Ewing's Sarcoma of the Cervical Spine

Paul H. Dahm¹ Meenakshi Bhattacharjee² Winston Huh³ Vandana Thapar⁴

¹Division of Critical Care Medicine, Department of Pediatrics, The University of Texas Health Science Center at Houston, Houston, Texas, United States

²Department of Pathology and Laboratory Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, United States

³Division of Pediatrics, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States

⁴Division of Pediatric Emergency Medicine, Department of Emergency Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, United States

Address for correspondence Paul H. Dahm, MD, Division of Critical Care Medicine, Department of Pediatrics, McGovern Medical School, The University of Texas Health Science Center at Houston, 6431 Fannin Street, MSB 3.242, Houston, TX 77030, United States (e-mail: paul.h.dahm@uth.tmc.edu).

J Pediatr Intensive Care 2018;7:86–89.

Abstract

Keywords

- Ewing's sarcoma
- cervical spine
- neck pain

In this article, we present the case of a 6-year-old female presented to the emergency department with progressive ascending motor weakness leading to cardiac arrest. The recent medical history included neck trauma 1 month prior to admission, 2 weeks of subjective fevers, and 1 day of urinary incontinence. After stabilization, and a review of the recent signs and symptoms, a magnetic resonance imaging of the neck revealed a posterior neck mass from C2 to T2. Neurosurgical removal of the mass was consistent with Ewing's sarcoma. Neck pain is a common presentation in the pediatric population, with the most common cause being traumatic. When coupled with neurological deficits, further studies are warranted to evaluate for organic causes.

Introduction

The Ewing's family of tumors account for approximately 33% of the primary bone tumors in young patients, and more commonly affect males versus females (1.5:1) between the ages of 4 and 15 years.¹ The most common sites of diagnosis are in the long bones of the extremities, with rare instances found in the ribs, scapula, and vertebrae.² The prevalence of vertebral Ewing's sarcoma is approximately 3.5%, with the highest prevalence occurring in the sacral region (55% of the tumors).^{3,4} Radiating pain is the most common presenting complaint in patients with spinal tumors.^{1,5}

Neck pain is a common complaint in the pediatric population. One survey indicates it as the second most common pain in the preadolescent population, and the most persistent pain symptom, recurring in 21% of preadolescents once a month and 6.3% once a week.⁶ The most common cause is trauma (62%), with the second most common being infectious (19%).⁷ During the evaluation, cervical spine radio-

graphy was utilized in 35% of the patients and cervical computed tomography (CT) utilized in only 5% (67% of these patients were noted to have pathological findings), while only two patients underwent magnetic resonance imaging (MRI) secondary to suspicion of C1 to C2 rotatory subluxation.⁷

Case Report

A 6-year-old Hispanic female presented to the emergency department with progressive ascending motor weakness occurring over a 3-day period that progressed to cardiopulmonary arrest. In the emergency department on the day of admission, the parents reported 2 weeks of subjective fevers with new onset of inability to walk or stand. Twenty-four hours prior she began having urinary incontinence. On physical exam, she was normotensive with slight tachycardia and oxygen saturation of 99% on room air. She was alert and oriented, without sensory defects. She complained

received

February 6, 2017

accepted after revision

July 24, 2017

published online

August 24, 2017

Copyright © 2018 by Georg Thieme
Verlag KG, Stuttgart · New York

DOI <https://doi.org/10.1055/s-0037-1606256>.
ISSN 2146-4618.

of neck stiffness and pain on palpation. Neurologically, cranial nerves were intact. Bilateral lower extremity weakness, with decreased reflexes, was noted. Negative Babinski was reported. She had normal range of motion in all extremities. Basic metabolic panel, complete blood count, blood cultures, urine cultures, and neck radiographs were ordered. Within 40 minutes of arrival, the patient was noted to be apneic, cyanotic, and pulseless. Cardiopulmonary resuscitation started with return of spontaneous circulation in 3 minutes. She was given one dose of atropine and intubated during the resuscitation. Upon stabilization, she was transferred to the pediatric intensive care unit (PICU).

