Treatment and Outcomes of Unifocal and Multifocal Osseous Pelvic Langerhans Cell Histiocytosis Lesions in a Pediatric Population

Parker Mitchell 1, Ekene U. Ezeokoli 2,3, Neritan Borici 4,2, Eva Schleh 5, Nicole Montgomery 2,1

1. Orthopaedic Surgery, Baylor College of Medicine, Houston, USA 2. Orthopaedic Surgery, Texas Children’s Hospital, Houston, USA 3. Orthopaedic Surgery, Oakland University William Beaumont School of Medicine, Rochester, USA 4. Orthopaedic Surgery, University of Medicine, European Hospital Villa Maria, Tirana, ALB 5. Orthopaedic Surgery, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, Buffalo, USA

Corresponding author: Ekene U. Ezeokoli, ekenex@gmail.com

Abstract

Introduction

Langerhans cell histiocytosis (LCH) is a rare, clonal disorder characterized by proliferation and tissue infiltration by myeloid dendritic cells, most commonly occurring in pediatric populations. It often manifests as skeletal lesions with possible pelvic involvement. Few studies have characterized and reviewed outcomes after treatment of isolated pelvic LCH lesions.

Methods

A retrospective single-institution review was conducted on diagnoses of patients younger than 18 with a diagnosis of unifocal or multifocal skeletal LCH lesions involving the pelvis. Clinical presentations, lesion sites, focal classification, radiographic findings, treatments, complications, and recurrence rates were reviewed.

Results

Twenty patients had unifocal or multifocal pelvic LCH lesions (11 males, nine females). The median age at diagnosis was 3.5 years (0.8-21.6). Eight cases (40%) involved unifocal lesions, and twelve (60%) involved multifocal lesions, with the most common associated skeletal disease occurring at the ilium. 100% of cases had a lytic bone lesion with no pathologic fractures. All cases were treated nonoperatively with chemotherapy medications, corticosteroids, or observation alone. 75% of cases were treated with chemotherapy with a 100% resolution rate. The median length of follow-up was 4.5 years (0.4-16.7).

Conclusion

Our study found that chemotherapy alone or chemotherapy with corticosteroid supplementation are appropriate options for unifocal pelvic LCH lesions. In contrast, pelvic lesions that are part of a multifocal presentation may be managed adequately with varied chemotherapy regimens. Corticosteroid therapy and observation alone may also be reasonable for a single organ system, multifocal, skeletal lesions that are anatomically accessible for biopsy and small in number or size.

Introduction

Langerhans Cell Histiocytosis (LCH) is a rare, neoplastic histiocytic disorder that most commonly affects bones and skin; however, it can also involve the lungs, pituitary gland, liver, spleen, central nervous system, lymph nodes, or other organs. LCH is considerably more common in the pediatric population, especially in white males, and is characterized by clonal proliferation of Langerhans dendritic cells [1]. Although the neoplastic cells of LCH resemble dendritic Langerhans cells in the skin and mucosa, the CD1a+ and Langerin+ neoplastic cells of LCH are found in bone, and visceral organs are derived from myeloid dendritic cells.

Initial presentation can range from isolated and unifocal skeletal lesions to multisystemic disseminated involvement, depending on the progression of the disease. In pediatric populations, LCH is limited to one organ system in approximately 55% of cases, with the remainder presenting with multisystemic disease [2]. The multisystem disease is most often seen in children under three years of age, while single-organ involvement is more common in older children and adults. The Histiocyte society classifies the disease as single-system single-site (SS-s), single-system multiple-site (SS-m), and multisystem (MS) [3]. Complete remission is sometimes possible without treatment, depending on the presentation, but some cases may
have treatment-resistant resistance, swift progression, post-disease complications, or even death [4-6]. SS-s usually have a better prognosis with more conservative treatment, while MS requires more aggressive management and is more likely to have a less desirable outcome.

