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Case Report

Multimodality imaging workup of classical Hodgkin lymphoma in an 8-month-old child ☆,☆☆

Maad Galal, MD[a], *Nader Ashraf Fawzy, MD*[a], *Areez Shafqat, MD*[a,*], *Hirdah Tauqir Rana, MD*[a], *Aljohara Aljabr, MD*[b]

[a] *College of Medicine, Alfaisal University, Al Takhassousi, Al Zahrawi Street interconnecting with, Riyadh 11533, Saudi Arabia*

[b] *Department of Radiology, King Fahad Medical City, Riyadh, Saudi Arabia*

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ABSTRACT

The incidence of Hodgkin lymphoma (HL) varies by age, most commonly affecting 15-19-year-olds. Cases in children less than 3 years old are exceedingly rare. We report a case of classical HL in an 8-month-old male; the youngest case reported thus far in the literature to our knowledge. Furthermore, while lymphadenopathy is a salient feature of HL, it was absent in our patient, who presented with immunodeficiency and delays in achieving neurologic milestones. A thorough radiologic workup demonstrated bilateral paravertebral masses, collapse of the T3 vertebrae, and severe spinal cord compression. Involvement of the lung, liver, and spleen was also noted. Histopathological evaluation of the paravertebral mass revealed a diagnosis of classical HL. Various non-neoplastic and malignant disorders, such as tuberculosis, Langerhans cell histiocytosis, leukemia, and neuroblastoma, amongst others, could be included in the differential diagnosis of our patient. Using an Illustrative case report, we review the multimodality imaging workup of Hodgkin lymphoma.

Introduction

Hodgkin lymphoma (HL) is a malignant lymphoma originating from B lymphocytes and accounts for about 7% of all childhood cancers and 1% of all childhood cancer deaths in the United States [1]. HL is categorized into classical HL (cHL) and nodular lymphocyte-predominant HL based on histopathology and immunophenotyping. The incidence of HL varies significantly by age, with estimated age-related annual incidence rates being 29/1,000,000 in 15-19-year-olds, 10/1,000,000 in 10-14-year-olds, 3.5/1,000,000 in 5-9-year-olds, and 1/1,000,000 in children between 0 and 4 years [6]. We present a case of HL in an 8-month-old infant, which, to our knowledge, is the youngest HL case reported in the literature.

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* Corresponding author.
E-mail address: ashafqat@alfaisal.edu (A. Shafqat).
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Case presentation

An 8-month-old male was referred to our hospital because of insidious onset weight loss and poor growth over the past two months. These symptoms were preceded by recurrent episodes of gastroenteritis and bronchiolitis that required multiple hospitalizations when he was 2 months old. At age 6 months, he developed coronavirus disease 2019 (COVID-19) complicated by multisystem inflammatory syndrome in children (MIS-C), drastically affecting his development, manifested as a lack of appetite and decreased movement. His developmental milestones were normal until his COVID-19 infection, after which he had motor regression, specifically in sitting with support, crawling, and rolling over. Review of systems was positive for constitutional symptoms, including fever, irritability, and decreased activity.

On physical examination, the patient appeared pale and weak. The chest was clear on auscultation and percussion bilaterally, with normal heart sounds. On abdominal examination, the abdomen was soft, nontender, and nondistended. No hepatosplenomegaly was noted. No cervical, supraclavicular, axillary, and inguinal lymph lymphadenopathy were present. A sensory examination of the upper and lower extremities revealed axial hypotonia.

Laboratory investigations revealed normocytic anemia and lymphocytopenia. An increased aspartate aminotransferase (AST) and erythrocyte sedimentation rate and low albumin levels were also seen. Hepatitis serology and HIV screening were both negative. Assessment of serum immunoglobulins revealed low IgA and IgM of 0.27 g/L (normal = 2.20-9.00 g/L) and 0.18 g/L (normal = 0.30-1.50 g/L), respectively.

The initial chest X-ray was normal (Fig. 1). However, abdominal ultrasound demonstrated a few anechoic cysts measuring 0.6 × 0.5 cm in the spleen (Fig. 2). A subsequent axial contrast-enhanced computed tomography (CT) scan revealed a right paravertebral cyst-like mass extending into adjacent neural foramina (Fig. 3A). Small, bilateral paravertebral solid lesions were also seen. Sagittal reconstruction demonstrated a paravertebral lesion extending to the neural foramen and T3 vertebra plana (Fig. 3B). CT also showed pulmonary and pleural-based nodules (Fig. 3C) and hypodense splenic lesions (Fig. 3D). Magnetic resonance imaging (MRI) of the spine showed a T3 vertebra plana with significantly enhancing prevertebral and intradural soft tissue components extending from the T1-T5 vertebral levels, occluding neural foramina bilaterally and causing severe spinal cord edema and compression (Fig. 4).