Reviewing the medical history, the patient was in good health until 1 month prior to admission when she experienced neck trauma. She underwent evaluation by her primary care physician and obtained neck radiographs which were noted for calcifications of the cervical spine. As symptoms did not improve, the patient returned within 2 weeks. Radiographs were repeated, remained unchanged, and the patient was referred to an orthopaedic surgeon. A CT without contrast of the cervical spine demonstrated no evidence of acute cervical osseous injury (►Fig. 1). One week prior to admission, the patient was noted to have a sore throat with odynophagia, without rhinorrhea, was diagnosed with an upper respiratory infection, and was prescribed amoxicillin. Throughout this course, the neck pain continued and was treated as musculoskeletal.

As the pain increased, the patient began to appear "clumsy" with increasing difficulty walking. This difficulty progressed to paralgia with inability to ambulate along with fever. On the day of admission, the patient could not walk secondary to bilateral lower extremity paraplegia and paralgia. Prior to admission to the emergency room, neither

upper extremity was involved. The paraplegia rapidly ascended to quadriplegia involving both upper extremities. She progressed to pulmonary failure requiring emergent intubation. Past medical history, family history, and social history were noncontributory.

Upon arrival to the PICU, she was noted to be tachycardic and hypertensive. She remained afebrile and sedated. Her pupils were equal and reactive. Her neck demonstrated no signs of trauma or lesions. No lymphadenopathy was appreciated. She had symmetrical breath sounds without rales. No murmur noted by auscultation. Her capillary refill was less than 2 seconds. Her abdomen was soft and nondistended. No organomegaly was noted. She was a Tanner's stage I.

Her initial laboratories revealed a leukocytosis of $14.3 \times 10^9/L$ with 79% segmented neutrophils without bandemia, 14.6% lymphocytes, 5.2% monocytes, and 0.6% eosinophils and basophils. Her hematocrit and hemoglobin were 32.4 and 10.9 g/dL, respectively. Her electrolytes were sodium 132 mEq/L, potassium 3.7 mEq/L, chloride 100 mEq/L, bicarbonate 24 mEq/L, and glucose 121 mg/dL. Her creatinine and blood urea nitrogen were 0.3 and 8 mg/dL. Her liver function tests were total protein 6.6 g/dL, albumin 3.8 g/dL, total bilirubin 0.5 mg/dL, direct bilirubin 0.1 mg/dL, alanine transferase 18 unit/L, and alkaline phosphatase 153 unit/L. Her protime was 13 seconds with a partial thromboplastin time of 28.6 seconds and an international normalized ratio of 1.07. Her urine was clear. She had an immunoglobulin A level of 161 mg/dL. She had been started on ceftriaxone and vancomycin. Blood and urine cultures were negative. A tracheal culture was noted to have many leukocytes, few squamous epithelial cells, and gram-positive cocci in clusters but was negative for growth at 2 days.

Given her initial presentation, she was treated for Guillain-Barre and given one dose of intravenous immunoglobulin. She underwent MRI of her brain and entire spine. In the cervical region, she had what was believed to be a posterior epidural hematoma from C2 to T2 causing severe spinal stenosis and cord compression with compressive myelopathy and cord edema (►Fig. 2). In addition, there was evidence of venous cord congestion. An abnormal signal in the medulla was suspicious secondary to the mass effect and venous hypertension. CT and CT angiography were performed of the neck with no evidence of arterial involvement. Neurosurgery was consulted.

She was taken for laminectomy and epidural mass removal. Upon opening the lamina, a congealed mass was noted, resected, and sent to pathology for frozen and permanent sectioning. A repeat cervical spine MRI with contrast was obtained the following day demonstrating removal of the mass, but an increase in the T2 signal from the brain stem to T6. This signal as compared with the previous study had worsened and increased along the length of the thoracic spine. She continued to be ventilator dependent and experienced paralysis. A third MRI was obtained demonstrating a likely cervical spine infarct.

