

Imaging of langerhans histiocytosis - Pictorial essay

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Abstract

Langerhans histiocytosis is the recent term used for the complex syndrome consisting of three sub types 1. Eosinophilic granuloma, 2. Hand-Schuller Christian disease and 3. Letterer-Siwe disease. The clinical manifestations vary with each entity. Although rare, radiological findings present a typical pattern. Advanced Imaging adds to the plain film diagnosis. The Imaging findings are illustrated in detail.

Keywords: Langerhans histiocytosis; Imaging of eosinophilic granuloma; Hand-Schuller Christian disease; Letterer-Siwe disease

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Introduction

Langerhans histiocytosis (LCH) is a complex syndrome with three subtypes, 1. Eosinophilic granuloma, 2. Hand-schuller Christian disease and 3. Letterer-siwe disease. It is a rare multi system disease and the incidence in India is not known. This term is replaced by the older term, Histiocytosis X. The etiology is unknown although, various theories have been proposed. Recent genomic studies showed activating, somatic BRAF mutations in most of the human specimens. This supports the concept of LCH as a myeloid neoplasm. Clinically the presentation depends upon the involved organ and the subtypes. Some of these may regress spontaneously and some of them have a rapid progressive course. In eosinophilic granuloma, there may be one or two skeletal lytic lesions. Around 70% of them are solitary. Although common in children, may be encountered in older age group also. The prognosis is good. In Hand-Schuller-Christian disease (HSC) clinically hepatosplenomegaly is noted with diabetes insipidus in some of the patients. Bone lesions are many. It is common in children and adolescents. The prognosis differs and depends on the severity of the lesions. In Letterer-Siwe disease, disseminated

lesions are noted in skin, bones and lungs. It runs a Fulminant course with poor prognosis. Infants in young children are affected.

Review of the literature

Langerhans histiocytosis (LCH) is a group of unknown disorders, characterized by the presence of cells with characteristics similar to bone marrow derived langerhans cells. In 1868, Paul langerhans has discovered the epidermal dendritic cells, which bear his name [1]. The term LCH is preferred to the older term histiocytosis X, since its cellular basis has been clarified [2- 4]. The etiopathogenesis of LCH is unknown. However LCH has been recently classified as a myeloid neoplasm, since cancer associated gene mutations of the ERK pathway are found in this disorder [5, 6]. LCH predominantly affects children and young adults [7, 8]. When the bones are involved the skull is the most common site and has typical radiographic appearance. In the spine, vertebra plana is the classical appearance. In the long bones, a lytic lesion confined to medulla and encroaching the endosteum is noted. Benign type of periosteal reaction may also be present [9-11]. MRI plays a major role in differentiating eosinophilic granuloma with other disorders [12].

The radiological investigations include the following

- Conventional films
- MD CT
- MRI
- Scintigraphy
- Pet CT

Radiological findings in eosinophilic granuloma (EG)

Conventional films show a lytic lesion of varying sizes between 1-3cms. However, multiple lytic lesions in the same bone or in multiple bones may be seen. In the long bones, lytic lesion is round or oval in shape with surrounding sclerosis and thick linear periosteal reaction (Figure 1a,b,c,d,e). In the flat bones such as skull, single or multiple large areas of lysis are seen. The bevelled edges in the skull are due to greater involvement of the inner than the outer table (Figure 1f,g). A button sequestrum is often noted in the lytic lesion (Figure 1h). The size of the lesion may be larger and multiple lesions may be seen. This appearance

has been described as “geographical” areas of lysis. The differential diagnosis of multiple lytic lesions of bones of calvaria is listed in Table 1. In the mandible, areas of lysis are seen along the alveolar margin with “floating teeth” (Figure 1i,j). Histopathology shows clusters of eosinophilic cells with admixture of neutrophils and occasional histiocytes (Figure 1k). MRI is not specific but confirms the plain film findings (Figure 1l,m,n).