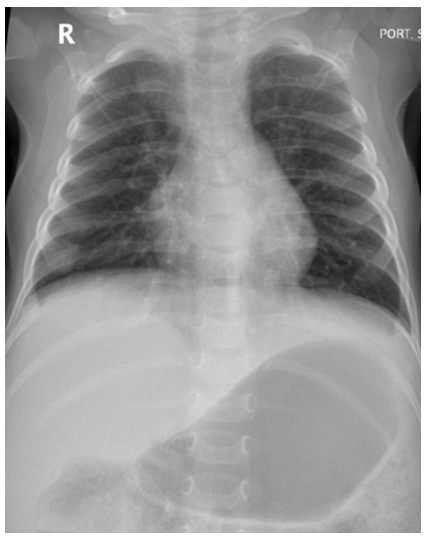

Fig. 1 – The initial chest X-ray was normal.

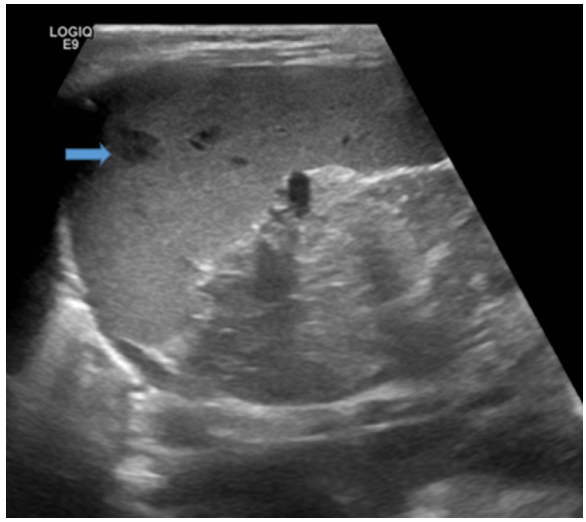

Fig. 2 – An abdominal ultrasound done after X-ray revealing anechoic cysts in the spleen, the largest measuring 0.6 × 0.5 cm.

Paravertebral masses in this age group are a rare entity, and with the constellation of findings, our prime differential was Langerhans cell histiocytosis (LCH). However, investigations of LCH came back negative with normal bone marrow on aspirate and biopsy. Acid-fast bacilli staining and culture for *Mycobacterium tuberculosis* were also negative, ruling out TB. Whole exome sequencing was done to investigate his low immunoglobulin levels and showed IL2RG gene deficiency related to atypical X-linked severe combined immunodeficiency. The patient was managed on intravenous immunoglobulin until further investigation.

A month later, our patient deteriorated and required admission for failure to thrive and neurological symptoms due to severe spinal cord compression. A posterior cervicothoracic decompression surgery with hemilaminectomy and tumor biopsy was done. The excisional thoracic spinal biopsy revealed a 2 × 1.5 cm aggregate of tan, white-red fragments. Histopathology showed classical HL staining positive for CD30, CD15, Fasin, MUM-1, and PAX-5. A whole-body PET scan revealed stage IV disease affecting the vertebral and paravertebral areas, lungs, spleen, and liver (Fig. 5).

The patient was transferred to oncology and started on chemotherapy with an initial cycle with OEPA (oncovin, etoposide, prednisone, and doxorubicin) followed by 2 cycles of COPDAC (cyclophosphamide, vincristine sulfate (Oncovin), prednisone, and dacarbazine). The patient showed signifi-

