CASE REPORT

Disseminated histiocytic sarcoma in a child: a clinicopathological dichotomy with 8 years survival

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SUMMARY

A 3-year-old girl presented with a non-healing ulcer, originating as a pustule over the right anterior chest wall of 1½ month duration associated with high fever. A subcutaneous nodule along with right apical and anterior axillary lymph nodes was palpable. Abdominal ultrasound and chest skiagram were normal. Fine needle aspiration cytology (FNAC) from the axillary lymph node was suggestive of embryonal rhabdomyosarcoma. Bone marrow aspirate was normal. The ulcer and subcutaneous nodule were excised completely with adequate margins. Histopathological examinations were compatible with malignancy of histiocytic origin with clear resected margins. The axillary nodes were free of tumour. Adjuvant chemotherapy was given for 13 months. The patient is doing well at 8 years follow-up.

BACKGROUND

Disseminated histiocytic sarcoma (DHS), also known as malignant histiocytosis (MH) is an aggressive, histiocytic neoplasm that arises in multiple sites simultaneously. Malignancy of histiocytic origin rarely occurs in children.¹ It is usually fatal with many patients succumbing even before a diagnosis is established. Here we describe the long-term outcome of a case presenting as multiple lesions with apparently complete cure.

CASE PRESENTATION

A 3-year-old girl presented with a non-healing ulcer on the anterior chest wall of 1½ month duration that had not responded to antibiotics. The non-healing ulcer had originated as a pustule over the right side of the anterior chest wall that had gradually and progressively increased in size with surrounding redness and minimal purulent discharge. The ulcer was associated with fever that was initially of mild to moderate grade but had become high grade since the past 2–3 weeks. She had received oral and intravenous antibiotics for more than a month. She had been extensively investigated for pyrexia of unknown origin with no improvement in symptoms. She had undergone a wedge biopsy elsewhere that showed non-specific chronic inflammation with no cellular atypia and no granuloma. She was thus referred for further treatment. Her pulse was 112/min, respiratory rate was 26/min and temperature was 101°C. The ulcer was 4×5 cm in size, with everted margins (figure 1).² The floor was fleshy, pink and purple. The base was fixed to the underlying muscle. There was a subcutaneous nodule palpable near the

anterior fold of the axilla. The right apical and anterior axillary lymph nodes were palpable.

INVESTIGATIONS

Haematological and biochemical values were normal: haemoglobin 12 g%, total leukocyte count 8100, P65L20E5M2, platelets 271 000, erythrocyte sedimentation rate 6 mm, urea 25 mg/dL, creatinine 0.6 mg/dL, Na/ K 143/5.3 and random blood sugar 104 mg/dL. Liver function tests including the prothrombin time were normal. Abdominal ultrasound and chest skiagram was normal. The urine routine and culture examination was normal. Tests for malaria parasite, Widal test and Montoux test were normal. The ulcer swab culture and blood culture were sterile. Fine needle aspiration cytology (FNAC) from the axillary lymph node was suggestive of malignancy with a possibility of embryonal rhabdomyosarcoma. A repeat FNAC/biopsy with immunocyto/histochemistry was advised. The bone marrow aspirate depicted cellular marrow with normal marrow components, prominent megakaryocytes and no metastatic deposits.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included a non-healing ulcer of tubercular or malignant origin. Rhabdomyosarcoma and peripheral neuroectodermal tumours are the most common malignancies involving the chest wall in children.

TREATMENT

A repeat wedge biopsy and lymph node biopsy was planned. On the operating table, it was decided to excise the ulcer and the subcutaneous nodule along with the two palpable lymph nodes completely. Consent was taken. The ulcer was excised with its base with a margin of 1cm of healthy skin all around. The fibres of the underlying muscle attached to the ulcer were also removed with a healthy margin of 0.5 cm from depth. A full-thickness flap was raised and the wound was closed with a suction drain. The histopathological findings depicted a malignant tumour with moderately pleomorphic histiocytes with high mitotic activity (10–12/HPF) with focal necrosis (figure 2). At places, the cells showed angiocentricity and infiltration into the overlying epidermis. The cells were immunopositive for CD 68 and focally for S-100 protein. A mixed population of CD 20 and CD 3 positive lymphocytes were also identified. Immunostaining for desmin was negative. The features were compatible with malignancy of histiocytic origin. Sections from the peripheral resected

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Figure 1 Clinical photograph showing (A) the ulcer with the excised subcutaneous nodule and anterior axillary lymph node placed on its anatomical location (B) Excised ulcer with its base with a healthy margin of 0.5 cm from depth and 1cm all around. (C) Wound closure with a full thickness flap closure over a suction drain (with kind permission from Publishers Jaypee Brothers, New Delhi).² (D) Scar of wound at follow-up.

margin of soft tissue, skin and deep resected margin were free of tumour. The subcutaneous nodule anterior to the axilla showed a similar malignant tumour. The two deep apical axillary nodes were free of tumour. The patient was given chemotherapy comprising vinblastine, prednisolone and 6 mercaptopurine for more than 13 months.

OUTCOME AND FOLLOW-UP

The patient is doing well and remained asymptomatic at 8 years follow-up, 7 years after completion of chemotherapy.

