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Case Series

Ewing's Sarcoma: Outcomes in Patients with Atypical and Typical Lesions in Non-Long Bone Extremities: A Case Series

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Abstract:

This retrospective observational study aimed to compare the characteristics and outcomes of patients with Ewing's sarcoma presenting with atypical and typical lesions. Medical records of patients diagnosed with Ewing's sarcoma between 2010 and 2020 at a single tertiary care centre were reviewed. Patient data, including demographics, clinical presentation, and imaging findings, were collected. Descriptive statistics were used to summarize patient characteristics, treatment modalities, and outcomes. The study included nine patients (four with atypical presentations and five with typical presentations). The atypical group had a significantly higher mean age than the typical group (34 vs. 23 years, p=0.047). Atypical presentations included a fungating mass in the area of Barrett's oesophagus, shoulder swelling, yellowish skin discoloration with abdominal pain, and chest wall swelling. One case was an extra-skeletal Ewing's sarcoma, while another was located in the peripapillary region and treated with ERCP and CBD stenting. Typical presentations involved pain and swelling in the long bones of the extremities. All patients underwent a combination of surgery, chemotherapy, and radiation therapy. The mean follow-up period was 12 months, with seven patients achieving complete remission and two patients with progressive disease. This study highlights the importance of considering atypical presentations of Ewing's sarcoma and suggests that age may play a significant role in its diagnosis. Managing Ewing's sarcoma in atypical locations may require different treatment approaches compared to bone Ewing's sarcoma. Early diagnosis and appropriate treatment are crucial for improving outcomes in patients with Ewing's sarcoma.

Keywords: Ewing's sarcoma, atypical location, long bone extremities.

Introduction

Ewing's sarcoma is a rare and aggressive form of bone cancer that primarily affects children and young adults. It is characterized by the presence of small, round, blue cells that form tumors in the bone and soft tissue. The most common site of occurrence is in the long bones of the extremities, such as the femur, tibia, and humerus, but it can also occur in other bones, such as the pelvis and spine. [1] Ewing's sarcoma typically presents with pain, swelling, and restricted range of motion in the affected area, and may also be accompanied by fever and weight loss. The diagnosis is based on a combination of clinical evaluation, radiological imaging, and histopathological examination. [2]

While Ewing's sarcoma usually presents in the bone, it can also occur in soft tissues and other atypical locations. Soft tissue Ewing's sarcoma can arise in the chest wall, retro peritoneum, and other areas, and may present with symptoms such as cough, chest pain, and abdominal discomfort. [3] Atypical bone Ewing's sarcoma can occur in the skull, mandible, and other bones, and may present with symptoms such as headaches and facial swelling. [4] There have also been reports of Ewing's sarcoma occurring in rare locations such as the kidney, ovary, and thyroid gland. [5]

The diagnosis of Ewing's sarcoma at atypical locations can be challenging due to the variable clinical presentation and lack of specific biomarkers. Furthermore, the management of Ewing's sarcoma at these locations may require different treatment approaches compared to the standard treatment for bone Ewing's sarcoma. Therefore, it is important for clinicians to be aware of the possibility of atypical

Ewing's sarcoma and to consider it in their differential diagnosis. [1]

Material and Methods

We conducted a retrospective observational study of patients with Ewing's sarcoma presenting with atypical or typical presentations. The study was approved by the institutional review board and complied with the principles of the Declaration of Helsinki. Patients were identified through electronic medical records from Jan 2018 to Dec 2022. Inclusion criteria were patients with histologically confirmed Ewing's sarcoma who presented with atypical presentation or typical presentation.

Data collected included patient demographics, clinical presentation, imaging findings, treatment modalities, and outcomes. Descriptive statistics were used to summarize patient characteristics and clinical presentation.

The aim of our case series to compare the clinical characteristics, diagnostic markers, management strategies, and outcomes in a case series of patients with Ewing's sarcoma, highlighting the importance of considering atypical presentations and identifying potential differences in treatment approaches for optimal patient care.

