AMERICAN JOURNAL OF MEDICAL CASE REPORTS

ISSN 2374-216X

Langerhans cell histiocytosis of bone

Rituparna Biswas; Anirban Halder*

***Anirban Halder**

Department of Radiation Oncology, IPGMER, Kolkata, Howrah, West Bengal-711303, India

Abstract

Langerhans Cell Histiocytosis (LCH), previously known as histiocytosis X, is a rare, proliferative disorder caused by accumulation of pathologic Langerhans cells leading to local tissue infiltration and destruction. In this article, we report two cases of LCH of bone; a four years old child with LCH of left scapula and another adolescent with LCH of right mid-humerus.

Keywords

langerhans cell histiocytosis; langerhans cells

Introduction

Langerhans Cell Histiocytosis (LCH) is a rare disorder characterized by proliferation and infiltration of histiocytes at various organs, causing local or systemic effects. The most common sites of involvement include the bone, lung, central nervous system, liver, thymus, skin, and lymph node [1]. Though the etiology is controversial, various theories have suggested contribution of environment, infections, immunology, genetics, and neoplastic process. Limited data are available regarding the epidemiology of LCH, mainly, because of its relatively low incidence. The incidence of LCH is estimated to be 0.2-0.5 cases per 100.000 per year. It is usually considered to be a disease of childhood, however the diagnosis frequently is made in adults and many cases of childhood onset progress into adult life [2]. LCH has a widely variable disease course and clinical presentation with the capacity for spontaneous remission or chronic disease. The Histiocyte Society now recommends the term Langerhans Cell Histiocytosis to unify this disparate group of disorders. The staging system proposed by Greenberger et al. is applied in many reports [3]. The diagnosis of LCH is solely based on microscopic examination and management and prognosis of LCH are based on the clinical presentation of the lesion. Here we present two cases of LCH of bone.

Case Series

Case 1

An otherwise well, four years old boy had complaint of swelling over left upper back for eight months. Skiagram showed almost entire left scapula was destroyed by multiloculated cystic area with thick irregular septations (Figure1a). Skeletal survey was unremarkable for other sites. Magnetic Resonance Imaging (MRI) of left shoulder showed focal heterogeneous signal changes involving superior.

portion of scapula with marginal cortical irregularity and bone destruction with mild soft tissue edema and shoulder joint space was uninvolved (Figure1b). Biopsy from swelling was done and Histopathologic Examination (HPE) revealed proliferation of large mononuclear cells interspersed with inflammatory cells, suggestive of LCH. Further Immunohistochemistry (IHC) confirmed diagnosis as tumor cells were positive for CD1a and S100. He was treated by conventional radiotherapy with dose of 10 Gy in 5 fractions over one week on tele-cobalt. On being followed up after one month, the swelling was completely subsided and skiagram at that point of time showed near complete resolution (Figure 1c).

Case 2

Another sixteen years old male with no comorbidities, presented with pathological fracture of right mid- humerus. Skiagram showed a radiolucent lesion at mid diaphyses of right humerus (Figure 2). No other osteolytic lesions were observed on skeletal survey. Curettage was done and HPE revealed proliferation of mononuclear cells, histiocytes and eosinophil infiltration suggestive of LCH. No adjuvant radiation was considered. There was complete healing of fracture at the end of three months of follow up.

Systemic examination was non contributory in both cases.

Discussion

LCH is a rare systemic granulomatous disease demonstrating infiltration with histiocytes characterized by single or multiple osteolytic bone lesions with variable clinical spectrum [4]. The etiology and pathogenesis for development of LCH are still disputed. Clonal proliferation has been reported with the presence of BRAF V600E oncogenic mutation in more than half of patients with LCH, which suggests a neoplasm [5]. Although the disease can present at any age, it usually presents within the first few years of life and has slight male preponderence [2], similarly both our presented cases are male and young. The clinical presentation can range from localized disease, which may spontaneously resolve, to widely disseminated disease with organ failure and death [2]. Both of our reported cases presented with localised bone disease. Illnesses characterized by clonal proliferation of histiocytes in various tissues were traditionally labeled as Eosinophilic Granuloma of bone, Hand-Schuller-Christian syndrome, and Letterer-Siwe disease [2]. The Histiocyte Society now recommends the term Langerhans Cell Histiocytosis to unify these diverse group of disorders. Pain is the most common presenting symptom [6]. Children more commonly develop localized soft tissue swelling than do adults [6]. Fractures of the affected bones may appear as the first sign of the disease [6]. In our report, the child presented with local swelling and the adolescent presented with fracture. Bone lesion is often detected by skiagram and characterized by a osteolytic defect without evidence of reactive sclerosis [7]. As LCH can be a multifocal disease, radiographic skeletal surveys is considered to be a reasonable procedure for a complete evaluation of the bone condition. In addition, extra skeletal involvement is more likely in patients with multiple bony lesions. A bone scintigraphy can also be useful to exclude or to detect additional bone lesions and to follow up patients [8]. Biopsy of the lesion is necessary to establish the diagnosis. Pathology demonstrates infiltration of bone by clusters of characteristic histiocytes with admixture of morphologically related giant cells, eosinophils and lymphocytes. Specific Langerhans granules (Birbec's granules) can be identified in the histiocytes by electron microscopy [1]. IHC shows strong S-100 protein, HLA-DR and CD-1a surface antigen positivity [9]. For patients with localised bony disease, curettage is usually sufficient for diagnosis and therapy, although some cases may need

