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Sometimes we need to think of zebras: An observational study on delays in the identification of bone tumors in children

Patients eventually diagnosed with osteosarcoma or Ewing sarcoma often spend many weeks receiving physiotherapy and visiting other health care professionals in the primary care setting before they are referred to a tertiary care centre.

ABSTRACT

Background: Pediatric bone sarcomas are rare and difficult to diagnose. Osteosarcoma is the most common and Ewing sarcoma is the second most common of these. Most cases are identified in individuals age 13 to 16 years. Common sites for osteosarcoma include the distal femur and proximal tibia. Patients typically present with chronic localized pain that is intermittent. There is often no fever, no weight loss, and no malaise. Because the presentation can be similar to what a clinician would expect for tendonitis and other benign pathologies, patients frequently receive physiotherapy rather than referral to a tertiary care centre for further workup. A quality improvement observational study was proposed to address a lack of research on delays in appropriate management of pediatric bone tumor and to increase awareness of osteosarcoma and Ewing sarcoma.

Methods: Six pediatric patients at BC Children's Hospital who were diagnosed with either osteosarcoma or Ewing sarcoma in 2018 were identified from the oncology database. The dates of their interactions with the health care system were used to create patient journey maps.

Results: Each patient saw an average of four health care professionals before referral to BC Children's Hospital, and three patients spent 4 to 9 weeks receiving physiotherapy. On average, 114 days elapsed from the time patients had their first symptoms to when they received chemotherapy, and 81% of this time was spent within the primary care system.

Conclusions: The study reveals an overall delay in diagnosis and treatment of pediatric bone tumors and highlights the need for general practitioners to further consider sarcomas in the differential diagnosis when patients present with chronic localized pain, especially when patients are in the at-risk age group and the pain is localized to one of the common sites. Practitioners should be even more suspicious if there is a history of night pain, an atypical pain pattern following minor trauma, or a soft tissue mass on examination.

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This article has been peer reviewed.

Background

Bone sarcomas make up 6% of all pediatric cancers, with the most common being osteosarcoma and the second most common being Ewing sarcoma.[1,2] Osteosarcoma is a malignant mesenchymal neoplasia characterized by the production of osteoid or bone by the malignant cells.[3] Ewing sarcoma is part of the Ewing sarcoma family of tumors, which share histological characteristics and chromosomal translocations. Ewing sarcomas are small round blue cell tumors that can develop in bone or soft tissue.[3] The peak incidence for both osteosarcoma and Ewing sarcoma coincides with the adolescent growth spurt. Most cases are identified in individuals age 13 to 16 years, and females tend to present at a younger age than males.[1] Both diseases most commonly occur in the metaphyses of long bones.[4,5] One large population-based series suggested that as many as 75% of osteosarcomas originate in the distal femur.[6] Other common sites for osteosarcoma include the proximal tibia, proximal humerus, middle femur, and proximal femur.[4]

Patients often present with chronic localized pain that is intermittent. Clinical diagnosis is difficult because there is often no family history to consider, no fever, no weight loss, and no malaise. The pain is often first noticed after trauma to the site.[7] A bone sarcoma patient's presentation will frequently be similar to what a clinician would expect for tendonitis, muscle injury, Osgood-Schlatter disease, meniscal lesions, and other benign pathologies.[7] The obscure nature of bone sarcomas can result in patients receiving inadequate pain management and attending physiotherapy sessions rather than being referred to a tertiary care centre for further workup.