Hematoxylin and eosin stained section was noted for classical Ewing's sarcoma morphology (►Fig. 3). The pathology revealed the tumor to be positive for synaptophysin, CD

Fig. 1 A CT sagittal image of cervical vertebrae without contrast of the patient 1 week prior to admission to the pediatric intensive care unit demonstrating no evidence of acute intraosseous injury. CT, computed tomography.

Fig. 2 A T2-weighted sagittal image of the cervical and thoracic spine of the patient on the day of admission to the pediatric intensive care unit with cord compression from a posterior epidural mass from C2 to T2.

56 and CD 99 (►Fig. 4). The differential diagnosis included peripheral neuroectodermal tumor/Ewing's sarcoma versus medulloblastoma or other neuroendocrine tumor. Cytogenetics could not be performed to demonstrate if the tumor had the characteristic t(11:22) translocation for Ewing's sarcoma, but the morphology and immunohistochemical pattern was felt to be most consistent with Ewing sarcoma.

Further evaluation demonstrated no metastasis. The patient was transferred to the regional cancer center for further evaluation and treatment.

Discussion

Neck pain is a common complaint in the pediatric population and is more commonly seen in females. Causes of neck pain

Fig. 3 A hematoxylin and eosin stained section from pathology at $\times 40$ magnification demonstrating small round blue cell morphology.

Fig. 4 An immunostained section for CD99 antibody at $\times 40$ magnification demonstrating diffuse tumor expression.

can be divided into four classifications: traumatic, infectious, postural, and miscellaneous. Of these, the most common is traumatic; which usually has a history of trauma. In one study, of the traumatic injuries, clinical exam revealed restricted neck movements in 46% of patients with another 27% patients having painful movements without restriction. None of the patients had associated neurological deficits on the initial physical exam. Among the population with infection, the most common causes are viral, upper respiratory viral infection, retropharyngeal abscess, nonstreptococcal angina, and streptococcal angina. These were diagnosed with history and physical examination, or laboratory studies.^{6,7}

The current guidelines for injuries to the cervical spine call for the initial evaluation by three view plain radiographs. The new guidelines for children younger than the age of 10 years recommend CT scans only in cases with severe head injury, where plain films are technically inadequate, or where there is a strong indication of injury despite normal plain films. MRI is warranted with evidence of ligamentous and disc injuries or evidence of soft tissue injuries suggested by plain radiographs or CT. The second case where the MRI is warranted is in the presence of neurological signs or symptoms and a suspicion of vascular injury.⁸

This case presents a complicated diagnostic challenge. The patient had a clear mechanism of injury and underwent appropriate evaluation. With the prolonged pain, referral to orthopaedic surgery was indicated. As this evaluation was ongoing, the diagnosis was further complicated by the development of fevers and the upper respiratory infection. With this development, the differential diagnosis grew to include viral myopathies and syndromes.

Over a brief period of time, this patient developed two of the most common symptoms of primary Ewing's sarcoma of the spine: neck pain and neurological deficits. When this pain is coupled with neurological dysfunction, more than 50% will have serious or organic causes. Headaches and neurological dysfunction are the most common complaints in pediatric patients with cancer.⁹ With rapidly progressing

neurological symptoms including urinary incontinence and muscle weakness, an MRI was warranted.

The Ewing's sarcoma family of tumors is part of the small, round blue cell group of tumors including lymphomas and neuroblastoma. The Ewing family of tumors includes extra-osseous and osseous Ewing's sarcoma, and Askin's tumor. Ewing's sarcoma is the second most common malignant primary bone tumor occurring in children. More than 90% of Ewing's sarcoma cases possess the characteristic t(11:22) translocation for the *EWS/FLI1* fusion gene. The most common sites of development are the diaphysis of the long bones, with rare occurrence in the spinal and paraspinal regions (3.5%) and when it occurs is most likely in the sacrum (55%). There are less than 30 cases of primary Ewing's tumor of the spine and paraspinal regions diagnosed annually in the United States. The most common cause of Ewing's sarcoma noted in the spine is as a metastatic lesion.¹⁰