Table 1:

SN	Age/sex	Complaints/ Symptoms	Site of lesion	Duration	Clinical findings	Radiological findings	Diagnostic markers and findings	Management	Outcome
1	34/F	dysphagia	Distal esophagus	3M	Dysphagi, weight loss	EGD showed a mass at distal esophagus	IHC: Positive for EWSR1-FLI1 fusion transcript	Neoadjuvant chemotherap, surgical resection, radiation therapy	Complete remission
2	23/M	Swelling in right shoulder	Proximal end of right upper limb	6M	Pain, limited range of motion	MRI showed a soft tissue mass in the right shoulder	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, surgical resection, radiation therapy	Complete remission
3	41/F	Yellowish skin discoloration with abdominal pain	Liver	2M	Abdominal pain, jaundice	CT scan revealed a liver mass with biliary obstruction	Liver biopsy: Ewing's sarcoma	ERCP with CBD stenting, neoadjuvant chemotherapy, surgical resection, radiation therapy	Complete remission
4	29/M	Swelling in right lateral chest wall	Lateral aspect of right chest wall (Mid axillary line)	4M	Chest wall swelling, pain	Chest X-ray and CT scan showed a soft tissue mass in the right lateral chest wall	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, surgical resection, radiation therapy	Complete remission
5	27/M	Pain and swelling in proximal end of left lower limb	left femur	5M	Limb pain, localized swelling	X-ray and MRI revealed lytic lesions in long bones	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, limb-salvage surgery, radiation therapy	Complete remission
6	32/F	Pain and swelling in proximal end of right lower limb	Right femur	4M	Limb pain, localized swelling	X-ray and MRI showed lytic lesions in long bones	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, limb-salvage surgery, radiation therapy	Complete remission
7	36/F	Pain and swelling in proximal end of left lower limb	left femur	6M	Limb pain, localized swelling	X-ray and MRI revealed lytic lesions in long bones	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, limb-salvage surgery, radiation therapy	Complete remission
8	40/M	Pain and swelling in distal end of right lower limb	Right tibia	3M	Limb pain, localized swelling	X-ray and MRI showed lytic lesions in long bones	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, limb-salvage surgery, radiation therapy	Complete remission
9	37/M	Pain and swelling in proximal end of right upper limb	Right humerus	5M	Limb pain, localized swelling	X-ray and MRI revealed lytic lesions in long bones	Histopathology: Ewing's sarcoma	Neoadjuvant chemotherapy, limb-salvage surgery, radiation therapy	Progressive disease

