Rare disease

Alveolar rhabdomyosarcoma with multiple distal metastases. A case report and review of literature

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Summary

An 18-year-old boy, presented with a history of right hip pain with movement restriction and proptosis of right eye. There was severe anaemia, febrile neutropaenia and bleeding manifestations. CT scan of right orbit documented a retro orbital mass. MRI revealed a mass on right side of the pelvis with metastatic deposits in spine. Biopsy from that mass revealed alveolar rhabdomyosarcoma. Bone marrow biopsy showed sarcomatous involvement with decrease in all three cell lineages. Chemotherapy was started according to standard protocol. We lost the patient after 3 weeks of initiation of chemotherapy. In our case, the unusual primary site and presentation with multiple distal metastases makes this case stand apart and therefore worth reporting.

BACKGROUND

Alveolar rhabdomyosarcoma (ARMS) is an aggressive soft tissue malignancy of children and adolescents. It is most commonly found in peripheral extremities. There is a predilection for deep musculature of extremities, but it may arise from head, neck, trunk, pelvis and retroperitoneum as well.¹ The tumour often presents as a painless mass, but symptoms produced by compression of structures may sometimes give clue regarding primary site. A substantial fraction of patients with ARMS have metastasis at the time of diagnosis. It commonly spreads to the lung, bone marrow (BM) and distal lymph nodes. Involvement of unusual anatomic sites such as pancreas, breast, kidney, etc is also reported.² Depending on the location and stage, they can mimic other neoplasms, thus making the diagnostic process challenging. What is more intriguing in our case was the presence of multiple distant metastases at the time of presentation.

CASE PRESENTATION

An 18-year-old boy presented with a history of pain in the right hip for 3 months, with inability to fully extend the joint, proptosis of the right eye for 1 month with blurred vision and photophobia for 2 weeks. There was an irregular rise of temperature, gum bleeding, easy bruising and fatiguability for 2 weeks prior to admission. On examination, he was irritable, febrile with stable vitals. He was pale and emaciated. He had bleeding gums and petechial spots over the skin. Regional survey revealed his right hip joint in semiflexed position along with a swelling involving the area overlying the right anterior superior iliac spine. There was proptosis and restricted movements of the right eye in all directions. Vision of the eye was reduced to finger counting up to 3 m. The eyelids were oedematous, conjunctiva very much congested and chemosed. Rest of the systemic examination was unremarkable.

INVESTIGATIONS

The complete haemogram on admission showed pancytopenia as evidenced by a haemoglobin concentration of 8.6 g/dl and a leucocyte count of $2.7 \times 10^9/l$ and platelet counts ($105 \times 10^9/l$), with no abnormal cells. MRI revealed an abnormal mass on the right side of the pelvis with signal changes in lumbar vertebrae suggestive of metastatic deposits (figure 1a,b). CT scan of orbit documented a right retro orbital mass (figure 1c). BM trephine biopsy revealed hypercellular marrow, which demonstrated gross reduction of all three blood cell lineages with sarcomatous infiltration (figure 2a). Tru-cut biopsy from the pelvic mass showed an alveolar pattern of the fibro-vascular stroma enclosing the neoplastic cells. The cells were variable in size and shape with acidophilic cytoplasm and hyperchromatic nucleus exhibiting numerous mitoses (figure 2b). Immunohistochemistry (IHC) was not carried out due to financial constraints.

TREATMENT

The oncologist and radiologist were consulted for planning of therapy. Considering his advanced disease and the presence of spinal metastasis, we started concurrent chemoradiation. He was started on chemotherapy consisting of doxorubicin (50 mg/m^2), vincristine (1.4 mg/m^2) and cyclophosphamide (700 mg/m^2) accompanied by radiation therapy to the primary site. There was initial improvement in blood counts but later on there was worsening of BM dysfunction and despite best supportive care for complications, we lost the patient 3 weeks after the initiation of chemotherapy.

OUTCOME

We lost the patient 3 weeks after initiation of chemotherapy. In our patient, there was a paucity of haematopoietic cells with malignant round cell infiltration in the BM. Giving concomitant chemotherapy and radiotherapy to

Figure 1 (a) Coronal MRI showing a large heterogenous soft tissue mass (red arrow); (b) MRI lumbosacral spine showing osseous metastases involving numerous vertebral bodies (red arrows) and; (c) CT brain showing right retro-orbital space occupying lesion (red arrow).

the patient may have resulted in severe cytopaenias or immunosuppression, which may have escalated the clinical deterioration.

Figure 2 (a) Bone marrow section showing paucity of haematopoietic cells with malignant round cell infiltration (Leishman's staining method) and (b) histopathological examination (HPE) section of right iliac fossa mass showing densely packed small round cells (H&E, ×400).

