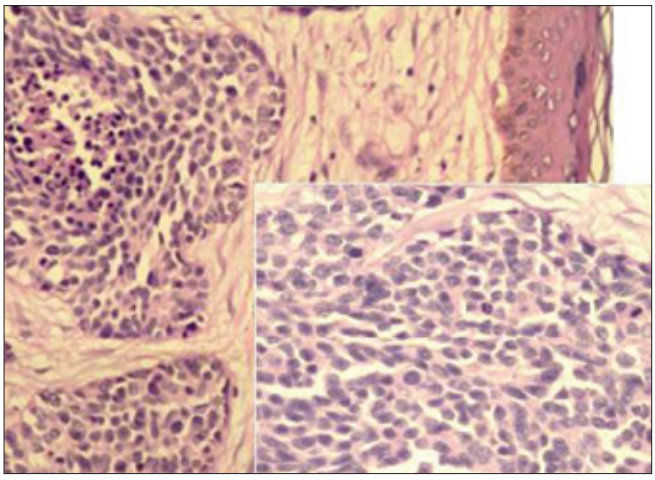

Figure 3: Shows islands of small blue round tumor cells surrounded by abundant desmoplastic stroma in the dermis. The overlying epidermis shows no involvement. (H and E, ×40). Inset shows mitotic figures in few tumor cells (H and E, ×100)

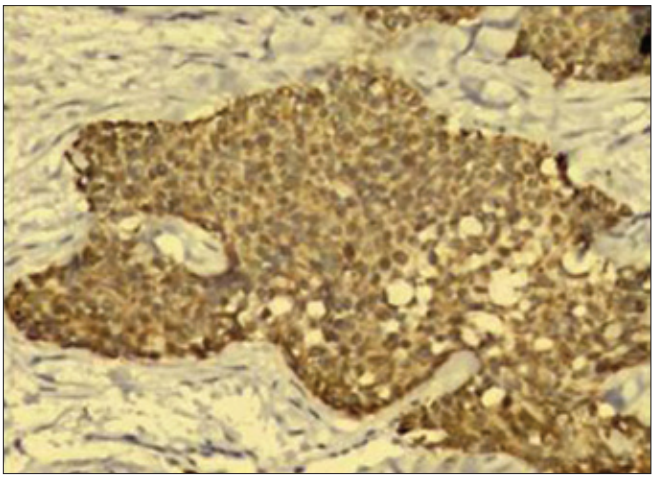

Figure 4: Tumor cells show cytoplasmic positivity for cytokeratin (Immunostain cytokeratin, ×100)

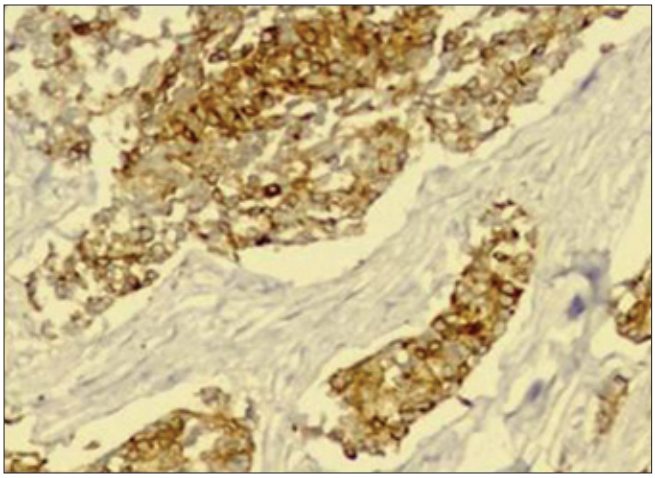

Figure 5: Neoplastic cell showing focal positivity for desmin (Immunostain desmin X40)

vaginalis as well as solid organs such as liver ovary, bone, pancreas, kidney, and even in non-abdominal locations like the nasal sinus and posterior cranial fossa.[4]