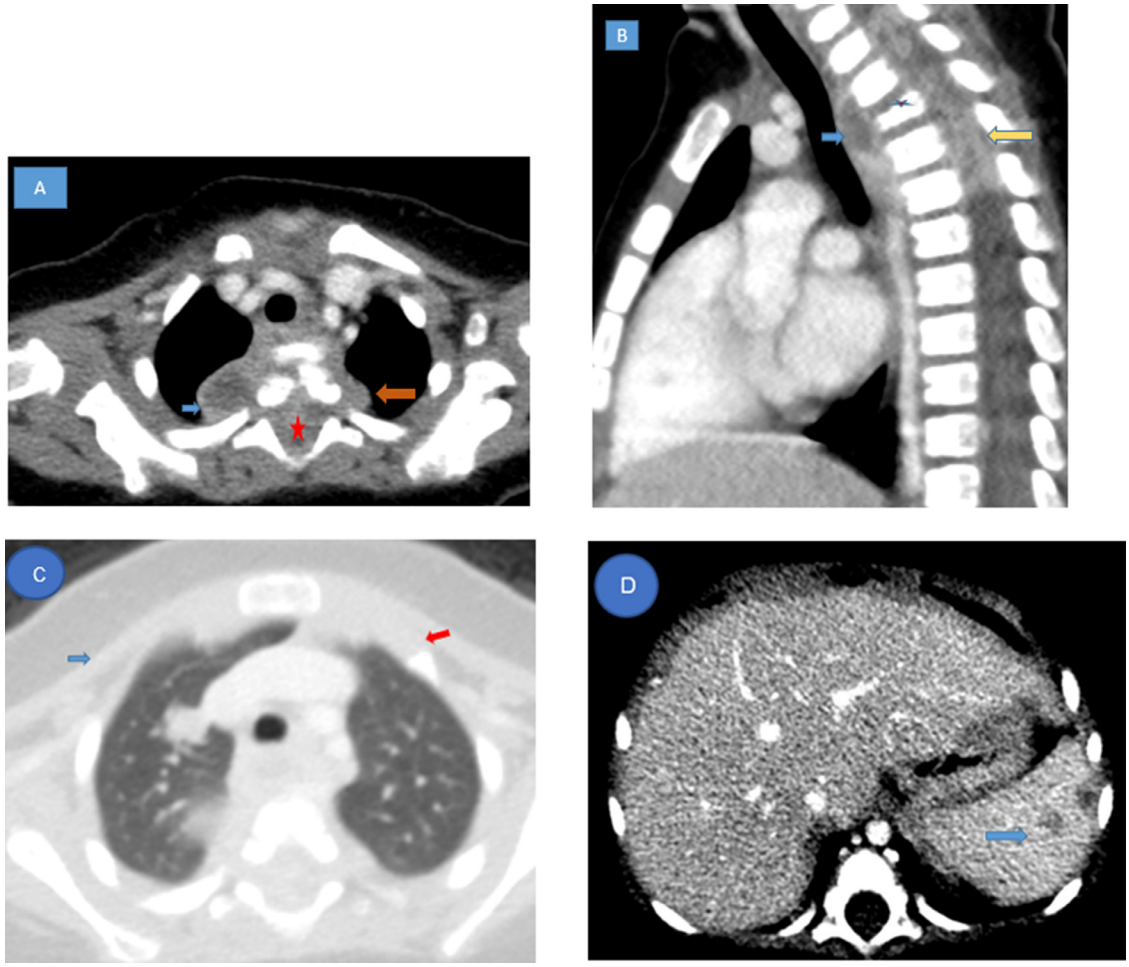

Fig. 3 – Contrast-enhanced CT scan of the chest and abdomen. (A) Axial view revealing a right-sided paravertebral cyst-like mass (blue arrow) extending into neural foramina (red star). Solid paravertebral mass also seen on the left side (orange arrow). (B) Sagittal reconstruction demonstrating a paravertebral lesion with cystic components (blue arrow) extending into neural foramen (yellow arrow) and T3 vertebra plana (black star). (C) Lung-window revealing a pulmonary nodule. (D) Abdominal CT showing few hypodense splenic lesions.

cant interval improvement on CT scan (Fig. 6) and complete metabolic response shown on FDG-PET scan (Fig. 7) after treatment completion.

Discussion

HL is the most diagnosed cancer in adolescents aged 15-19 years but is uncommon overall; HL is rare in children <5 years old and adults. Childhood HL (an HL diagnosis in those <14 years of age) demonstrates a male predominance. Childhood HL is more likely to be histologically classified as mixed cellularity and lymphocyte predominant than HL affecting adolescents and adults. The primary risk factor for childhood HL is Epstein-Barr virus infection [2]. Others include low socioeconomic status, large family size, chronic HIV, HBV, and HCV infections. The Ann Arbor classification with Cotswolds modifications remains the standard for clinically staging HL patients into limited, intermediate, and advanced risk categories based on age, clinical presentation, blood chemistry, metabolic profile, and radiologic findings [3].