Bone involvement is one of the most common findings of LCH. Although some bone lesions are asymptomatic, pain with accompanying skeletal lesions and raised, soft, tender spots are also common initial presentations [7]. LCH can involve any bone in the body, but the most common sites vary with age. Children’s most frequent sites are the skull, femur, rib, vertebra, and humerus [8]. The main sites of bone involvement in adults are the jaw, skull, pelvis, vertebra, extremities, and rib [9]. While the pelvis is not an uncommon site of LCH lytic lesions in adult studies, few studies have characterized and reviewed the eventual outcomes after treatment at these sites, especially in pediatric populations. The few studies looking at isolated pelvic lesions were all case reports in an older patient population or investigations characterizing radiographic findings for differential diagnosis [10-17]. The incidence and sequential investigation of outcomes of this rare disorder at the pelvic site are poorly defined and followed.

This study’s primary goal includes (1) clinical and radiographic characterization of a series of unifocal and multifocal LCH lesions involving the pelvis and (2) determining success and recurrence rates with different treatment modalities in a pediatric population at a tertiary children’s hospital.

**Materials And Methods**

We obtained approval from the Baylor Institutional Review Board (H-45616) for a retrospective review of patients under 18 years old diagnosed with LCH at a significant, level 1 children’s hospital before June 1, 2021. Patients were captured from February 22, 2005, to June 1, 2021. The main inclusion criteria included patients with a unifocal or multifocal skeletal lesion. After inclusion criteria were met, patients without a pelvic lesion were excluded. Additional exclusion criteria included the involvement of the bone marrow and multisystemic LCH disease, which included patients with visceral involvement, concurrent malignant diagnoses, and lack of data. Twenty patients met all criteria to be included in the study.

All patients had a skeletal survey and a positron emission tomography (PET) scan. The diagnosis was confirmed through biopsy and histology via a positive CD1a, CD207 (Langerin), or S100 immunoassay in all cases, except for Case 10, as no test was documented. Clinical presentations, lesion sites, additional skeletal lesions, biopsy site, focal classification, radiographic findings, lesion size, treatments, complications, recurrence rates, and lengths of follow-up, if present, were abstracted from the chart. We also determined whether the associated skeletal lesion was diagnosed at the initial consultation and which intervention was used in clinical care.

**Data analysis**

All statistics were descriptive and were reported as counts with percentages or means with range values or where applicable.

**Results**

**Demographics**

In our study, there were 686 patients diagnosed with Langerhans cell histiocytosis during the study period between 2009-2021. Twenty patients were found to have unifocal or multifocal LCH lesions involving the pelvis. There were 11 males and nine females identified. The median age at diagnosis was 3.5 years (0.8-21.6) (Table 1). The most common reasons for exclusion were multisystemic cases or bone marrow involvement.
### TABLE 1: Demographics and Characteristics

