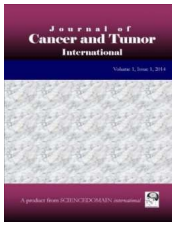

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Technetium-MDP Bone Scan/SPECT CT Findings in Erdheim-Chester Disease: A Case Report of Skull and Ribs Involvement

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Authors' contributions

This work was carried out in collaboration between both authors. Author CAA designed the study, gathered necessary case information and wrote the first draft of the manuscript. Author GE reviewed the manuscript. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Erdheim-Chester disease (ECD) is a rare disorder of the non-Langerhans cell histiocytes with associated infiltration of multiple organ systems. Skeletal involvement is characteristically bilateral and symmetric, exhibiting an osteosclerotic pattern in the metaphysis and diaphysis of the long bones, usually sparing the epiphysis. It is quite a rare disease with less than one hundred cases reported in the literature. We report a case of a 31 year old retroviral disease positive female patient who presented with a history of right sided hemiplegia and aphasia and subsequently diagnosed to have ECD histologically following a brain biopsy. A technetium-99m methylene diphosphonate ((99m)Tc-MDP) bone-scan done showed osteoblastic lesions in the left lateral parietal skull and in the right 4th-6th ribs anteriorly and the right 10th rib antero-laterally. The patient had irradiation of the intracranial mass and is presently on interferon. ECD though a rare disorder also presented with a rare skull and ribs involvement in this patient.

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Keywords: Technetium-MDP; bone scan/SPECT-CT; erdheim-chester disease; skull and ribs involvement.

1. INTRODUCTION

Erdheim-Chester disease (ECD) is a rare disorder of the non–Langerhans cell histiocytes first described in 1930 with poorly understood specific etiology and pathogenesis [1-4]. There is associated infiltration of multiple organ systems (skin, lung, bone, heart, central nervous system, pituitary, retroperitoneum, (retro-) orbital tissue) by xantogranulomatous lipid-laden histiocytes [2]. Skeletal involvement is characteristically bilateral and symmetric, exhibiting an osteosclerotic pattern in the metaphysis and diaphysis of the long bones, usually sparing the epiphysis. It was first reported in 1930 by the pathologist Jakob Erdheim and physician William Chester in two patients [1]. It is quite a rare disease with less than one hundred cases reported in the literature. We report a bone scan/ SPECT/CT findings in a 31 year old retroviral disease positive female patient who presented with a history of right sided hemiplegia and aphasia and subsequently diagnosed to have ECD histologically following a brain biopsy.

2. CASE REPORT

A thirty one year old female, a known retroviral disease patient on Anti Retroviral treatment who presented with a three day history of right sided hemiplegia and aphasia with no signs of meningeal irritation and altered consciousness. Patient was afebrile with normal vital signs. Blood sample result included a low white blood cell count (2.15 x 10^9/L) with low neutrophils (1.02 X 10^9/L) and lymphocytes (0.80 X 10^9/L) count but high basophils (7.42 x 10^9 /L). There was also an associated low red cell count (3.04 x 10^{12}/L), high MCV (114.1 FL), MCH (41.4 pg) and MCHC (36.3 g/dl) level. The absolute CD4 level was Normal (938).The Serum ALP, AST, ALT and GGT were all elevated with a low serum albumin. The brain contrast enhancing CT (CECT) scan revealed a large contrast enhancing tumor in the left basal ganglia and portion of the frontal and parietal lobe while the abdominal CECT demonstrated two small hypodensities in the liver segment 4A, measuring 4mm across which was suggested to be hepatic cysts. A brain biopsy of the left basal ganglia with subsequent histopathological analyses revealed an infiltration of lipid storing macrophages with non- Langerhans' features (CD 68+, CD1a–, S100 –), which is consistent with ECD. A technetium-99m methylene diphosphonate ((99m)Tc-MDP) SPECT/CT bone-scan showing osteoblastic lesions in the right 4^{th}-6^{th} ribs anteriorly, the right 10^{th} rib antero-laterally and in the left lateral parietal skull. The patient subsequently had irradiation of the intracranial mass and is presently on interferon. The patient made clinical improvement with minimal side effects of interferon and was then discharged to follow up with the medical team including rehabilitative therapies like speech therapy.

3. DISCUSSION

Erdheim-Chester disease (ECD) has a poorly understood specific etiology and pathogenesis [1-4]. It is documented to be more common between the 5^{th} and 7^{th} decades of life with a mean age of 53-54 years [5-7] and slight male predominance [7-8]. The reason for this slight male predominance is not understood however most of the work done reported male predominance. Our patient in this report is a 31 year old female which may not be the typical pattern of age and sex presentation of ECD; however reports of presentation below the age of forty years have been documented [9,2,7,10]. It is also reported that male patients are diagnosed at a more advanced age than female patients [2,11].

ECD is associated with a variety of general and non specific symptoms which may be a reflection of the involved organ-system and may include amongst others fever, weakness, weight loss, night sweats, Diabetes insipidus, bone pain, exophthalmos and failure to thrive in children [7, 2,12,10]. Skeletal involvements have been reported in as many as 70-96% of cases [4,3] and are characteristically bilateral and symmetric, involving mostly long bones [13,14, 15]. Extra-skeletal involvement is correlated with increased morbidity and mortality [2]. Our patient presented with a history of right sided hemiplegia and aphasia reflecting a central nervous system involvement. The low white cell count and red cell count may be associated with other inter-current illness like HIV infection which the patient had.