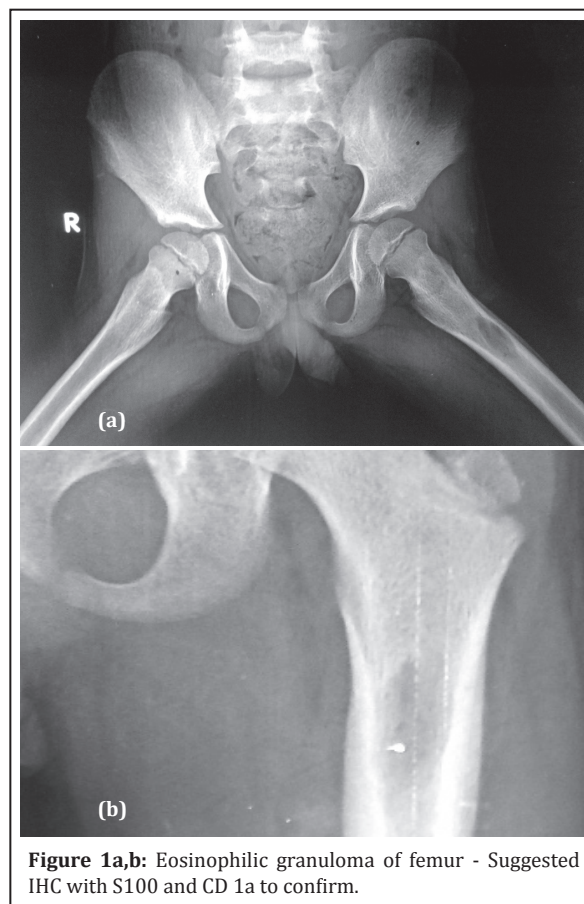


Figure 1a,b: Eosinophilic granuloma of femur - Suggested IHC with S100 and CD 1a to confirm.

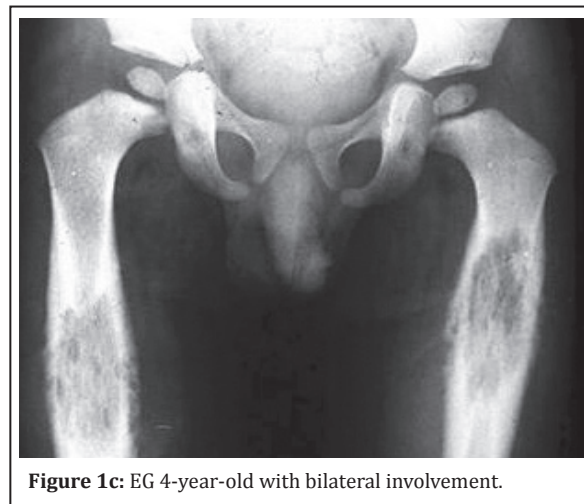


Figure 1c: EG 4-year-old with bilateral involvement.



Figure 1d: EG in humerus.



Figure 1e: EG of calcaneum.

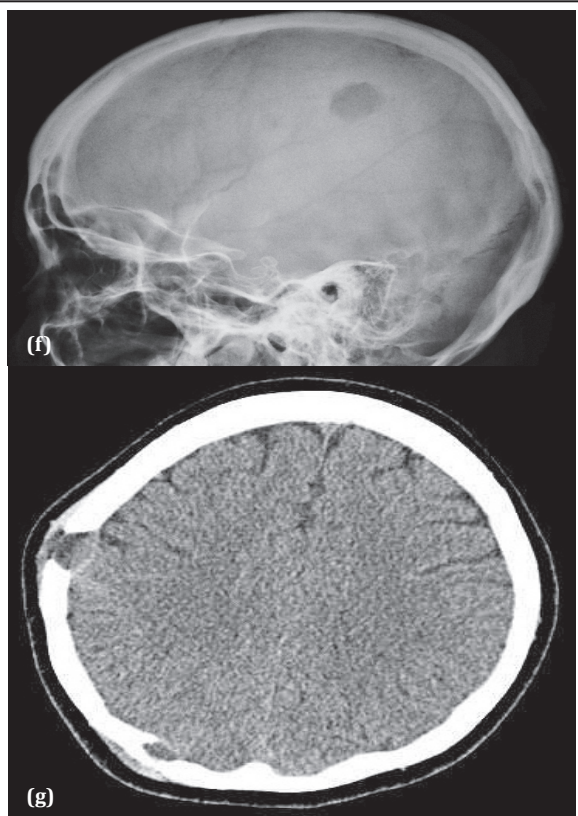


Figure 1f,g: EG skull (f) plain, (g) CT note the bevelled edges.