| Case | Age at diagnosis/Sex | Presentation | Lesion Site | Other skeletal lesion(s) | Classification | Biopsy site(s) |
|------|----------------------|--------------|-------------|--------------------------|----------------|----------------|
| 1    | 2.3/F                | Restricted range of motion, limitation | Ilium | N/A | Unifocal | Hip |
| 2    | 8.2/M                | Upper leg pain | Sacrum | Femur, sternum | Multifocal | Femur |
| 3    | 15.4/F               | Sided weakness, dizziness, fatigue | Ilium | Vertebrae | Multifocal | Vertebrum |
| 4    | 3.2/F                | Painless limping | Ilium | N/A | Unifocal | Ilium |
| 5    | 1.7/F                | Painful limping | Ilium | N/A | Unifocal | Ilium |
| 6    | 0.9/M                | Appetite change, fever, irritability, rash | Ilium | Clavicle, rib | Multifocal | None |
| 7    | 3.9/M                | Limping, fatigue, sweating | Ilium | Left parietal | Multifocal | Ilium |
| 8    | 3.0/F                | Limping 8-9 weeks | Ilium | Vertebrum, femur, sacrum | Multifocal | Ilium |
| 9    | 0.8/M                | Leg pelvic pain | Ilium | Mediastinum | Multifocal | Acetabulum |
| 10   | 10.5/M               | Back pain | Acetabulum | Vertebrum, skull | Multifocal | Vertebral |
| 11   | 5.4/F                | Headaches, nausea | Pubis, acetabulum | N/A | Unifocal | Acetabulum |
| 12   | 21.6/M               | Scalp mass | Bilateral ilium, pubis | Femur, rib, skull | Multifocal | Skull |
| 13   | 13.2/M               | Hip pain | Ilium | N/A | Unifocal | Ilium |
| 14   | 8.6/F                | Leg pain | Ilium | N/A | Unifocal | Ilium |
| 15   | 2.1/M                | Limping, leg mass | Ilium | femur, rib, humerus, metacarpal | Multifocal | Femur |
| 16   | 1.8/M                | Fever, rhinorrhea | Ilium | skull | Multifocal | Skull |
| 17   | 11.7/M               | Arm pain | Sacrum | clavicle, rib, vertebra | Multifocal | Clavicle |
| 18   | 11.3/F               | Hip pain, limping | Ilium | N/A | Unifocal | Ilium |
| 19   | 1.1/M                | Scalp rash | Ilium | Pelvis, femur, parietal bone | Unifocal | Skin |
| 20   | 1.7/F                | Hip pain | Ilium | Pelvis, femur, parietal bone | Multifocal | Ilium |

**Characterization**

Of the 20 pelvic LCH cases identified, there were 8 (40%) unifocal lesions and 12 (60%) multifocal lesions, with the most common associated skeletal lesion occurring at the ilium (15 cases, 60%). Other sites included ischium (3 cases, 15%), acetabulum (2 cases, 10%), and sacrum (2 cases, 10%). The most common multifocal lesion site occurred at the ilium (7 cases, 35%), along with sacral (2 cases, 10%), ischial (2 cases, 10%), and acetabular (1 case, 5%) lesions. Of the eight unifocal lesions, the ilium was the most common site (6 cases, 75%). Case 12 included bilateral ilium and pubis involvement, and Case 11 included acetabular and pubis lesions. The ileum was typically chosen as a biopsy site in unifocal cases (4 cases, 50%). The most common radiographic finding was a lytic bone lesion (100% of cases, Figure 1). Measurements of pelvic lesions were not consistently assessed radiographically. The most common clinical presentations associated with pelvic lesions were pain and limping with lower extremity or hip pain occurring in 8 patients and limping in 7 patients with pelvic lesions. Other bony lesions primarily included the femur (5 cases, 25%), vertebrae (4 cases, 20%), ribs or mediastinum (6 cases, 30%), and skull (4 cases, 20%).
FIGURE 1: 8-year-old female presenting with hip and lower extremity pain (Case 14). (A) AP PET/CT demonstrating hyperintensity of the right ilium. (B) Axial CT demonstrating an osteolytic lesion at the right ilium.