intralesional steroid or low dose radiation. Radiation dose for bony disease in children: 6-10 Gy and in adults: 15- 20 Gy are usually recommended [3,6,7]. Extensive or multiple bone lesions or multi-system disease is treated with immunomodulatory therapy which includes systemic glucocorticoids (prednisolone), chemotherapeutics (like the vinca alkaloids), the folate antagonists (methotrexate) and the purine analogues (6-mercaptopurine) [10].

The prognosis is variable. It has been seen in most studies that poor prognostic factors are age less than two years and patients with certain organ involvement, i.e. bone marrow, liver, spleen or lung. The estimated 10-year survival for single organ disease has been reported as high as 100% while the survival for multi-organ disease is 77% [11].

Figures

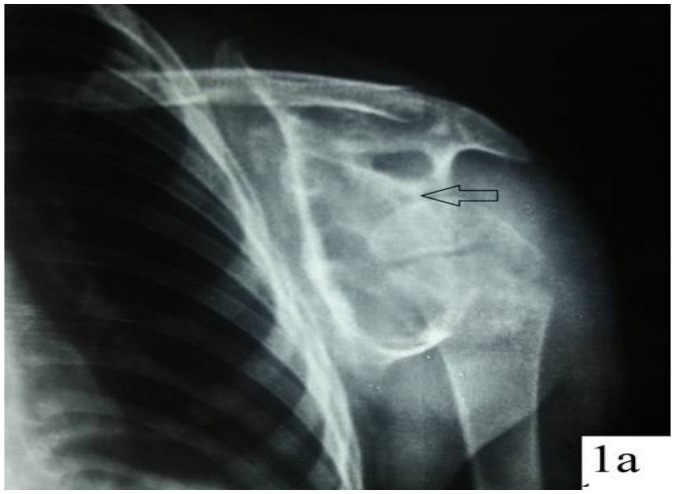

Figure1a: Skiagram showing lytic lesion in scapula.

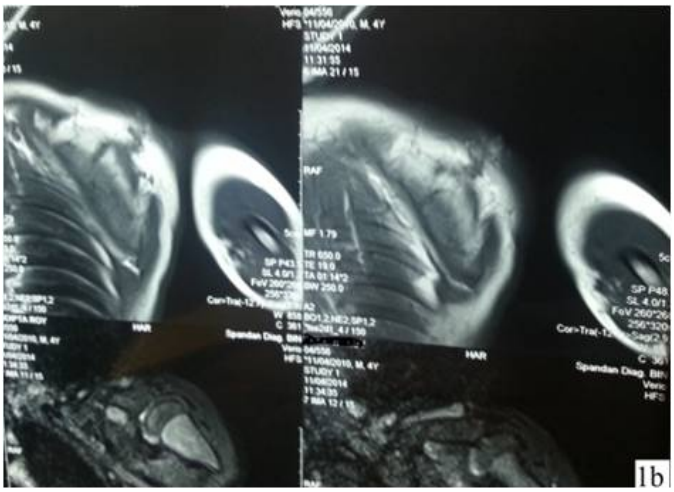

Figure1b: MRI of lt shoulder region showing scapular lesion.

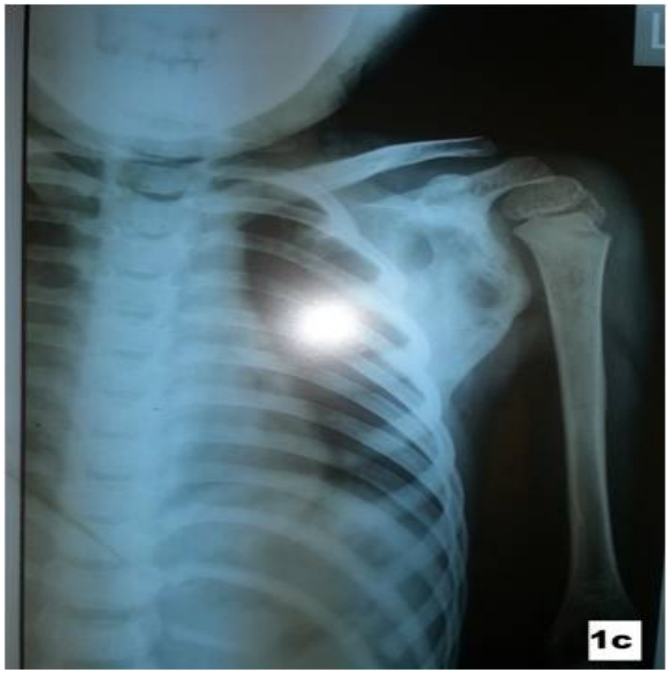

Figure 1c: One month post radiation skiagram showing near complete resolution of lesion.