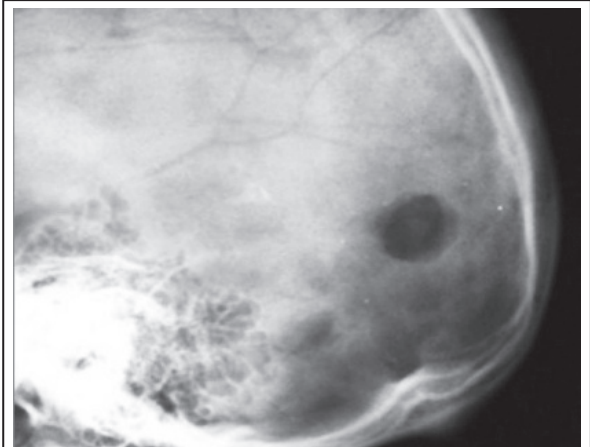


Figure 1h: EG with a button sequestrum.

Table 1: Differential diagnosis of multiple lytic lesions of bones of calvaria.

- Langerhan's histiocytosis
- Tuberculosis
- Osteomyelitis
- Hyperparathyroidism
- Lukemia/lymphoma
- Cystic angiomas
- Fibrous dysplasia
- Myeloma
- Metastasis

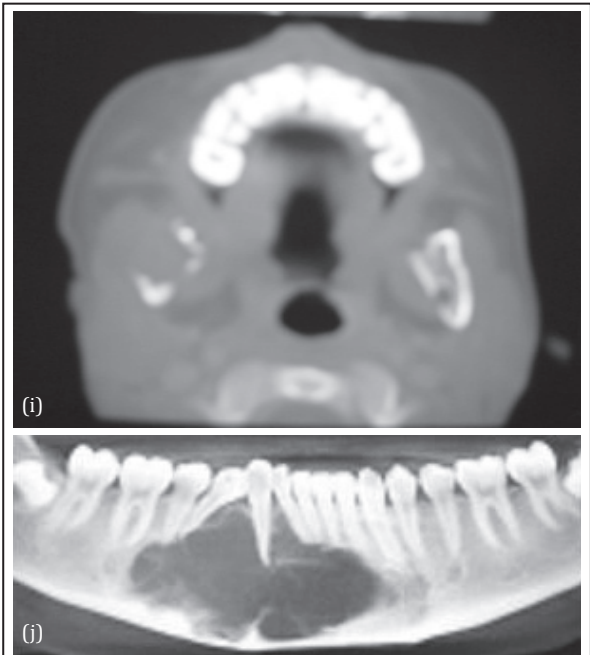


Figure 1: (i) CT-EG involving both sides of the mandible, (j) Floating tooth.

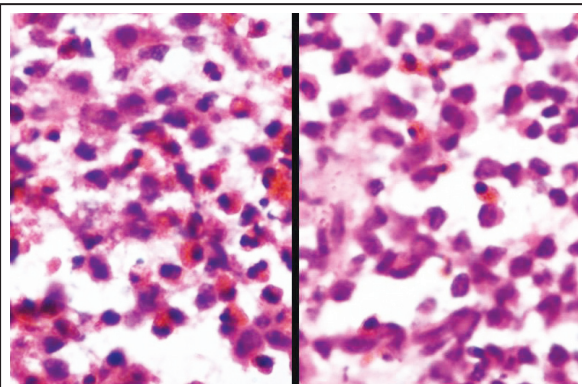
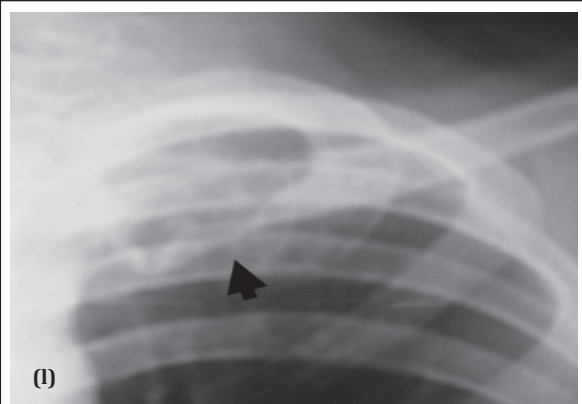
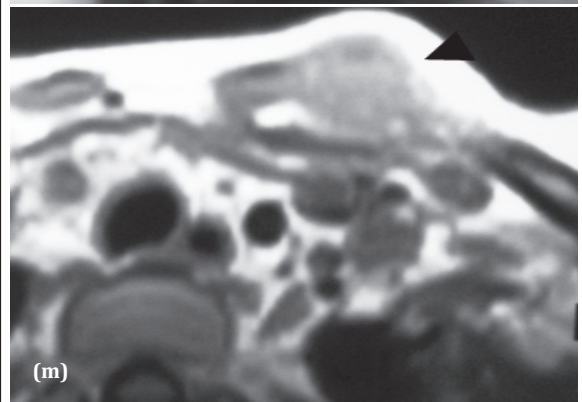


