CASE REPORT

Primary cutaneous Ewing sarcoma presenting as a chest wall lesion

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SUMMARY

A 10-year-old boy presents with a rare case of primary cutaneous Ewing sarcoma. The left-sided chest wall lesion was initially thought to be a benign haemangioma and treated with cryotherapy. Within 4 months, the lesion returned and post excision was found to be primary cutaneous Ewing sarcoma on histology. Few cases of primary cutaneous Ewing sarcoma exist in the literature, and although it is a rare differential for paediatric skin lesions, it is an important consideration due to the associated mortality risk in this young cohort.

BACKGROUND

Ewing sarcoma is the second most common primary bone tumour in the paediatric population.¹ Histologically, Ewing sarcoma comprises small round blue cells which express CD99. It is characterised by a chromosomal translocations of the EWS gene, namely t(11;22)(q24;q22).²

While a well-known tumour when seeded in the bone and soft tissue, few cases have been reported of primary cutaneous Ewing sarcoma. In the few cases documenting cutaneous disease, patients were generally older (17 years old) and were female. Clinically, lesions were described as slow growing, soft and haemorrhagic in appearance.³

This is in stark contrast to our patient, a young boy who presented with a raised, vascular appearing lesion on his chest wall which was initially misdiagnosed as a haemangioma.

CASE PRESENTATION

A 10-year-old boy presents with a 12-month history of a left-sided chest wall lesion (figure 1). It was initially thought to be benign haemangioma and removed via cryotherapy by his general practitioner but was noted to return within 4 months. Due to its recurrence and darker colour, the patient was referred in for surgical review.

Of note, our patient possessed an unremarkable medical history, with no known regular medications or known allergies. He had no known family history of hereditary illness or paediatric malignancy.

An ultrasound investigation revealed a 11×10×12 mm exophytic lesion, anterior to the pectoralis muscle. The lesion was noted to be hypervascular, solid and hypoechoic. A feeding artery was identified, which appeared to supply

the lesion and further intensified suspicions that this may be a malignant lesion.

A subsequent MRI was performed 2 months later, whereupon the lesion had rapidly increased in size to 15×18×13 mm with extension into the pectoralis muscle belly and had two prominent feeding vessels which likely arose from the left internal thoracic artery.

Due to these findings and rapidity of growth over the previous 2 months, the lesion was excised with a 3 mm margin 2 weeks later and sent for histopathology. This subsequently revealed primitive neuroectodermal tumour (PNET) and the patient was referred to paediatric oncology.

Paediatric oncology confirmed the lesions had histological and immunohistochemical characteristics of PNET. Cytogenetics reported disruption of the EWSR1 gene. The patient was eligible for and consented to the Euro Ewing 2008 treatment protocol which included subsequent central review of the histopathology. The consensus was that of a malignant tumour with morphological features of Ewing sarcoma.

INVESTIGATIONS

To complete staging, a fluorodeoxyglucose positron emission tomography (FDG-PET) and CT scan were organised which reported no metastatic disease. Further investigation with bone marrow aspirates and trephines showed no evidence of disease.

TREATMENT

Once the diagnosis of Ewing sarcoma was confirmed, the patient commenced chemotherapy 1 month postexcision. Six cycles of vincristine, ifosfamide, doxorubicin, etoposide (VIDE) chemotherapy was commenced and the patient is currently on his last cycle. Concurrently, he is on pneumocystis and antifungal prophylaxis in light of his immunocompromised state.

Once induction chemotherapy is completed, the lesion will require re-excision to ensure a wide tumour clearance and safeguard against local recurrence and limit the potential long-term consequences of chest wall radiotherapy. This will be followed by further chemotherapy in accordance with the Euro Ewing protocol.

Psychosocial support was offered to the patient and family throughout chemotherapy due to the confronting diagnosis and treatment.

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Figure 1 Left-sided anterior chest wall lesion.

OUTCOME AND FOLLOW-UP

The patient tolerated chemotherapy treatment well with no significant complications. He continues to be followed up by paediatric oncology post his initial diagnosis and management.

DISCUSSION

Primary cutaneous Ewing sarcoma is extremely rare, and due to its benign appearance, is predisposed to being underdiagnosed.⁴ Few case reports exist, with only 78 cases reported in the literature since it was first described in 1969.⁵

Due to the disease's external visibility and ease of excision, most cases present early and if diagnosed, are managed and treated successfully. But if left undetected, Ewing Sarcoma metastasise easily and is associated with a poor prognosis in a paediatric population. Therefore, awareness of this disease process must be emphasised and clinicians should exercise a high degree of suspicion when confronted by an acquired rapidly increasing lesion to ensure a diagnosis is not missed, and the child has a good prognosis. Diagnosis can be made by taking a small biopsy of the lesion for histopathology. Without a proper diagnosis, clinicians should not attempt to manage the lesion locally via cryotherapy or excision.

In this case, an MRI was organised prior to surgical excision to determine whether this was a malignancy, which led to a 10-week delay in histological diagnosis. It must be emphasised that early diagnosis and treatment is essential, and an MRI was not mandatory prior to cutaneous excision. Excision or biopsy of larger lesion should be taken without delay on any suspicious skin lesion to ensure early diagnosis and treatment.

Initially, cryotherapy was used, with the lesion growing at an accelerated rate postcryotherapy. The authors are not aware of a relationship between cryotherapy and accelerated tumour growth, and no literature was found to support this.

The luxury of external disease is that if recognised, the lesion is typically smaller at diagnosis than internal bony sarcoma. As tumour size is directly related to Ewing sarcoma prognosis,

smaller lesions are less likely to have metastasised and therefore could potentially avoid aggressive chemotherapy.