Treatments and outcomes

No patients with pelvic LCH had their lesions resected or debrided surgically. All cases were treated nonoperatively either exclusively or in tandem with chemotherapy medications, corticosteroids, or observation alone. Most cases were treated with vinblastine and prednisone (11 cases, 55%). Other treatment options included cytarabine (7 cases, 35%) or no treatment (3 cases, 15%). Two cases were eventually transitioned to cladribine (Case 1 and 8). Case 1 was transitioned from vinblastine and prednisone to cladribine due to a history of neutropenia with prior chemotherapy and LCH-S-98 study protocol. Case 8 was transitioned to cladribine due to complaints of bilateral heel and feet pain with mild foot drop secondary to vinblastine. Three chemotherapy regimens switched to clofarabine (Case 10, 12, 17) due to new skeletal lesions or increased size of lesions. Of the 8 unifocal cases, 5 cases were treated with vinblastine and prednisone, 2 cases had no treatment, and 1 case was treated with steroid injection alone. One patient had a documented disease recurrence. The recurring case (Case 13) included a unifocal lesion of the ischium that returned as cervical adenopathy. The initial ischial lesion was treated solely with triamcinolone acetonide injections, and the recurrent adenopathy was treated with hydroxyurea. The median length of follow-up was 4.5 years (0.4-16.7 years) (Table 2). There was no mortality in this cohort. No complications from treatment were recorded.
| Case | Radiographic findings | Size of the lesion (on imaging) | Immune Findings | Treatment | Recurrence frequency | Total f/u (years) |
|------|------------------------|--------------------------------|-----------------|-----------|---------------------|------------------|
| 1    | Lytic lesion (expansile with edema) | 2.8x2.5x2.1 cm | CD207+ | Vinblastine, prednisone, cladribine | 0 | 6.32 |
| 2    | Lytic lesion | N/A | CD1a+, S100+ | Vinblastine, prednisone | 0 | 3.05 |
| 3    | Lytic lesion | 0.5x0.6x0.9 mm | CD1a+, CD207+, S100+ | None | 0 | 0.36 |
| 4    | Osteolytic lesion | 4.2x1.6 cm | CD1a+, S100+ | Vinblastine, prednisone | 0 | 9.55 |
| 5    | Lytic lesion | N/A | CD1a+ | None | 0 | 0.52 |
| 6    | Lytic lesion | N/A | CD1a+, S100+ | Cytarabine | 0 | 1.56 |
| 7    | Lytic lesion | N/A | CD1a+ | Cytarabine | 0 | 3.14 |
| 8    | Lytic lesion (slight sclerosis) | 2.0x1.5x2.4 cm | CD1a+, CD207+ | Vinblastine, and prednisone, were switched to cladribine. Continued 6-mercaptopurine and methotrexate for maintenance therapy | 0 | 10.97 |
| 9    | Lytic lesion | 2.7 cm | CD207+ | Vinblastine, cytarabine | 0 | 16.13 |
| 10   | Lytic lesion | N/A | N/A | Vinblastine, prednisone, cytarabine clofarabine | 0 | 5.86 |
| 11   | Lytic lesion | 3.5x3.3x2.1 cm | CD207+ | Vinblastine, prednisone | 0 | 11.77 |
| 12   | Lytic lesion (sclerotic) | 6.7mm x 2.6mm | CD1a+, CD207+, S100+ | Cytarabine + zoledronic acid, switched to clofarabine, after 3 months | 0 | 0.88 |
| 13   | Lytic lesion | N/A | CD1a+, S100+ | Steroid injection | 1 | 1.42 |
| 14   | Lytic lesion | N/A | CD1a+ | Vinblastine, prednisone | 0 | 1.21 |
| 15   | Lytic lesion | 2x0.8x0.2 cm | CD1a+, CD207+, S100+ | Cytarabine | 0 | 8.78 |
| 16   | Lytic lesion | N/A | CD207+ | Vincristine | 0 | 11.41 |
| 17   | Lytic lesion | 2cm | CD207+ | Cytarabine switched to Clofarabine | 0 | 6.77 |
| 18   | Lytic lesion (cortical disruption) | 2.2x2.1x1.8 cm | CD1a+, CD207+ | None | 0 | 0.83 |
| 19   | Lytic lesion | N/A | CD1a+ | Vinblastine, prednisone | 0 | 1.81 |
| 20   | Lytic lesion | N/A | CD1a+ | Vinblastine, prednisone | 0 | 16.67 |

**TABLE 2: Radiology, Histology, and Outcomes**

**Discussion**

Langerhans cell histiocytosis is a rare disease expressed as abnormal histiocytic proliferation, often occurring with skeletal lesions or skin involvement. In pediatric patients, treatment is usually adapted to presentation depending on disease progression and organ involvement. Isolated lesions have different treatment options, while multisystemic or disseminated disease usually requires chemotherapy [8]. Some
studies have even demonstrated that minimally-invasive radiofrequency ablation may support safe and effective treatment for unifocal LCH bone lesions [17]. LCH presentations may not be benign, with disseminated disease associated with increased mortality and recurrence rates [18-21].