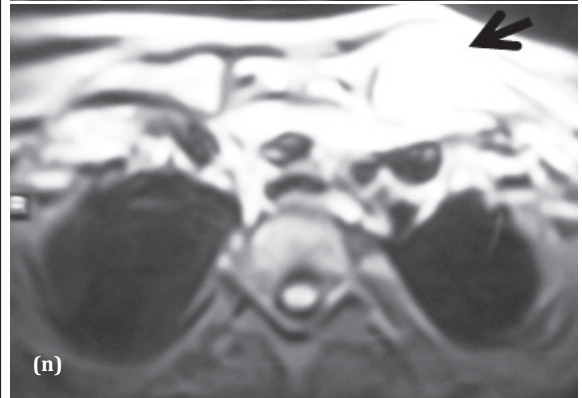
Figure 1k: Higher magnification of EG with eosinophilic clusters admixed with neutrophils and occasional histiocytes.



(l)



(m)



(n)

Figure 1: (l) EG of clavicle - Plain film, (m, n) MRI.

In the spine, vertebra plana is common finding (Figure 1,o).

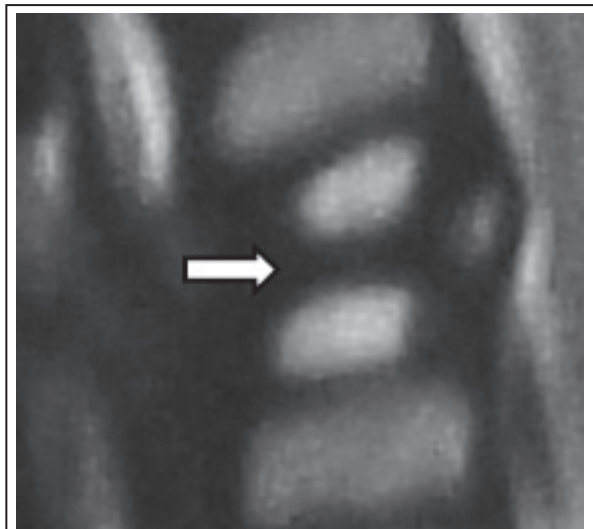


Figure 1o: MRI cervical spine-vertebra plana in EG.

Radiology of Hand-Schuller Christian disease (HSC)

In this type of Langerhans histiocytosis, the skeletal lesions are multiple and disseminated associated with lymphadenopathy and hepatosplenomegaly. Interstitial pulmonary changes with mediastinal lymphadenopathy may be seen. Diabetes insipidus may occur. A chronic course may be seen. Radiological findings include multiple lytic lesions involving flat and long bones with areas of confluence (Figure 2a,b,c). CT shows the characteristic appearance with bevelled edges (Figure 2d). Skull shows lytic areas simulating eosinophilic granuloma (Figure 2e,f,g). Scintigraphy reveals multiple hot spots (Figure 2h,i).

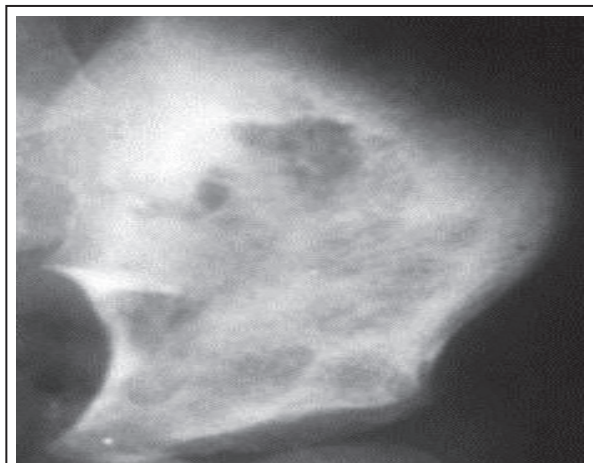


Figure 2a: LH in a 10-year-old boy involving iliac bone.