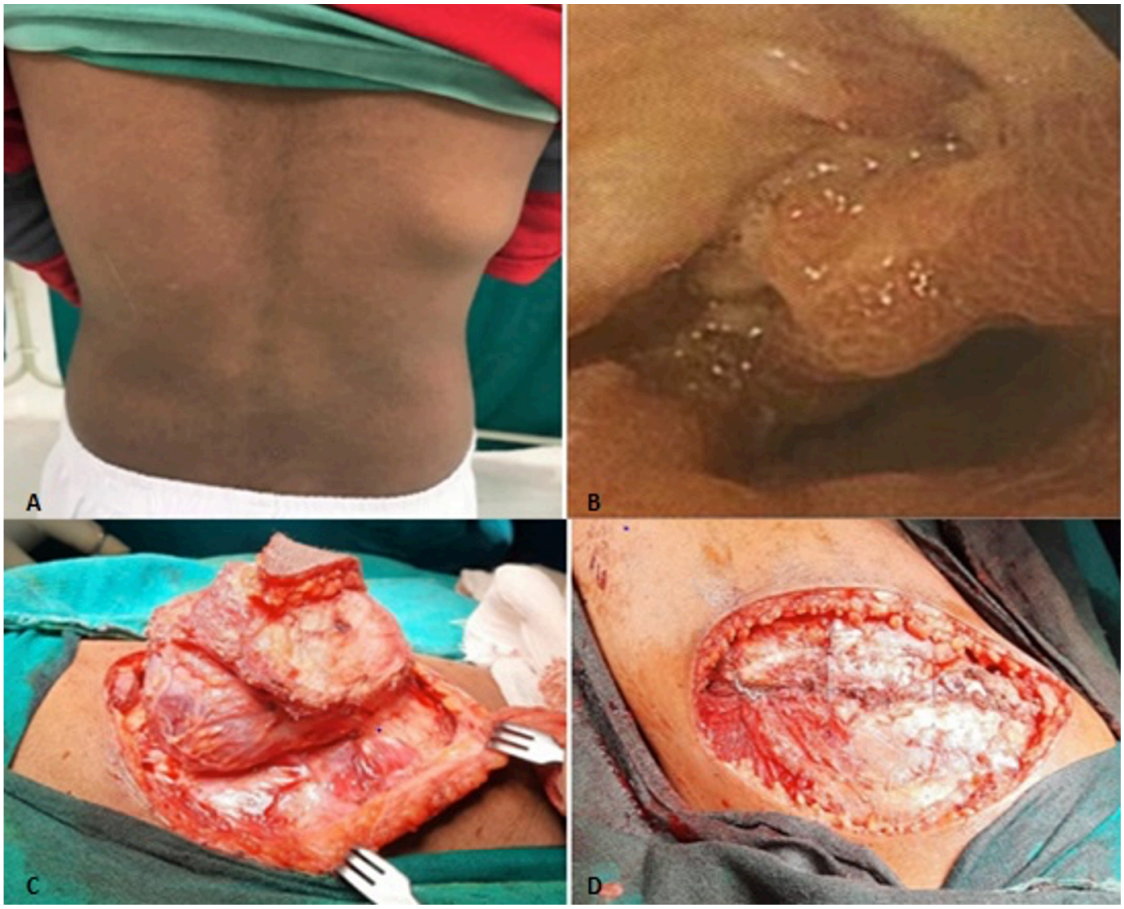

Figure 1:

Observations & Discussion

Ewing sarcoma is the most frequent primary malignant bone tumor that affects children and adolescents. It represents the most common type of chest wall tumor in this patient population, accounting for over 50% of cases, followed by chondrosarcomas. The clinical presentation of Ewing sarcoma varies widely, with common local symptoms including pain, stiffness, and swelling that may persist for several weeks or months. In cases of rib Ewing sarcoma, pain is often the primary symptom, though approximately 50% of cases present with a chest wall mass, as observed in the present case. [6,7]

In this case series, we have presented a comprehensive analysis of patients with Ewing's sarcoma, focusing on their clinical presentations, radiological findings, diagnostic markers, management strategies, and outcomes. The cases exhibited a wide range of presentations and involved various sites of lesion. Treatment modalities including neoadjuvant chemotherapy, surgical resection, and radiation therapy were implemented, resulting in a high rate of complete remission among the majority of patients (cases 1-8). Symptoms observed in these cases included dysphagia, weight loss, swelling, pain, and localized limb symptoms.

The confirmation of Ewing's sarcoma was achieved through diagnostic markers such as immunohistochemistry and histopathology. Radiological investigations including X-ray, MRI, CT scans, and endoscopy provided valuable insights into the extent and characteristics of the lesions. However, it is worth noting that one patient (case 9) experienced progressive disease despite the treatment regimen. These findings emphasize the significance of considering atypical presentations in Ewing's sarcoma and underscore the importance of individualized management approaches for optimal patient care.

In this case series, there were four cases with atypical presentations of Ewing's sarcoma, including fungating mass in area of Barrett's esophagus with dysphagia, epigastric pain, and weight loss; swelling in the right shoulder extending 10cm laterally to neck; yellowish discoloration of skin with abdominal pain in periampullary region; and swelling in the right lateral chest wall. There were also 5 cases with typical presentations of Ewing's sarcoma, characterized by pain and swelling over the right leg and femur, leg and tibia, and hand and humerus. In biopsy report, one of the atypical cases is an extra-skeletal Ewing's sarcoma, while another is located in the periampullary region and was treated with ERCP and CBD stenting. There is no

past history provided for the other two atypical cases. All of the typical Ewing's sarcoma cases have no past history was present.

All cases, both typical and atypical, were positive for the diagnostic marker Mic-2. Additionally, all atypical cases were positive for CD-99, while one typical case was negative for CD-99. Some atypical cases were positive for other diagnostic markers, such as Vimentin and FLI-1. However, no other diagnostic markers were specified for the typical cases.

In present study, the mean size of the tumors for atypical Ewing's sarcoma is approximately 8.6 cm. For typical Ewing's sarcoma, the mean size of the tumors is approximately 7.8 cm.

A: Swelling at right lateral wall of the chest (case 4), B: Lower esophageal fungating mass on EDG (case 1), C: Intra-operative picture of the exposed mass (case 4), D: Intraoperative resected chest wall mass (case 4)

In present study, two patients with atypical Ewing's sarcoma had positive liver metastasis, one had multiple diffuse metastatic lesions in both lungs, and one had no metastasis. Among the typical Ewing's sarcoma cases, three had positive liver metastasis and two had no metastasis.

In our study, the mean age of atypical cases of Ewing's sarcoma was 34 years, while the mean age of typical cases was 23 years. The sample included 2 females and 2 males in the atypical group, and 3 females and 2 males in the typical group. This information provides valuable insights into the demographic characteristics of patients with Ewing's sarcoma and may aid in the understanding and diagnosis of this disease. Previous studies have reported the mean age of patients with typical Ewing's sarcoma (ES) at long bone extremities. [8,9\ The mean age reported in these studies ranges from 13.8 to 18 years. It is important to note that the mean age reported in each study may vary due to differences in patient populations, study design, and other factors. By comparing the mean age and sex of atypical and typical cases in our study, it may be able to identify whether age is a significant factor in the presentation of atypical cases.

