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TEST YOURSELF: ANSWER

Answer: Multiple lesions of the skull in a 30-month-old girl

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Discussion

Langerhans cell histiocytosis (LCH) is rare, affecting 5–10 children per million (mostly under 15 years old). LCH is even rarer in adults, with an incidence of 1–2 adults per million per year, with an increased incidence in males and Hispanics [1–5]. The exact aetiology of this disease is unknown, with the debate still ongoing over whether it is a neoplastic or reactive disease in nature [2, 3]. Clonal proliferation and specific mutations, potential mortality and response to chemotherapy argue in favour of a neoplastic origin, whereas the possibility of spontaneous remission, inflammatory infiltrates and large amounts of cytokine production argues in favours of a reactive origin [3].

LHC is clinically categorized into single or multi-system disease [3]. In single-system, the disease only affects a single organ or system at diagnosis [3]. This can then be subcategorised into uni-focal, or if multiple bone lesions exist or multiple lymph nodes are involved, multi-focal disease [3]. In multi-focal disease, multiple organs systems are affected at the time of diagnosis [3].

Patients under five years old have a greater chance of systemic involvement, while patients between 5 and 15 usually only present with solitary bone lesions [2, 3].

LCH presents with lytic bone lesions, often with accompanying soft tissue swelling (80%), rash (20 to 40%), soft tissue swelling near bone lesions, lymph nodes or thymus enlargement, external ear drainage and gum hypertrophy and premature tooth eruption [1–3, 5, 6]. The liver and spleen can be affected in some cases [1, 3, 4]. Patients presenting with only single-site skeletal, lymph node or skin lesions have a better prognosis compared with those with spleen and lymph node involvement [2, 3]. Neurological symptoms can appear at onset or during remission, causing cognitive and cerebellar involvement caused by space-occupying lesions within the central nervous system, as well as leukoencephalopathy and atrophic changes [1, 3, 7]. Patients presenting with skull lesions at the diagnosis are considered high-risk for central nervous system involvement if the mastoid, temporal, sphenoid or orbital bones are affected [1, 3].

Diagnosis is based on biopsy using specific histopathological markers such as CD1a, S100 or Langerin [3].

Full body radiographic skeletal survey (RSS) and chest radiographs are recommended at the diagnosis as a first workup. Bone scan indication for the initial workup is controversial, with some guidelines still including it as a part of the initial workup, whilst others, such as the International Histiocyte Society, have seen it side-lined due to limited sensitivity [2]. CT-scan and FDG PET-CT are useful for both initial staging as well as follow-ups [1, 2]. FDG PET-CT studies in particular are used to assess disease activity in addition to initial staging [2].

A variety of modalities can be used to detect LHC, each with their own characteristics. When using FDG PET-CT studies the lesions may appear as high activity zones [2]. On radiographs, 80% of LCH patients present with solitary or multiple bone lesions, predominantly located at the skull and, less frequently, spine, pelvis and ribs. Feet and hands are rarely affected [3]. Lesions affecting the skull typically have a bevelled appearance on radiographs [2]. Vertebra plana is the typical appearance of LCH of the spine [2]. When the appendicular skeleton is affected, endosteal scalloping or fusiform periosteal reactions can be observed [3, 5]. If MRI is used, the bone lesions will typically present as bone marrow oedema, with or without accompanying periostitis, these lesions being best seen on STIR sequences [2]. Bone scintigraphy will show either increased uptake, in lesions with osteoblastic activity, or decreased uptake in healed or inactive lesions as well as in lesions without osteoblastic activity [2]. Cervical lymphadenopathy occurs