HL typically presents with lymphadenopathy of supradiaphragmatic lymph nodes and B symptoms, including fever, drenching night sweats, and significant weight loss. In our case, lymphadenopathy was absent on physical examination and imaging [4,5]. Our patient presented with weight loss, poor growth, and B symptoms over 2 months. These systemic symptoms followed an episode of COVID-19 infection complicated by MIS-C. His clinical course was punctuated by deterioration and failure to thrive, requiring hospital admission and further investigations that revealed underlying advanced HL—imaging showed stage IV disease with metastasis involving the spleen, lungs, and liver.

Our primary differential was LCH, a rare systemic disease characterized by the clonal proliferation of CD1a/CD207+ dendritic cells. LCH typically affects children, with a median age of diagnosis of 3 years old [6]. LCH is the most common cause of vertebra plana in children and can extend from the spine to involve paravertebral soft tissues [6,7]. Therefore, the presence

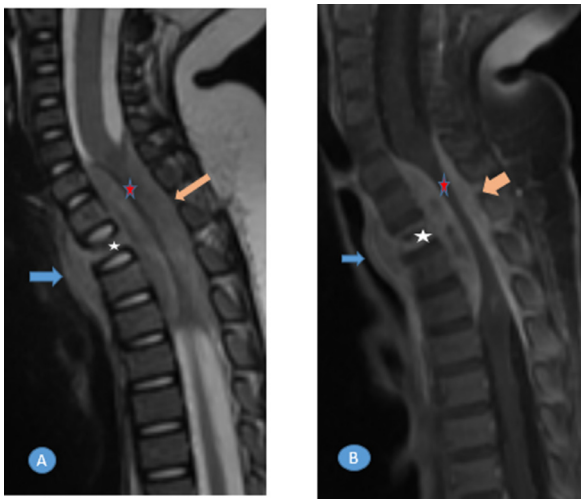

Fig. 4 – MRI done as part of the initial imaging workup after CT scan. T2-weighted images showing T3 vertebra plana (white star) with large enhancing prevertebral (blue arrow) and intradural soft tissue components extending from T1-T5 levels (orange arrow), obliterating bilateral neural foramina and causing severe cord compression and edema (red star).

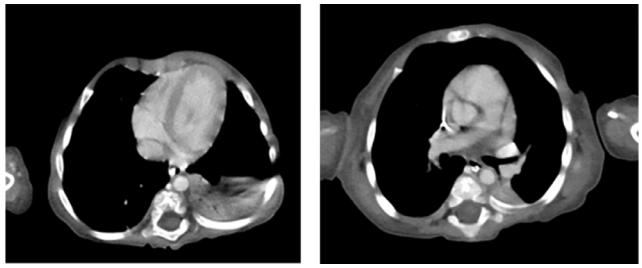

Fig. 6 – A CT scan of the chest showing significant interval improvement 2 months after treatment initiation.

of paravertebral soft tissue lesions, vertebra plana, multiorgan involvement, and neurological deficits may indicate a possible diagnosis of LCH. A biopsy ruled out LCH in our case. B symptoms are also absent in LCH. Neuroblastoma and leukemia are other malignancies common in the age group of our patient and can involve the spine to cause vertebra plana and neurologic deficits. TB can also manifest with vertebra plana as part of Pott's disease. The clinical, laboratory and imaging findings for these diseases are often sufficient to point to the underlying cause.