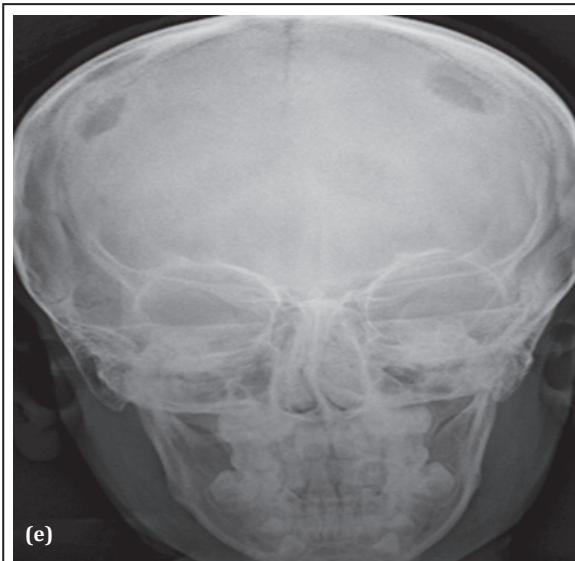
Figure 2b: HSC multiple lytic lesions.



Figure 2c: HSC with pathological fracture.



Figure 2d: CT multiple lytic areas involving both iliac bones in HSC.



(e)

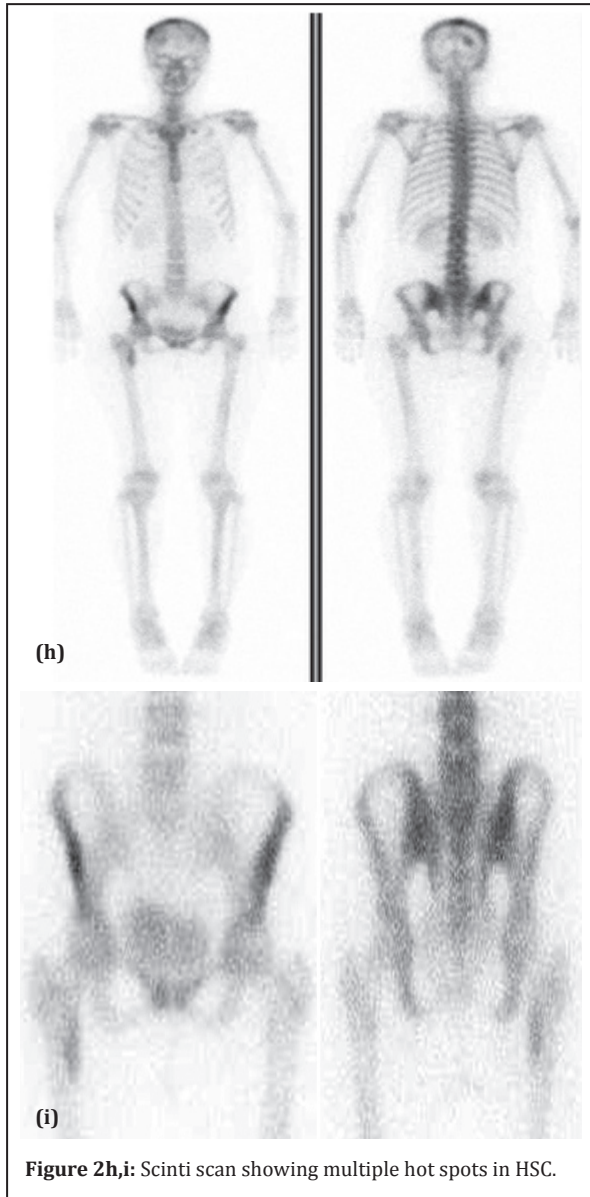


(f)



(g)

Figure 2e,f,g: Multiple lytic lesions in the skull in HSC disorder.



(h)

(i)

Figure 2h,i: Scinti scan showing multiple hot spots in HSC.