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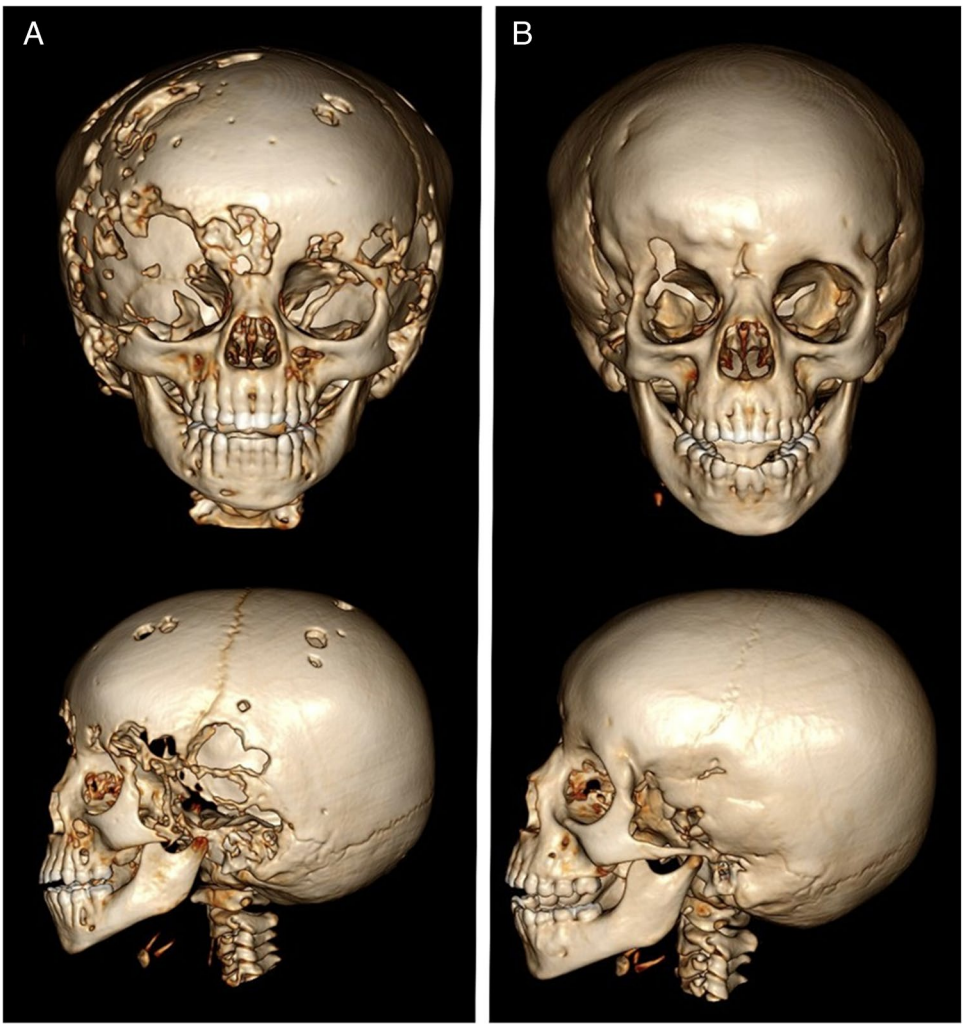

Fig. 1. 3D VRT CT-scanner reconstructions showing pre-treatment (**A**) and post-treatment (**B**) improvement of the lytic skull lesions

in around 13% of cases, though other regional lymph nodes may also be involved, with those draining bone or skin commonly affected [3].

In our case, the patient presented with multiple osteolytic lesions during the initial standard radiograph workup located on the scapula, femur, and hip bone (not shown). Further imaging revealed multiple bilateral necrotic, rim enhancing, lymph nodes in the neck. Furthermore, the patient presented numerous osteolytic lesions of the skull of variable appearances ranging from well marginated and bevelled to moth-eaten in appearance.

In cases where LCH presents as a solitary lesion, the differential diagnosis includes epidermoid and dermoid cysts and metastasis [5, 8].

Once diagnosed, treatment ranges from watchful waiting to vinblastine/prednisone or targeted therapy, depending on the spread of the disease and organs affected [1, 3]. The prognosis for LCH patients has improved over the last 40 years and is now thought to be excellent [9]. For patients younger than 2 years, the 10-year survival rate is over 80%, rising to 97% for patients over 2 years old [9]. Figure 1 illustrates post-treatment improvement in our patient with the reduction of the lesions.

Declarations

Conflicts of interest The authors declare that they have no conflict of interest.

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