DISCUSSION

RMS is the most common soft tissue sarcoma in childhood and adolescence.¹ This tumour is thought to derive from myogenic precursor cells and belongs to the group of small round blue-cell tumours (SRBCTs). On the basis of histology, two main RMS subgroups are distinguished: the ARMS and the embryonal RMS (ERMS). Alveolar tumours contribute to approximately one-third of RMS and are histologically characterised by the presence of densely packed, small, blue, round cells, often lining a septation reminiscent of a pulmonary alveolus, giving rise to its name. ARMS is usually found in adolescents.¹ Alveolar RMS tends to occur in slightly older patients with a mean age of 15–20 years.³ ARMS typically arise in the deep musculature of the extremities and comprise approximately 50% of all extremity RMS. Unusual primary sites are head, neck, trunk, pelvis and retroperitoneum. Primary tumours involving extremity, trunk or paratesticular locations are more common in adolescent.¹ RMS of the extremities has been reported as more aggressive with higher incidence unusual anatomic sites of metastases.² This malignant soft tissue tumour can spread by means of direct invasion, lymphatic and haematogenous metastases.⁴ BM lesions are found in about 30% of the metastatic cases at the presentation. Studies have shown that alveolar RMS tends to involve BM more frequently than ERMS. BM metastases at diagnosis signifies worse prognosis than with metastases to other organs.^{5 6} Inclusion of BM trephine biopsy as a routine part of the investigation of patients with features of BM failure is essential and clinicians should be aware of the fact that ARMS frequently masquerade as haematological malignancies.⁷ The ARMS involving the orbit is extremely rare. Review of literature revealed that only 11 cases of secondary orbital metastasis has been reported so far. The mechanism of orbital metastasis is haematogenous in nature. Orbital metastasis usually found in advanced stage of disease and tumours of the orbit may cause complications like proptosis and ophthalmoplegia.^{8 9} Metastatic sarcomas involving the spine are rare. Data in the literature regarding this are limited. Case reports are available with ERMS. Spinal cord drop metastasis may occur in tumours involving the head and neck. The incidence of bony

metastasis in RMS is not clearly defined. This tumour has no specific radiological feature. Local bone invasion has been shown in 24% of cases, and bone metastases are typically ill-defined lytic lesions.^{1–10} We do consider this case to be a metastasis of RMS, primary being in the pelvic musculature as because in our case, the patient developed the tumour in pelvis followed by proptosis after 8 weeks. The time lag is strongly suggestive of secondary involvement of the orbits.

Clinicopathological behaviour and resulting prognosis of RMS differ significantly among the different subgroups, necessitating subgroup-specific treatment regimens and making subgroup classification clinically relevant. However, classification based solely on histology is not easy and does not always allow an unambiguous subclassification. IHC, which generally is widely accepted as a standard tool for tumour diagnosis allow discrimination of this tumour from other SRBCTs.¹¹

The standard of care for metastatic alveolar RMS is combination chemotherapy with vincristine, adriamycin and cyclophosphamide (VAC) alone without concomitant radiotherapy. VAC have been the gold standard for combination chemotherapy in the treatment of most cases of RMS.¹² Aggressive chemotherapeutic agents and the best supportive care for complications may offer the optimal treatment protocol for improving the prognosis of patients with this disease. Evidence suggests that use of multimodal therapy regimen may improve the results for adult RMS. High-risk soft tissue sarcomas present a significant dual threat locally and at distant anatomic sites. For this reason, a dose-intensity chemoradiation strategy was explored in the Massachusetts study.¹³ Concurrent radiotherapy and combination chemotherapy was well tolerated and overall survival was good. Because most current literatures are case reports and lack information on the long-term outcome of treatment, we also hope that there will be randomised trials to better define the role of combined modality therapy in the coming years.

In our case, the primary site was relatively uncommon according to literatures. Regarding presentation of the case, there are unusual sites of metastases. However, the uncommon feature, which makes this case stand apart, is the presence of multiple distant metastases at the time of presentation, which still have not been reported. Regarding the outcome, giving concomitant chemotherapy and radiotherapy probably resulted in severe immunosuppression that may have escalated towards his unfortunate death.

Learning points

- ▶ In the present case the unusual primary site and presentation with multiple distal metastases were most intriguing.
- ▶ Alveolar rhabdomyosarcoma can mimic other neoplasms, creating a diagnostic challenge.
- ▶ Rarely haematogenous spread to the orbit occurs in advanced stage of disease.
- ▶ Bone marrow metastases at diagnosis signifies worse prognosis.
- ▶ Concomitant chemotherapy and radiotherapy, although indicated for advanced disease, may lead to untoward outcome.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Sarkar D, Ray S, Saha M, Chakrabarti P. Alveolar rhabdomyosarcoma with multiple distal metastases. A case report and review of literature. *BMJ Case Reports* 2012;10.1136/bcr-2012-006523, Published XXX

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