Morphologically, DSRCTs appear as multiple nodules at the affected site, with sometimes a larger dominant nodule. The cut surface of the tumor is firm, grey-white showing areas of necrosis and hemorrhage. Characteristic patterns noted on histology include islands of neoplastic cells arranged in diffuse sheets surrounded by a dominant desmoplastic stroma. Other patterns include infiltrative (Indian – file appearance), rosetting, and gland formation. Tumor cells appear uniformly small, round to elongated, with scanty cytoplasm. Nuclei typically are round hyperchromatic with inconspicuous nucleoli. The desmoplastic stroma is composed of fibroblasts and myofibroblasts embedded in loose collagenous tissue. Positivity with histochemical (Masson's Trichrome) and immunostains for muscle (smooth muscle actin) confirms its myofibroblastic origin.[5]

The differential diagnosis of DSRCT on histopathology include other round cell malignancy, eg, non-Hodgkin's lymphoma (NHL), Ewing's/primitive neuroectodermal tumor (PNET), Wilms' tumor and embryonal rhabdomyosarcoma. The distinguishing features of DSRCT are clinical presentation and multiphenotypia of tumor cells, with combined expression of epithelial/neural/mesenchymal markers and expression of EWS-WT1 genetic abnormality. Desmoplastic small-round-cell tumor demonstrates immunoreactivity for cytokeratin (CK), epithelial membrane antigen, vimentin, and neuron-specific enolase. Although the tumor cells express characteristic dot-like intracytoplasmic perinuclear positivity with desmin, it is consistently negative for myogenin and myoD1. Immunoexpression of WT1 antigen by tumor cells serves as a sensitive and specific marker for DSRCT. The WT1 gene is important for normal kidney and mesothelial development, and strong WT1 expression is noted in the splanchnic mesoderm during embryogenesis. This may be a reason for the DSRCT predilection for mesothelial surface. Its association with mesothelial sites may further be strengthened by the fact that these tumor cells co-express desmin and CK, a feature also exhibited by fetal mesothelial cells.[6]

In contrast to polyphenotypia in DSRCT, the neoplastic cells in NHL are positive for lymphoid markers such as CD45 and B-cell or T-cell immunostains. Ewing's family or PNET is positive for CD99, while embryonal rhabdomyosarcoma show positivity for desmin, myoD1, and myogenin. Renal involvement with triphasic pattern on the histology and positivity for WT1 immunostains are the distinguishing features for Wilms' tumor.

Cytogenetics

A recurrent specific chromosomal abnormality that has been reported in DSRCT is t(11:22) (p13:q12). The breakpoints in this translocation involve two genes: EWS, which is altered in the t(11;22) (q24:q12) that is characteristic of Ewing's family of tumors, and WT1, which is the gene for Wilms' tumor. EWS-WT1 chimeric transcripts (that can be demonstrated by reverse transcriptase polymerase chain reaction (RT-PCR) and fluorescence *in situ* hybridization (FISH)) are considered characteristic of the disease.[6]

Treatment

These are very rare tumors and therefore no comparison of treatment modalities is available to provide evidence-based data. The three modalities available for DSRCT are surgical de-bulking, combination chemotherapy, and radiotherapy. Most lesions present too late for a surgical resection to be possible. However, studies indicate a 34-month survival for those with a resection as against 14-month survival in those who have undergone only biopsy, while others indicate no such benefit.[7] Surgical de-bulking is of value in patients who have obstructive symptoms.

High-dose chemotherapy with ifosfamide, vincristine, and epirubicin showed only a marginal survival benefit. Combination chemotherapy shows some response. Protocol 6 uses seven cycles of chemotherapy, with cycles 1-3, and 6 using cyclophosphamide, vincristine, doxorubicin, while cycles 4, 5, 7 using ifosfamide and etoposide.[8] Local radiotherapy is not effective and whole abdominopelvic irradiation (WAPI) gives a median survival of 32 months and a median time to relapse of only 19 months.[9] Quaglia *et al.*, showed a survival benefit when all three modalities were combined as against either of them in isolation (3-year survival of 55% vs 27%).[9,10] Further new experimental treatment modalities include stem cells, monoclonal antibodies, and continuous hyperthermic peritoneal perfusion (CHPP) with cisplatin.[10]

Conclusion

The possibility of DSRCT should be considered in the differential diagnosis of umbilical nodule that shows round cells on histology, especially in the young. Immunohistochemistry helps to identify this rare tumor associated with a very poor prognosis.

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