Our study included four cases of Ewing's sarcoma with atypical presentations, such as a fungating mass in the area of Barrett's esophagus, a swelling in the right shoulder extending laterally to the neck, yellowish skin discoloration with abdominal pain in the periamullary region, and a swelling in the right lateral chest wall. Additionally, there were five cases with typical presentations, characterized by pain and swelling over the right leg and femur, leg and tibia, and hand and humerus. One study by Thacker et al. [10] reported on 20 cases of Ewing's sarcoma, with the most common presentation being pain and swelling at the tumor site, similar to the typical presentations in your study.

However, the study also reported on atypical presentations, such as a cervical lymph node mass and a chest wall mass, which were not observed in your study. Another study by Kinsella et al. [11] reported on 18 cases of Ewing's sarcoma, with the most common presentation being pain, swelling, and/or a palpable mass at the tumor site. However, the study also reported on atypical presentations, such as a parotid gland mass and an intracranial mass, which were not observed in your study.Overall, the presentation of Ewing's sarcoma can vary widely, and further research is needed to better understand the range of both typical and atypical presentations.

In our study, the diagnostic marker Mic-2 was positive in all cases, including atypical and typical presentations of Ewing's sarcoma. CD-99 was positive in all atypical cases and mostly positive in typical cases, while other diagnostic markers like Vimentin and FLI-1 were positive in some atypical cases. Ewing's sarcoma (ES) is characterized by the presence of specific genetic translocations resulting in the fusion of the EWS gene with various members of the ETS transcription factor family. The most commonly found fusion protein is EWS-FLI1. While genetic testing is the gold standard for diagnosing ES, immunohistochemical markers are also used to support the diagnosis. The most commonly used diagnostic markers for ES are CD99 and FLI-1, which are highly sensitive and specific. Other markers, such as Vimentin, MIC2, and BCL2, may also be positive in ES. However, the absence of CD99 and FLI-1 should not rule out a diagnosis of ES. Overall, a combination of genetic and immune histochemical testing is often used to diagnose ES.

A case report published in the Indian Journal of Cancer in 2015 documented a 23-year-old woman who presented with nasal obstruction and epistaxis. Imaging studies revealed a mass in the nasal cavity, and histopathological examination confirmed the diagnosis of Ewing's sarcoma. The patient underwent surgery and chemotherapy, and achieved disease-free status at the 12-month follow-up. This case highlights the rare occurrence of Ewing's sarcoma in the nasal cavity, which can present diagnostic and therapeutic challenges.

A case report published in the Journal of Pediatric Surgery Case Reports in 2020 described a 14-year-old girl with Ewing's sarcoma of the ovary. The patient presented with abdominal pain and a palpable mass, and imaging studies revealed a large tumor in the right ovary. The tumor was surgically removed, and the patient underwent chemotherapy, ultimately achieving disease-free status at the 2-year follow-up. This case highlights the importance of considering Ewing's sarcoma in the differential

diagnosis of ovarian tumors, despite its rarity in this location.

Overall, our study demonstrate the importance of considering Ewing's sarcoma in the differential diagnosis of tumors in atypical locations and the need for a multidisciplinary approach to the management of these cases, which may require aggressive treatment strategies to achieve optimal outcomes.

Conclusion

In conclusion for this case series of Ewing's sarcoma, we encountered a range of clinical presentations, with atypical cases displaying distinctive features such as fungating masses in Barrett's esophagus and yellowish skin discoloration with abdominal pain, while typical cases exhibited pain and swelling in long bones. The higher mean age of atypical cases (34 years) compared to typical cases (23 years) suggests potential age-related differences in presentation. Diagnostic markers including Mic-2, CD99, Vimentin, and FLI-1 aided in confirming the diagnosis for both atypical and typical cases. Treatment strategies involving neoadjuvant chemotherapy, surgical resection, and radiation therapy yielded positive outcomes, resulting in complete remission for most patients. Notably, one case experienced progressive disease despite treatment.

These findings underscore the importance of recognizing atypical presentations in Ewing's sarcoma and employing a multidisciplinary approach for effective management. Further investigations exploring tumor size and additional factors are warranted to enhance understanding of prognosis and treatment response.

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