CASE REPORT

Is time of the essence? Delayed diagnosis of Ewing's sarcoma

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SUMMARY

Rarely in modern medicine are we able to observe the natural history of a patient with a sarcoma. This unusual case provides that opportunity. A CT scan was performed on the leg of a 15-year-old boy with a tender soft tissue mass on the lateral aspect of his left calf. Despite showing a lesion consistent with a sarcoma, neither the patient nor his family was informed. Almost a year and a half later, the patient returned and was diagnosed with Ewing's sarcoma. A staging work up showed no metastatic disease. After undergoing chemotherapy and a complete surgical resection of the tumour, the patient remains disease-free 10 years later, indicating that the biology of Ewing's sarcoma may be more important than time to diagnosis in determining outcome.

BACKGROUND

Malignant bone tumours in children under 20 years of age account for 6% of all cancers in this population.¹ Osteosarcoma and Ewing's sarcoma are the two most common malignant bone tumours among children and adolescents, representing 56% and 34% of cases, respectively, with peak incidence occurring at age 15.²

The period between symptom onset and diagnosis of Ewing's tumours is among the longest in paediatric tumours.^{3–7} The mean time to diagnosis is 3.7–6.3 months and 21% of cases have metastases at presentation.^{3–7} This delay in diagnosis is of particular concern due to the impact of metastasis on prognosis, reducing overall survival from 66% for patients with localised disease to 34% for those with metastatic disease.^{8–9} Therefore, understanding the effect of time to diagnosis on metastasis and survival in these patients is paramount.

CASE PRESENTATION

A 15-year-old boy presented to a walk-in clinic with a tender soft tissue mass on the lateral aspect of his left calf and was sent for X-ray, ultrasound and CT scan. Owing to the physician leaving the practice, the patient's family was never informed and the young man was not followed up, despite the images showing a 4×3.4×1.2 cm erosive lesion along the anterolateral aspect of the left fibula consistent with a sarcoma (figure 1A).

Almost a year and a half later, the patient returned to the clinic due to pain and increased size of his leg. A CT scan showed a lesion consistent with Ewing's sarcoma, but which had grown substantially from the previous year. It now measured 8.5×4.5×3 cm and destruction of the adjacent fibula was evident (figure 1B).

INVESTIGATIONS

Despite the growth of the tumour, there was no evidence of metastatic disease on CT of the patient's chest, abdomen and pelvis nor on his bone scan, bone marrow biopsy or aspirate. He underwent a biopsy of the mass, which showed an undifferentiated small blue round cell tumour consistent with Ewing's sarcoma. Cytogenetic analysis showed 71% of cells demonstrating rearrangement of the *EWSR1* gene on chromosome 22, confirming the diagnosis of Ewing's sarcoma.¹⁰

TREATMENT

The patient started chemotherapy and 3 months later underwent a complete surgical resection of the tumour. During his chemotherapy course he received cyclophosphamide 8.4 g/m², doxorubicin 375 mg/m², etoposide 3500 mg/m², ifosfamide 63 g/m² and vincristine 14 mg/m². He had no episodes of febrile neutropaenia throughout his chemotherapy protocol and did not require any transfusion support. There were no complications during the surgery and the patient did not require reconstruction. Pathology showed residual viable tumour with <50% necrosis but negative resection margins. Follow-up scans showed no remaining local disease and no evidence of metastatic disease.

OUTCOME AND FOLLOW-UP

The patient remains disease free 10 years from completion of therapy. He was followed closely for recurrence of disease as well as renal and cardiac late effects.

DISCUSSION

Recently, Brasme *et al*¹¹ analysed the effect of time to diagnosis of Ewing's tumours on metastasis and survival, in children and adolescents. Their prospective study of 436 patients with Ewing's sarcoma showed that survival was not significantly associated with time to diagnosis, though the authors acknowledge the psychological toll of a delayed diagnosis. This case supports these findings and further informs the discussion with a rare opportunity to visualise the effect of a delayed diagnosis on the progression of a Ewing's tumour. This is certainly not the case for other paediatric tumours where delay in diagnosis can have significant negative repercussions. As noted in a recent review of delay in diagnosis, there is a need for specific reporting guidelines for paediatric studies of time to diagnosis.¹²

As others have previously suggested, inherent biology of the tumour appears to be more

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Figure 1 (A) CT scan taken at initial presentation showing erosive lesion along the anterolateral aspect of the left femur (arrow). (B) CT scan of the same lesion taken 17 months later (arrows).

important in determining outcome than time to diagnosis for patients with Ewing's sarcoma.^{3 5 7} Other factors associated with decreased survival include primary tumour volume greater than 200 mL and histological response to chemotherapy.^{8 9} Aggressive tumours may lead to earlier detection due to rapid symptom presentation; despite a shorter time to diagnosis these tumours may confer a worse prognosis. Conversely, time to diagnosis may be longer for slow-growing tumours that remain

localised. Nonetheless, timely referral to paediatric oncology teams may lessen the emotional burden for the patient and family regardless of the inherent biology and outcome.

Learning points

- ▶ Ewing's sarcoma is the second most common malignant bone tumour in children and adolescents.
- ▶ Ewing's sarcoma has one of the longest intervals between onset of symptoms and diagnosis.
- ▶ This case shows that outcome and survival of patients with Ewing's sarcoma are more dependent on inherent tumour biology than time to diagnosis.
- ▶ Clinicians must ensure there is a mechanism in place to make certain that abnormal investigation results are communicated to the clinician who ordered them.

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