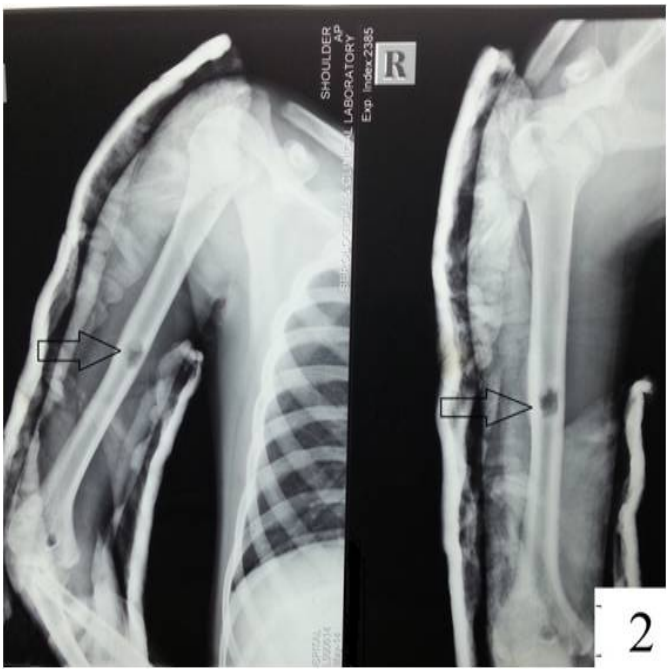

Figure 2: Skiagram showing radiolucent, lytic lesion in mid-diaphysis of right humerus.

Conclusion

The clinical spectrum of Langerhans Cell Histiocytosis (LCH) can be very diverse. Although, single bone lesion of LCH is one of the rarest cause of bone neoplasm, it should be considered in the differential diagnosis of solitary osteolytic lesion, as it can be successfully managed by partial resection or low dose radiotherapy. Optimal therapy is still unknown because no prospective controlled study has been performed. Further studies with large sample sizes are required to establish uniform treatment guidelines.

References

1. Azouz EM, Saigal G, Rodriguez MM, Podda A: Langerhan's cell histiocytosis: pathology, imaging and treatment of skeletal involvement. Pediatr Radiol. 2005; 35: 103-115.

2. Pavan Kumar Y, Jayshree Agrawal J. Mohanlakshmi P. Suresh Kumar. Langerhans cell histiocytosis revisited: Case report with review. Contemp Clin Dent. 2015; 6: 432–436.

3. Greenberger JS, Crocker AC, Vawter G. Results of treatment of 127 patients with systemic histiocytosis Letterer-Siwe syndrome, Schuller Christian syndrome, multifocal eosinophilic granuloma. Medicine. 1981; 60: 311-338.

4. Grois N, Fahrner B, Arceci RJ, Henter JI, McClain K, Lassmann H, et al. Histiocyte Society CNS LCH Study Group. Central nervous system disease in Langerhans cell histiocytosis. J Pediatr. 2010; 156: 873-881.

5. Routy B, Hoang J, Gruber J. "Pulmonary Langerhans Cell Histiocytosis with Lytic Bone Involvement in an Adult Smoker: Regression following Smoking Cessation". Case Reports in Hematology. 2015; 201536.

6. Ewa Wasilewska-TeÊluk, Zbigniew Szutkowski, Andrzej Kawecki. Langerhans cell histiocytosis of bone – a case report and review of the literature. Nowotwory Journal of Oncology. 2003; 53: 161–164.

7. Selch MT, Parker R. Radiation therapy in the management of Langerhans cell histiocytosis. Med Pediat Oncol. 1990; 18: 97-102.

8. Eckardt A, Schultze A. Maxillofacial manifestations of Langerhans cell histiocytosis: A clinical and therapeutic analysis of 10 patients. Oral Oncology. 2003; 39: 687-694.

9. Gabbay LB, Leite Cda C, Andriola RS, Pinho Pda C, Lucato LT. Histiocytosis: a review focusing on neuroimaging findings. Arq Neuropsiquiatr. 2014; 72: 548-558.

10. The French Langerhans' Cell Study Group. A multicentre retrospective survey of Langerhans' cell histiocytosis: 348 cases observed between 1983 and 1993. Arch Dis Child. 1996; 75: 17-24.

11. Bernstrand C, Sandstedt B, Ahstrom L, Henter JI. Longterm follow-up of Langerhans cell histiocytosis: 39 years' experience of a single centre, Acta Paediatr. 2005; 94: 1073-1084.