Patients with Ewing's sarcoma may present with leukocytosis, increased sedimentation rate, or other signs of systemic inflammation. Neurological symptoms become apparent with compression of the nerve roots and are seen in 50% of the patients at the time of diagnosis. The initial weakness may be mild and not recognized. Pathological fractures are rare. Plain radiographs may have features of variable degrees of osteolysis or sclerosis with partial or complete vertebral collapse. Radiographic evidence of calcification is rare with only a few previously described cases of metastases from the long bones or scapula.⁵

Once discovered, prompt treatment must be performed to preserve function. Complete surgical removal of primary tumor is the preferred method of local treatment, whenever a marginal or wide resection is possible.¹¹ With the introduction of chemotherapy prior to surgical resection, survival has increased to nearly 70%. Currently, this has involved into neoadjuvant chemotherapy first for treatment of systemic disease followed by surgery for complete resection.¹² However, primary Ewing's tumors of the spinal region present a greater challenge. Complications from spinal cord compression from the tumor and the surgical resection, and, although a late effect, central nervous system radiotoxicity are all recognized. Because of the difficulty in obtaining adequate local tumor control for these tumors, the prognosis is often poor. When patients present with neurological deficits, one treatment option is prompt decompression with biopsy. This

may relieve the symptoms but increases the risk of venous thrombosis.²

Radiation therapy has been another modality of treatment for Ewing's sarcoma. Adequate treatment requires doses ranging from 55 to 60 Gy. However, this radiation dose is harmful to the adjacent spinal cord. Even under the best circumstances, at the full dose, there is an elevation of myelopathy.²

In pediatric patients presenting with persistent neck pain, once suspicion of trauma has been dismissed, careful evaluation must be undertaken, especially in the setting of neurologic symptoms.

References

- 1 Qureshi AA, Qureshi GA, Hassan M. A case of Ewing's sarcoma involving cervical spine. *Am Eur J Sci Res* 2007;2(01):57–59
- 2 Indelicato DJ, Keole SR, Shahlaee AH, et al. Spinal and paraspinal Ewing tumors. *Int J Radiat Oncol Biol Phys* 2010;76(05):1463–1471
- 3 Hao DP, Xu WJ, Wang ZC, Liu JH, Yang BT. Primary Ewing's sarcoma of the cervical vertebra: one case report and literature review. *J Pediatr Orthop B* 2010;19(03):276–280
- 4 Weinstein JB, Siegel MJ, Griffith RC. Spinal Ewing sarcoma: misleading appearances. *Skeletal Radiol* 1984;11(04):262–265
- 5 Akeda K, Kasai Y, Kawakita E, Seto M, Kono T, Uchida A. Primary Ewing sarcoma of the spine mimicking a psoas abscess secondary to spinal infection. *Spine* 2009;34(09):E337–E341
- 6 Ståhl M, Mikkelsson M, Kautiainen H, Häkkinen A, Ylinen J, Salminen JJ. Neck pain in adolescence. A 4-year follow-up of pain-free preadolescents. *Pain* 2004;110(1-2):427–431
- 7 Pharisa C, Lutz N, Roback MG, Gehri M. Neck complaints in the pediatric emergency department: a consecutive case series of 170 children. *Pediatr Emerg Care* 2009;25(12):823–826
- 8 Head Injury: Triage, Assessment, Investigation and Early Management of Head Injury in Infants, Children and Adults. London: National Institute for Health and Clinical Excellence; 2007
- 9 Whitefield J. A 12-year-old girl with sudden onset of numbness and tingling feet. Osseous Ewing's sarcoma of T2. *Pediatr Ann* 2010;39(05):271–273
- 10 Theeler BJ, Keylock J, Yoest S, Forouhar M. Ewing's sarcoma family tumors mimicking primary central nervous system neoplasms. *J Neurol Sci* 2009;284(1-2):186–189
- 11 Gaspar N, Hawkins DS, Dirksen U, et al. Ewing sarcoma: current management and future approaches through collaboration. *J Clin Oncol* 2015;33(27):3036–3046
- 12 Biswas B, Bakhshi S. Management of Ewing sarcoma family of tumors: current scenario and unmet need. *World J Orthop* 2016;7(09):527–538