Early identification of patients is important because bone tumors frequently metastasize. Before treatment protocols changed to include both neoadjuvant and adjuvant chemotherapy, 80% to 90% of patients with osteosarcoma died as a result of their disease metastasizing. It has been hypothesized that the majority of these patients had subclinical metastases that went undetected.[8,9]

The current treatment protocol for osteosarcoma is surgery combined with 12 weeks of neoadjuvant and 29 weeks of adjuvant chemotherapy.[10] Ewing sarcoma is more sensitive to chemotherapy and radiotherapy than osteosarcoma, so radiation can be considered in place of or in addition to surgery.[11] As a result of modern multimodal therapies for osteosarcoma, 66% of patients without metastases, 50% with limited pulmonary metastases, and 25% with more advanced metastases are expected to be long-term survivors.[12]

System-wide awareness of osteosarcoma and Ewing sarcoma is needed along with timely referral. Only seven articles about delays in appropriate management of pediatric bone tumors have been published to date, and none of them are based on research in Canada or the United States.[7,13-18] A quality improvement observational study of patients treated at BC Children's Hospital (BCCH) was proposed to address this lack of research and to expedite the identification and referral of affected individuals.

Methods

To prevent biased selection of study subjects, the last six pediatric patients diagnosed in 2018 at BCCH with osteosarcoma or Ewing sarcoma were identified in the hospital's oncology database. The medical records of these patients were then reviewed to determine the dates of appointments, imaging, and interventions. Patient journey maps were created to illustrate all relevant interactions with the health care system from the time of first symptoms to the initiation of chemotherapy. The visual representations of important events for all patients were then compared to determine if there were patterns that might help physicians considering these diagnoses. Information that could be used to identify patients or the health care professionals involved in their care was not included in the research records. The study was approved by the UBC Children's and Women's Health Centre of British Columbia Research Ethics Board.

Results

One of the patient journey maps created using BCCH data reveals that the patient saw primary health care physicians seven times before being referred to tertiary care **[Figure 1]**. Before referral, the patient saw walk-in clinic physicians, family physicians, and a sports medicine physician. In addition, this patient received 9 weeks of physiotherapy. Another patient saw all the professionals named above as well as an emergency room physician before referral.