DISCUSSION

Histiocytoses, formerly histiocytosis X, are rare diseases involving histiocytes derived from bone-marrow stem cells. In 1987, the Histiocyte Society classified these into three groups based on the type of histiocyte cells:³

1. Dendritic cell disorder, Langerhans' cell histiocytosis (LCH). Rare diseases, juvenile xanthogranuloma and Erdheim-Chester Disease.
2. Macrophage cell disorder, haemaphagocytic lymphohistiocytosis and Rosai-Dorfman disease.

Figure 2 Photomicrograph shows dense dermal infiltration of a pleomorphic population of cells with focal ulceration of the overlying epidermis (A, H&E×40). The epidermis shows marked spongiosis, pseudo-epitheliomatous hyperplasia and infiltrate by the tumour cells (B, H&E×40). Higher power photomicrograph shows a discrete population of round to epithelioid cells with vesicular nucleus, prominent nucleoli and moderate amount of dense eosinophilic cytoplasm. Frequent mitotic figures are also noted. The tumour cells are interspersed by occasional small mature lymphocytes (C, H&E×400). Focal necrosis is identified in the lesion (D, H&E×40). The tumour cells show distinct peritheliomatous arrangement as well as vascular infiltrate (E and F, H&E; ×100; ×200). The tumour cells are strongly positive for CD 68 immunostain (G, IHC, CD 68×100), while the cells show very occasional positivity for S-100 immunostain (H, IHC, S-100 protein×100).

3. MH and includes certain kinds of leukaemia and malignant tumours.

MH is now referred to as DHS, when involving multiple sites. Histiocytic sarcoma refers to a lesion occurring at one site and not spreading beyond the local lymph node. Histiocytic sarcoma may be associated with acute lymphoblastic leukaemia and lymphoma.^{4 5}

The most common form of histiocytosis encountered in children is LCH followed by haemophagocytic lymphohistiocytosis, involving mononuclear phagocytes. There are only anecdotal cases of malignancy of histiocytic origin reported in children, involving central nervous system, lungs and bones.^{6–8} These have been histiocytic sarcomas involving only one site. Any similar case to one described here, presenting as a disseminated disease, involving the chest wall has not been reported hitherto.

Histiocytic proliferations in childhood have been a subject of curiosity and various workshops have been organised to study the distinguishing features.⁹ It is vital to distinguish between LCH and malignant lesions as the prognosis varies. Histologically, LCH lesions are granulomatous and have uniform distribution with orderly recruitment of cells to tissues; unlike the haphazard spread of malignant neoplasms. Regression of LCH lesions is frequent but rare in true malignancies.

It has been realised that most childhood malignancies in the past classified as ‘histiocytic’ were actually anaplastic large cell (Ki-1) lymphomas of T-cell type and that true histiocytic malignancies are exceedingly rare in the paediatric age group.^{1 10} Histological guidelines have been laid to distinguish between the two.¹¹ The differential diagnosis include malignant fibrous histiocytoma inflammatory variant and malignant rhabdoid tumour.¹²

The case described presented as a chest wall lesion and was treated as a malignant lesion. The clear distinction between benign and malignant chest wall tumours may not always be possible clinically and radiologically. It is wiser to consider all tumours of the chest wall as malignant until proven otherwise and carry out a wide excision, enabling an adequate diagnosis and improved chances of complete cure. Peripheral primitive neuroectodermal tumours including Ewing’s sarcoma that express MIC2 glycoprotein (CD99) and show the specific chimeric gene of EWS-FLI1 form an important differential diagnosis of chest wall tumours in children.

True MH as described here is an exceedingly rare disease, and only a few reports have clearly identified the histiocytic origin of malignant cells.¹³ These lesions are usually quite aggressive, clinically behave like different types of lymphoma and can present as single tumours or can be quite widespread. Despite unresolved nosological and terminological difficulties, they should be classified according to the lineage of the aberrant cells in a given tumour.¹⁴ As per the latest WHO classification of histiocytic and dendritic cell tumours, a negative expression of accessory/dendritic cell markers CD1a, CD21 and CD35 is seen in histiocytic sarcoma.^{15 16} Histiocytic sarcomas should be CD163 (+) CD68 (+) Lysozyme (+) CD1a (–) CD21 (–) CD35 (–) and CD33(–).¹⁶

Patients are usually best treated with combinations of chemotherapy, especially in disseminated forms, such as used for lymphoma and aggressive histiocytic disorders. For localised disease, sometimes surgery, with or without radiation therapy, is effective. Successful treatment for HS in children with surgery, chemotherapy and radiotherapy has been described.^{6–8 17} However, though disseminated HS is a potentially lethal disease, combination chemotherapy has offered a chance for cure in some patients.¹⁸ In the case described, early surgical excision of the lesions with clear margins followed by chemotherapy and stringent follow-up contributed to successful treatment.

Learning points

- Malignant histiocytic lesions are extremely rare in children.
- A rare case of disseminated histiocytic sarcoma presenting as a chest wall ulcer and subcutaneous nodule is described.
- A strong suspicion of malignancy for a non-healing ulcer can expedite the treatment and hope for complete cure.
- Early surgical excision of the lesions with clear margins is the mainstay of therapy.
- Adjuvant chemotherapy helps reduce the risk of local recurrence and widespread metastases.

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