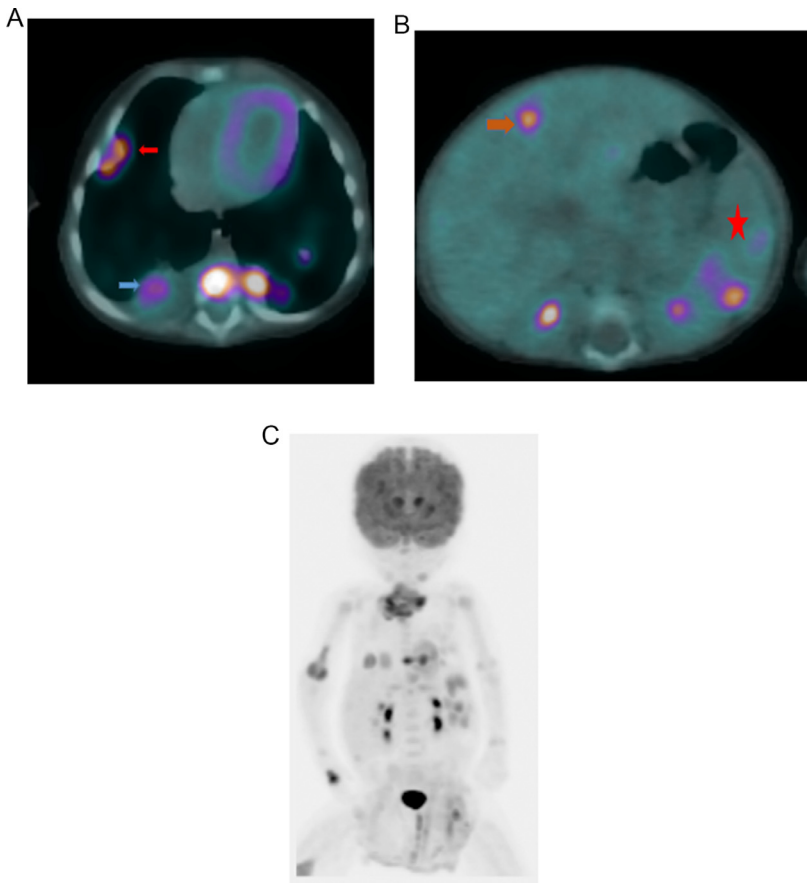

Fig. 5 – A whole-body PET scan done after histopathological cHL diagnosis demonstrating hypermetabolic lesions in the paravertebral area (blue arrow), lung (red arrow), spleen (red star), and liver (orange arrow).

Fig. 7 – FDG-PET scan showing a complete metabolic response upon treatment completion.

An FDG PET scan or PET/CT is the cornerstone of initial HL staging; it is performed mid-treatment cycle and upon treatment completion to assess treatment response [8,9]. But beyond PET/CT, other imaging modalities are also essential. Ultrasound is beneficial for confirming cervical lymphadenopathy and guiding excisional nodal biopsy. Ultrasound can also assess the involvement of extranodal sites such as the liver and spleen and guide biopsy [10]. Chest X-rays can provide preliminary evidence of mediastinal lymphadenopathy and bulky disease [11]. Contrast-enhanced CT can further characterize mediastinal adenopathy detected on X-ray, detect abnormalities not obvious on radiographs, and precisely delineate lesions for guiding further management, including biopsy and radiation planning [3]. Plain or contrast-enhanced MRI of the spine is the gold standard for identifying spinal cord compression due to edema [12].

Tremendous progress has been made in treating HL, with projected 5-year survival rates exceeding 98% in children and adults after chemotherapy alone or chemoradiation [13]. HL is exquisitely radiosensitive, and complete remission can often be achieved with radiotherapy alone. But this is avoided in children and adolescents due to high systemic toxicity. Our patient responded remarkably to the initial chemotherapy cycle of OEPA followed by 2 cycles of COPDAC.

Complications of Hodgkin lymphoma can result directly from the disease or as paraneoplastic syndromes. For example, CNS complications are common, including metastases, compression syndromes like cauda equina syndrome, and paraneoplastic syndromes causing cerebellar degeneration [14]. Alternatively, treatment regimens containing bleomycin may cause pulmonary toxicity [15]. Indeed, childhood HL cancer survivors suffer significant long-term morbidity and early mortality due to treatment-related complications, including cardiopulmonary toxicity, thyroid abnormalities, infertility, and secondary neoplasms [1]. Therefore, a multidisciplinary approach to HL treatment with stringent monitoring for post-therapy side effects is required.

Conclusion

We presented a case of classical HL in an 8-month-old male. This case reflects the diverse clinical presentation and challenging nature of diagnosing childhood HL, which requires a high index of clinical suspicion, thorough radiologic workup, and biopsy.

Availability of data and materials

Not applicable.

Code availability

Not applicable.

Author contributions

Maad Galal, Nader Ashraf Fawzy, Areez Shafqat, and Hirdah Tauqir Rana drafted the manuscript. Areez Shafqat and Aljohara Aljabr reviewed and finalized the manuscript. All authors have reviewed this manuscript and approved it for submission.

Ethics approval

Not applicable.

Patient consent

Informed written consent was obtained by the patient's father.

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