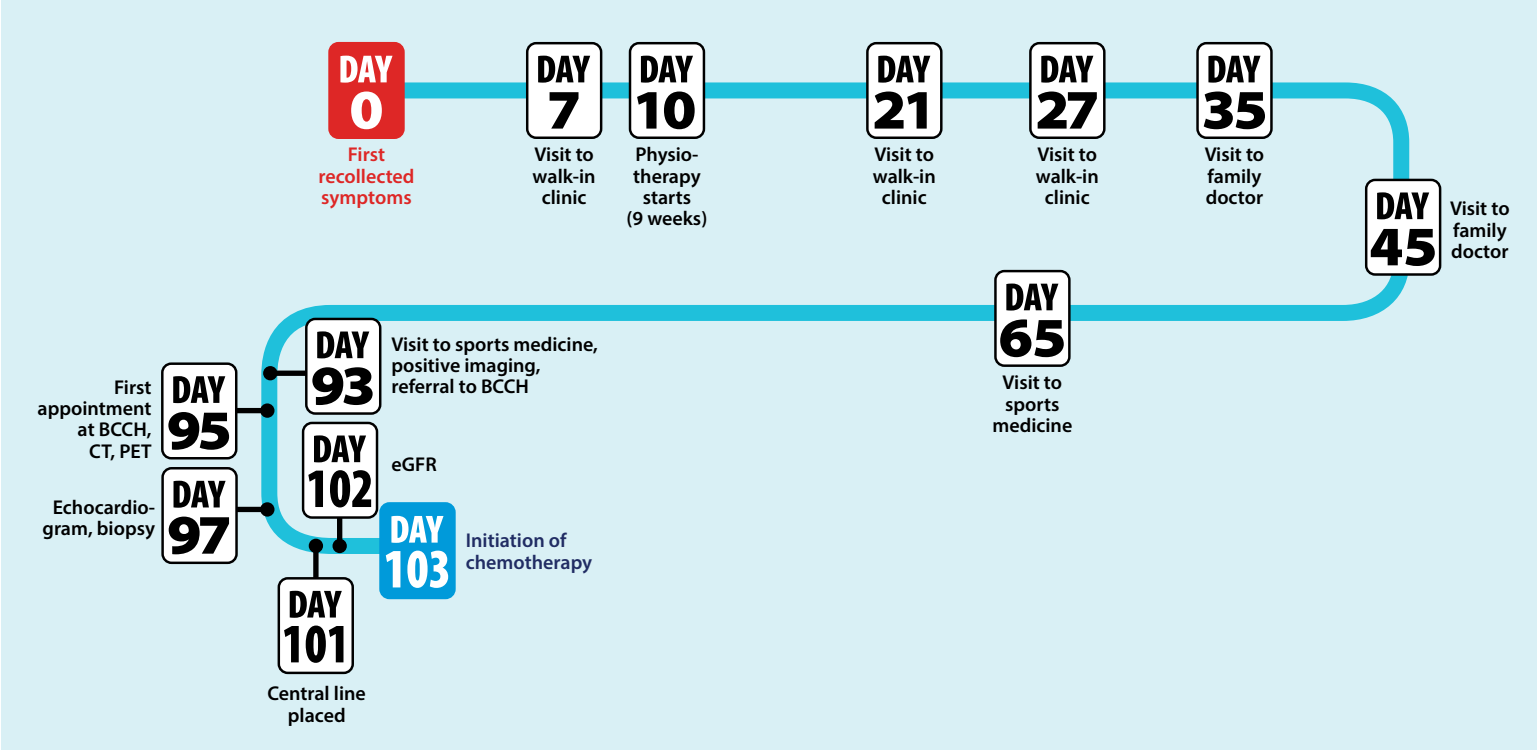

FIGURE 1. Patient journey map of all relevant health care encounters for one study subject with Ewing sarcoma.

On average, 114 days elapsed from the time patients had their first symptoms to when they were treated for their bone tumors, and patients spent 81% of this time in the primary care system visiting multiple health care professionals **[Figure 2]**. The six patients whose records were reviewed had an average of four interactions with health care professionals, not including regular physiotherapy. Physiotherapists were seen by three of the six patients for 4 to 9 weeks. On average, patients were seen 1.5 days after referral to BCCH and began chemotherapy 10.5 days after their first appointment.

A symptom common among all patients was chronic localized pain that progressed to become very severe. Three of the patients recalled night pain and two noted that they began to notice the pain after minor trauma.

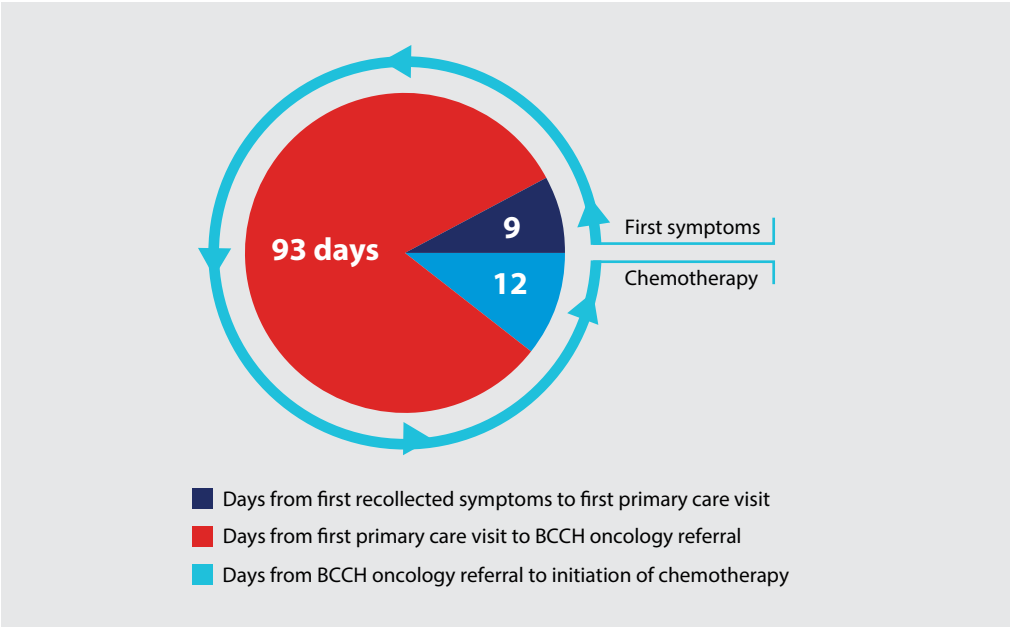

FIGURE 2. Average time in days that six study subjects with osteosarcoma or Ewing sarcoma waited at three points during their patient journeys: from first symptoms to first primary care visit, from first primary care visit to BCCH referral, and from referral to chemotherapy.