We only identified and analyzed unifocal (SS-s) or multifocal (SS-m) pelvic lesions; therefore, no patients displayed disseminated or visceral disease signs. Of the 686 patients initially queried for a diagnosis of LCH, twenty included lesions involving the pelvis (2.9%), with 8 being unifocal pelvic lesions (1.2%). All unifocal lesions were treated via vinblastine, corticosteroids, corticosteroids alone, or observation. Current literature suggests that resection of the skeletal lesion and steroid injection lead to positive outcomes in unifocal LCH lesions [22-24]. In various cases, resection and steroid injection can be used as an adjunct to chemotherapy or radiotherapy depending on the lesion site or associated complications [18,25]. Other studies have shown that skeletal, unifocal LCH lesions do not likely require aggressive surgical or medical management. A recent study by Rivera et al. [26] further demonstrated that biopsy alone confirms the diagnosis of unifocal osseous LCH and can rapidly resolve symptoms.

In comparison, all multifocal lesions in our study were treated with various chemotherapy regimens, primarily vinblastine and prednisone, cytarabine, cladribine, clofarabine, or observation alone of additional lesion quantity or location. Depending on the disease progression and location or the number of additional lesions, treatment was varied in a case-by-case manner. All patients experienced successful outcomes in our cohort regardless of treatment, except Case 13, who displayed a recurrent LCH lymphadenopathy event. However, three patients had under a year of follow-up.

Due to the location of the lesions in our study, most of the cases presented with acute lower back, hip, or leg pain and limping on the affected side. Despite the location of lesions in the cohort and several primary presentations, including acetabular involvement and deformity, there was no documented flank pain, constipation, buttocks pain, restriction of hip movement, associated fractures, functional impairment, or other complications expected from pathologies in the pelvis or acetabular joint.

Currently, no available case reports discuss longitudinal outcomes in pediatric patients with isolated, pathologic pelvic fractures. Furthermore, there is limited literature on pelvic LCH lesions in pediatric patients. Previous studies have investigated radiographic findings and imaging factors to differentiate diagnoses [10-14]; however, few studies thoroughly investigate LCH pelvic lesions through management, outcomes after treatment, or subsequent follow-up assessment. As LCH is often highly treatable, with many patients exhibiting favorable outcomes, timely diagnosis and management are essential, especially in patients with uncomplicated, superficial bony lesions. Although treatment can vary on a case-by-case basis, varying options in adults with isolated skeletal LCH have included curettage and corticosteroid injections [2,15,27] with or without supplemental radiation [28], and non-operative observation [29].

Limitations
A weakness of our study is its retrospective nature which relies on a chart review of available imaging and documentation. This retrospective case series was limited by the infrequency of LCH pelvic lesion presentations and would benefit from a higher-powered randomized trial to compare treatment options and outcomes of LCH lesions involving the pelvis. This was a single-institution study. Furthermore, there were only 20 patients that fit the criteria for our series. Though most literature reports of LCH are case reports, our study cohort is still of a relatively low quantity. Only 8 of our patients had a unifocal and isolated pelvic lesion, and four had under one year of follow-up. While we found an association of LCH pelvic lesion resolution with non-operatively treated methods, our study did not evaluate pelvic lesions treated operatively, which might reveal different rates of resolution and recurrence.

Conclusions
Our study found that chemotherapy regimens alone or with adjuvant corticosteroid supplementation are an appropriate option for unifocal pelvic LCH lesions. Multifocal pelvic lesions may be managed adequately with varied chemotherapy regimens, and surgical resection was not demonstrated as a suggested treatment option for LCH lesions involving the pelvis. Steroid therapy or observation alone may also be reasonable for pediatric, single-system, multifocal, skeletal lesions that are small in number and size, in contrast with a complete chemotherapy regimen and its associated adverse effects.