Letterer-Siwe disease (LS)

This subtype of LHS is often seen in younger age group below the age of 2years. Clinically, the affected is quite ill presenting with skin rash, anemia leucocytosis, fever, mediastinal adenopathy and disseminated pulmonary infiltrates. The skeletal lesions are often wide spread simulating metastasis from neuroblastoma or leukemia (Figure 3a). With steroid and chemotherapies the children are surviving longer. Radiologically the skeletal lesions are similar to multiple diffuse lytic lesions in the skull and vertebra. Vertebra plana may be noted (Figure 3b,c). Chest radiograph shows diffuse interstitial infiltrates (Figure 3d).

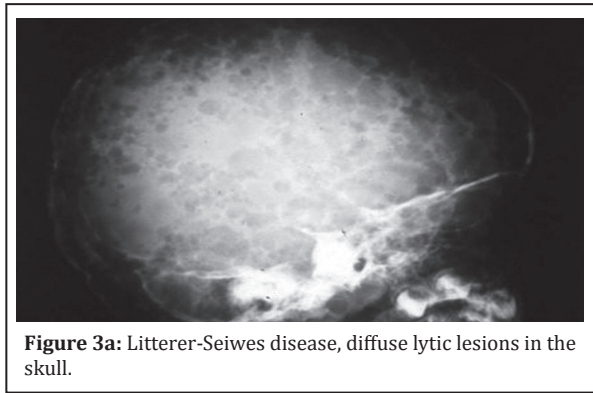
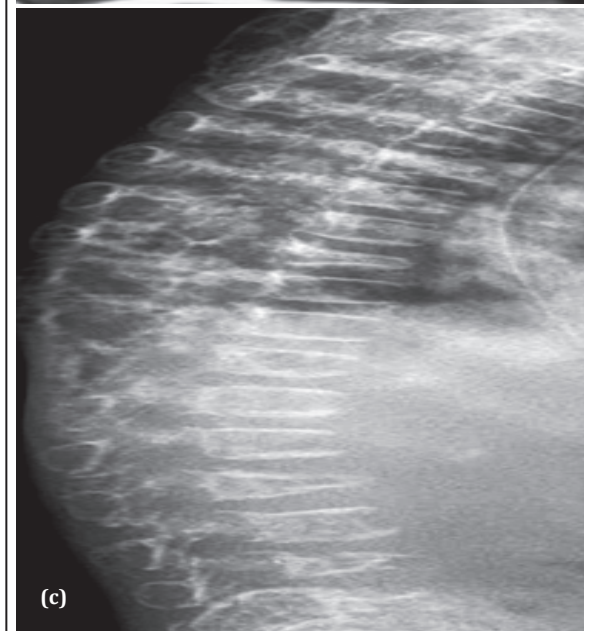


Figure 3a: Litterer-Seiwes disease, diffuse lytic lesions in the skull.



(b)



(c)

Figure 3: (b) CT lytic lesions in the spine, (c) compression fractures in LS disease.

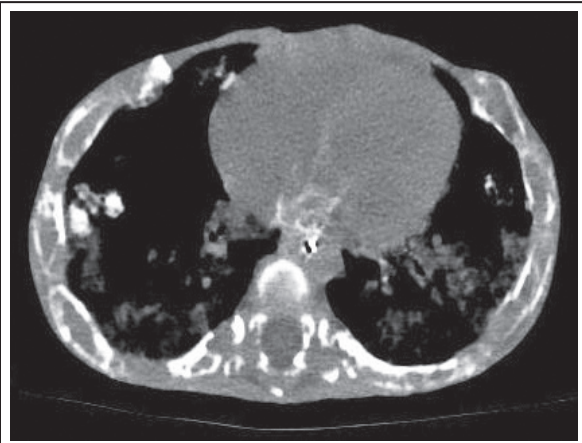


Figure 3d: CT reticulonodular shadowing of the lungs in LS disease, note the bone lesions.

Conclusion

Langerhans cell histiocytosis includes three subtypes 1. Eosinophilic granuloma, 2. Hand-schuller Christian disease and 3. Letterer-Siwe disease. The clinical findings differ with each type. Conventional radiography often reveals lytic lesions. Advanced imaging methods such as MDCT may help in characterising the lytic lesion. MRI and scintigraphy help in revealing multiple lesions. Differential diagnosis of multiple lytic lesions of the skull is listed.

Acknowledgements

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Conflicts of interest

The author declares no conflict of interest.

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