Conclusions

Bone sarcoma is often overlooked as a possible diagnosis. The patient journey maps created from BCCH data reveal an overall delay in diagnosis and treatment of pediatric bone tumors, with most of the delay in the primary care setting. This accords with findings from Widhe and Widhe, and Goedhart and colleagues, who conclude that timely care of bone sarcoma patients is needed between the first primary care visit and referral to a tertiary care centre.[7,13] In fact, Widhe and Widhe found that when bone sarcomas were identified on radiographs, the radiographs had usually been ordered to assess for more common pathologies such as fractures.[7]

Existing studies have found it difficult to correlate the delays in diagnosis and management with worse prognoses, as more aggressive tumors are usually diagnosed before less aggressive ones.[13,14] However, when metastases are due to a delayed diagnosis, earlier detection would increase survival and the possibility of limb-saving procedures.[7,16] Also, as treatment modalities improve, the speed of diagnosis may play a more important role in patient prognoses.[17]

Study limitations

The size of our study population was limited by the rarity of the diseases studied. As well, the patient journey maps created from BCCH records do not reveal the emotional and physical tolls that delays have on patients and their families, which can be inferred but not quantified from the time depicted between health care encounters. Despite these limitations, the study findings still point to the importance of identifying bone tumor cases sooner.

Recommendations

While the early diagnosis of a bone sarcoma is difficult, we believe that increased awareness could reduce delays. General practitioners should be aware that bone sarcoma patients typically present with localized chronic intermittent pain at the age of 13 to 16 years. The onset of the pain may follow a minor traumatic injury to the region with the sarcoma. Moreover, as Widhe and Widhe note, the post-trauma pain history of bone sarcoma patients is atypical because the pain from trauma seems to resolve over several days only to return in a more progressive and severe form. Nocturnal pain should increase suspicion.[15]

General practitioners conducting physical examinations should look for a tender soft tissue mass that is firmly fixed to the underlying bone, even though in the majority of cases these masses are not palpable on a patient's first visit.[7] Common sites for osteosarcoma in order of decreasing prevalence are the distal femur, proximal tibia, proximal humerus, middle femur, and proximal femur.[4,6]

Obtaining a plain radiograph is the recommended first step in the workup when bone tumors are a possibilty.[19] Goedhart and colleagues suggest that delays in care could be reduced if general practitioners lower the threshold at which they order plain radiographs.[13] If the radiograph findings are negative but suspicion remains high, a CT or MRI scan is warranted. The definitive diagnosis is made after biopsy, but it can be accurately predicted by considering clinical features with imaging results.[12]

Summary

General practitioners should further consider bone sarcomas in the differential diagnosis for chronic localized pain, especially when patients are in the at-risk age group and the pain is localized to one of the common sites. Practitioners should be even more suspicious if there is a history of nocturnal pain, an atypical pain pattern following minor trauma, or a soft tissue mass on examination. In accord with Goedhart and colleagues, we recommend that general practitioners consider lowering the threshold at which they order plain radiographs. We believe

that heightened awareness of bone sarcoma symptoms can reduce the delay in diagnosis and treatment. Although osteosarcoma and Ewing sarcoma are rare causes of chronic localized pain, it is critical to consider them since outcomes are heavily dependent on the stage when a tumor is first identified. ■

Competing interests

None declared.

The obscure nature of bone sarcomas can result in patients receiving inadequate pain management and attending physiotherapy sessions rather than being referred to a tertiary care centre for further workup.

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