Additional Information
Disclosures
**Human subjects:** Consent was obtained or waived by all participants in this study. Baylor College of Medicine Institutional Review Board issued approval H-45616. The Institutional Review Board has reviewed the above-referenced research proposal and documents (if applicable) which were submitted for exemption consideration. A Research Waiver of Authorization is granted only for the stipulation of identification/data collection of the specific data variables for this study. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no
financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Kim BE, Koh KN, Suh JK, et al.: Clinical features and treatment outcomes of Langerhans cell histiocytosis: a nationwide survey from Korea histiocytosis working party. J Pediatr Hematol Oncol. 2014, 36:125-33. 10.1097/MPH.0000000000000854
2. Grois N, Pöttscher U, Proesch H, et al.: Risk factors for diabetes insipidus in langerhans cell histiocytosis. Pediatr Blood Cancer. 2006, 46:228-33. 10.1002/bpc.20425
3. Haupt R, Minkov M, Antigarraga I, et al.: Langerhans cell histiocytosis (LCH): guidelines for diagnosis, clinical work-up, and treatment for patients till the age of 18 years. Pediatr Blood Cancer. 2013, 60:175-84. 10.1002/bpc.24367
4. Murata S, Yoshida Y, Adachi K, Morita E, Yamamoto O: Solitary, late-onset, self-healing Langerhans cell histiocytosis. Acta Derm Venereol. 2011, 91:105-4. 10.2540/00015555-09090
5. Minkov M: Multisystem Langerhans cell histiocytosis in children: current treatment and future directions. Paediatr Drugs. 2011, 15:75-86. 10.2165/11538540-000000000-0000
6. Chow TW, Leung WK, Cheng FW, et al.: Late outcomes in children with Langerhans cell histiocytosis. Arch Dis Child. 2017, 102:830-5. 10.1136/archdischild-2016-312185
7. Lau LM, Stuurnau K, Weitzman S: Skeletal Langerhans cell histiocytosis in children: permanent consequences and health-related quality of life in long-term survivors. Pediatr Blood Cancer. 2008, 50:607-12. 10.1002/pbc.21322
8. Slater JM, Swarn OJ: Eosinophilic granuloma of bone. Med Pediatr Oncol. 1980, 8:151-64. 10.1002/mpo.2950080208
9. Baumgartner I, von Hochstetter A, Baumert B, et al.: Langerhans’cell histiocytosis in adults. Med Pediatr Oncol. 1997, 28:9-14. 10.1002/(sici)1096-911x(199701)28:1<9::aid-mpo3>3.0.co;2-p
10. Singh I, Rajakuilasingam R, Safuddin A: Langerhans cell histiocytosis of the shoulder girdle, pelvis and extremities: a review of radiographic and MRI features in 85 cases. Skeletal Radiol. 2020, 49:1925-37. 10.1007/s00256-020-05472-2
11. Rama KVV, Leong MV, Tan AM, Quan DLW, Teo EL: Langerhans cell histiocytosis: another cause of a fluid-fluid level within an appendicular bony lesion. BJR Case Rep. 2016, 2:20150408. 10.1259/bjrcre.20150408
12. Samet J, Weinstein J, Fayad LM: MRI and clinical features of Langerhans cell histiocytosis (LCH) in the pelvis and extremities: can LCH really look like anything?. Skeletal Radiol. 2016, 45:607-13. 10.1007/s00256-016-2350-x
13. Winfeld M, Alawat S, Safdar N: Utilization of chemical shift MRI in the diagnosis of disorders affecting pediatric bone marrow. Skeletal Radiol. 2016, 45:1205-12. 10.1007/s00256-016-2403-9