Histologically, Ewing sarcoma is composed of small round cells, which express CD99. While sensitive, CD99 is not a specific marker and can be attributed to other disease processes that must be ruled out, such as Merkel cell carcinoma and lymphoma.⁶

In a paediatric population, multiple disease processes can be excluded. But rhabdomyosarcoma and malignant extrarenal rhabdoid tumour must be considered as they both express CD99 positivity. Testing for muscle markers and IN11 staining tests can exclude these diagnosis.

The importance of molecular biology becomes apparent when considering the differential diagnosis of poorly differentiated synovial sarcoma (PDSS) which is morphologically similar to cutaneous Ewing sarcoma. A difference in chromosomal translocation between Ewing sarcoma (EWSR1) and PDSS (SYT) can be detected in molecular biology and aid in the final diagnosis.⁷

Essentially, strong membrane staining for CD99 and negative staining of other markers can establish the diagnosis in most cases. The gold standard for diagnosis remains as confirming the presence of the EWSR1 gene rearrangement.⁶

While Ewing sarcoma of the bone affects the paediatric population, the key demographic for the cutaneous disease has been described as a teen female (51F:28M) presenting with a superficial soft skin lesion. This lesion traditionally slowly evolves and enlarges over 5 months and is predominantly located in the lower extremities, being described as brown in colour.⁷ Treatment traditionally involves surgical excision, followed by chemotherapy. If surgical margins are not sufficient to avoid local recurrence, radiotherapy may be used.

The Euro Ewing 2008 trial is a prospective, randomised, international, multicentre study which aims to optimise Ewing sarcoma treatment and outcomes.⁸ It is open to all patients diagnosed with Ewing sarcoma (including bony, cutaneous, localised or metastatic) who are eligible for chemotherapy. All patients receive six cycles of VIDE, subsequently patients are separated into three treatment arms. The first arm involves patients with localised disease who respond well histologically or an initial tumour volume <200 mL; these patients are randomised into two groups with the intervention being zoledronic acid added to the treatment regime. The second treatment arm includes patients with localised Ewings sarcoma that have a poor histological response or have an initial tumour volume >200 mL. These patients are randomised into a control group and a group who have Busulfan added to their therapy. The final treatment arms reviews whether the addition of treosulfan improves survival in patients with primary disseminated disease. Our patient fits the criteria for localised disease with an initial treatment volume of <200 mL; therefore, VIDE therapy was commenced and the decision to begin zoledronic acid is dependent on the trial randomisation process.

Currently, cutaneous Ewing sarcoma is treated aggressively as per Ewing sarcoma of the bone. Due to the smaller size at presentation and early detection, review articles have postulated less toxic regimes for cutaneous Ewing sarcoma may be plausible.³ But due to the rarity of this disease, no trial with a definitive conclusion about a safe less toxic regime exists and more information is required on this clinical entity before de-escalating therapy in a paediatric population. Hence, it is important that potential new treatment

protocols for cutaneous Ewing's is evaluated through international clinical trial groups. Awareness among clinicians is therefore required to ensure these primary cutaneous Ewing sarcomas are included.

Compared with Ewing sarcoma of the bone, the cutaneous disease appears to have a more favourable prognosis. Ninety-one per cent of patients survive at 10 years which is significantly better than the 10-year survival of Ewing sarcoma of the bone.^{3 4} This is likely due to the visibility of the disease—early detection of a large superficial skin nodule allows for treatment prior to the onset of metastatic disease. If the disease is detected early, and has appropriate management (local excision +/-systemic chemotherapy), then the outcome is favourable. Unfortunately, 11% of

primary cutaneous Ewing sarcoma cases have described metastatic disease at presentation.³ This is likely due to lack of clinician education and awareness of this very rare disease, which leads to delayed investigation and management. Thus, it must be emphasised that any acquired vascular lesion in a child must be investigated for malignancy with frozen tumour biopsy +/-imaging prior to any local intervention. Once malignancy has been excluded, the lesion may be treated locally as appropriate.

Our patient did not fit the key demographic of a typical cutaneous Ewing sarcoma lesion presentation. The rate of growth was also significantly faster, with significant lesion growth in the 2 months between his initial ultrasound and subsequent MRI. Early detection of this lesion is likely due to the location and size of the lesion, in addition to strong clinical suspicion from all his treating health professionals.

Contributors JX performed the literature review and analysed the current data, drafted and revised the paper. She is the corresponding author. VA reviewed and revised the paper. KS initiated the collaborative project, analysed current data, reviewed and revised the paper. ALR performed the literature review and analysed the current data, reviewed and revised the paper. All authors gave final approval before submission.

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Learning points

- Primary cutaneous Ewing sarcomas are very rare with very few cases described in the literature. Disease awareness among clinicians is essential due to the sinister progression of Ewing sarcoma and the favourable prognosis associated with it if treated early.
- Any acquired suspicious cutaneous lesion in a child must be thoroughly investigated (excision or biopsy of lesion) immediately and should be considered malignant until proven otherwise. This ensures early diagnosis and management.
- Disease prognosis is directly related to tumour size. Primary cutaneous primitive neuroectodermal tumour are usually smaller than bone lesions at diagnosis due to their external nature and disease visibility. Currently primary cutaneous Ewing is treated the same as bony Ewing sarcoma, but further international clinical trials are required to establish a less toxic management strategy prior to de-escalating therapy in the community.
- Molecular biology can be used to aid in the diagnosis of Ewing cutaneous sarcoma. The gold standard investigation is isolating a disruption in the EWSR1 gene.
- Once the diagnosis is made, staging investigations (fluorodeoxyglucose positron emission tomography scans, CT scans, bone marrow and trephine aspirates) must be organised immediately to determine the extent of disease and therefore the aggressiveness of treatment.

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