14. Nguyen BD, Roarke MC, Chivers SF: Multifocal Langerhans cell histiocytosis with infiltrative pelvic lesions: PET/CT imaging. Clin Nucl Med. 2010, 35:824-6. 10.1097/RLU.0b013e3181e0f851
15. Christopher Z, Binitie O, Henderson-Jackson E, Perno J, Makanji RJ: Langerhans cell histiocytosis of bone in an adult: a case report. Radialt Case Rep. 2018, 15:310-4. 10.1016/j.radar.2017.11.020
16. Song YS, Lee JS, Yi H, Choo KH, Kim DK, Song JW: Radiologic findings of adult pelvis and appendicular skeletal Langerhans cell histiocytosis in nine patients. Skeletal Radiol. 2011, 40:1421-6. 10.1007/s00256-010-1078-y
17. Tomasian A, Hillen TJ, Jennings JW: Unifocal Langerhans cell histiocytosis of bone: percutaneous navigational bipolar radiofrequency ablation for curative treatment. Clin Imaging. 2021, 72:55-7. 10.1016/j.clim.2020.11.031
18. Rodríguez-Galindo C: Clinical features and treatment of Langerhans cell histiocytosis. Acta Paediatr. 2021, 110:2892-902. 10.1111/apa.16014
19. Krooks J, Minkov M, Weatherall AG: Langerhans cell histiocytosis in children: history, classification, pathobiology, clinical manifestations, and prognosis. J Am Acad Dermatol. 2018, 78:1035-44. 10.1016/j.jaad.2017.05.059
20. Monseerenuosom C, Rodriguez-Galindo C: Clinical characteristics and treatment of patients with Langerhans cell histiocytosis. Hematol Oncol Clin North Am. 2015, 29:855-73. 10.1016/j.hoc.2015.06.005
21. Dhar S, Srinivas SM, Dhar S, et al.: Langerhans cell histiocytosis in children: a retrospective case series of 126 cases. Pediatr Dermatol. 2020, 37:1085-9. 10.1111/pde.14389
22. Bezdzian A, Alarfaj AA, Varma N, Daniel SJ: Isolated Langerhans cell histiocytosis bone lesion in pediatric patients: systematic review and treatment algorithm. Otolaryngol Head Neck Surg. 2015, 155:751-7. 10.1016/j.otohns.2015.07.0096
23. Egeler RM, Thompson RC Jr, Voite PA, Nesbit ME Jr: Intralesional infiltration of corticosteroids in localized Langerhans’ cell histiocytosis. J Pediatr Orthop. 1992, 12:811-4. 10.1097/01241398-199211000-00021
24. Sahin C, Uçpinar BA, Öc Y, Kahvecioglu F: Radiologic findings of scapular Langerhans cell histiocytosis successfully treated with CT-guided corticosteroid injection. J Coll Physicians Surg Pak. 2020, 30:754-6. 10.29271/jcpsp.2020.07.754
25. Aflahammi DM, Talon I, Rod J, et al.: Thoracoscopic rib resection in children. J Laparoendosc Adv Surg Tech A. 2018, 28:106-10. 10.1089/lat.2017.0131
26. Rivera JC, Wylie E, Dell’Orfano S, et al.: Approaches to treatment of unifocal Langerhans cell histiocytosis: biopsy-alone enough?. J Pediatr Orthop. 2014, 34:820-4. 10.1097/bpo.0000000000000150
27. Yanko AW, Fanning CV, Ayal A, Carrasco CH, Murray IA: Percutaneous techniques for the diagnosis and treatment of localized Langerhans-cell histiocytosis (eosinophilic granuloma of bone). J Bone Joint Surg Am. 1998, 80:219-28. 10.1099/0004625-199802000-00009
28. Howarth DM, Gilchrist GS, Mullan BP, et al.: Langerhans cell histiocytosis: diagnosis, natural history,
management, and outcome. Cancer. 1999, 85:2278-2290. 10.1002/(sici)1097-0142(19990515)85:10<2278::aid-cncr25>3.0.co;2-u

Abdelaal AH, Sedky M, Gohar S, Zaki I, Salama A, Hassanain O, El Ghoneimy AM: Skeletal involvement in children with Langerhans cell histiocytosis: healing, complications, and functional outcome. SICOT J. 2020, 6:28. 10.1051/sicotj/2020024