The diagnosis of ECD is made by identifying distinctive histopathological findings in the appropriate clinical and radiologic context. The initial step towards a diagnosis of ECD is either

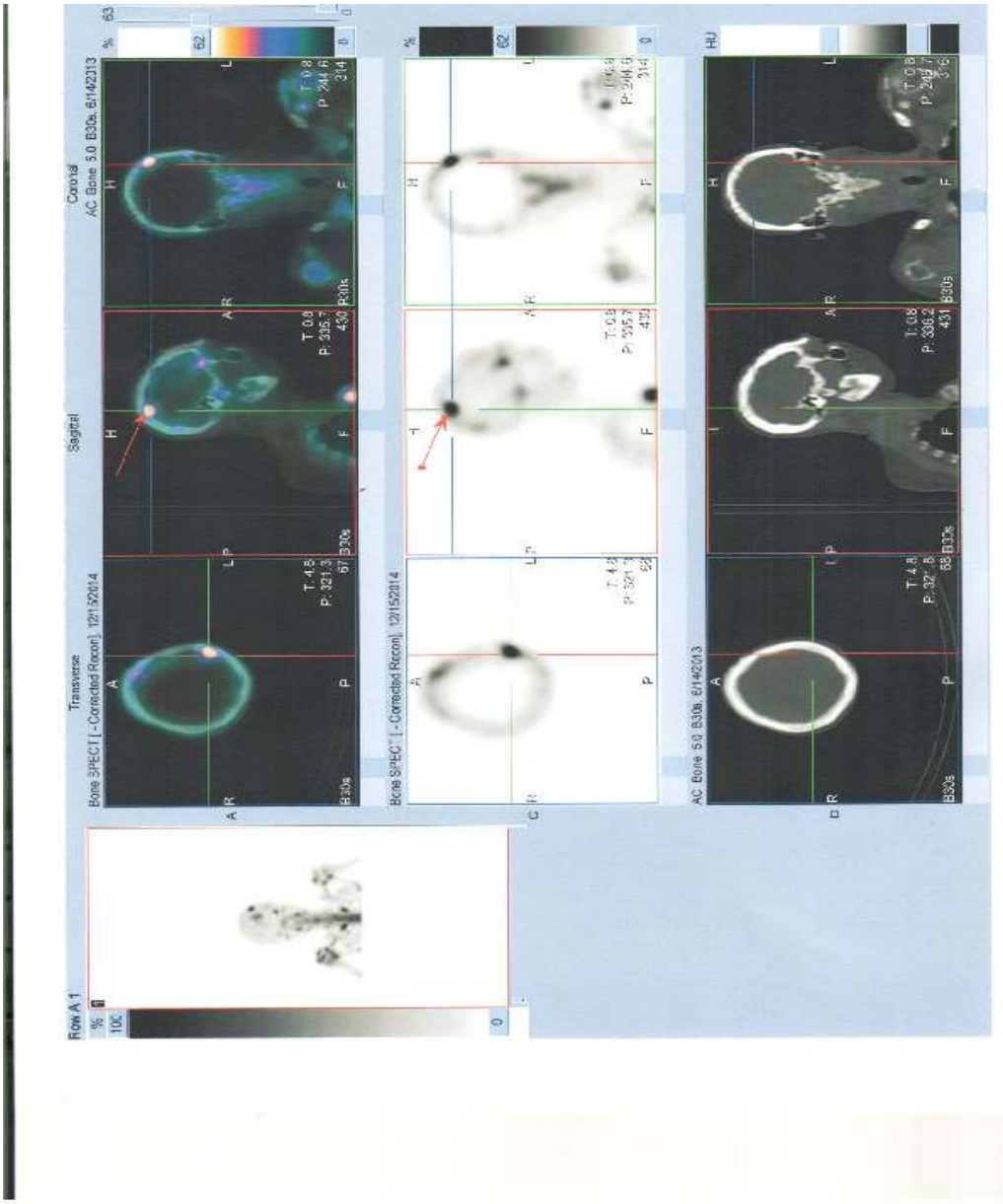

Fig. 1. A technetium-99 m methylene diphosphonate ((99 m)Tc-MDP) SPECT/CT bone-scan showing osteoblastic lesions in the left lateral parietal skull

99 mTc bone scintigraphy and\or radiography findings that are virtually pathognomonic to the disease with the conventional radiography exhibiting an osteosclerotic pattern and the bone scintigraphy showing osteoblastic lesions in the metaphysis and diaphysis of the long bones, usually sparing epiphysis in a bilaterally symmetric pattern [13-16]. However in this report, scintigraphy revealed ribs and skull osteoblastic involvement which is a rare and atypical pattern of skeletal involvement in this rare disease. This is however also reported by various other authors who have documented such atypical bone involvement of flat bones of the skull, ribs etc. [9,17-19]. Technetium-99m methylene diphosphonate ((99 m)Tc-MDP) bone-scan is a radioparmaceutical which has good affinity in the bones and hence can be used to image the entire skeletons of the body searching for mitotic, metastatic lesions amongst other uses.

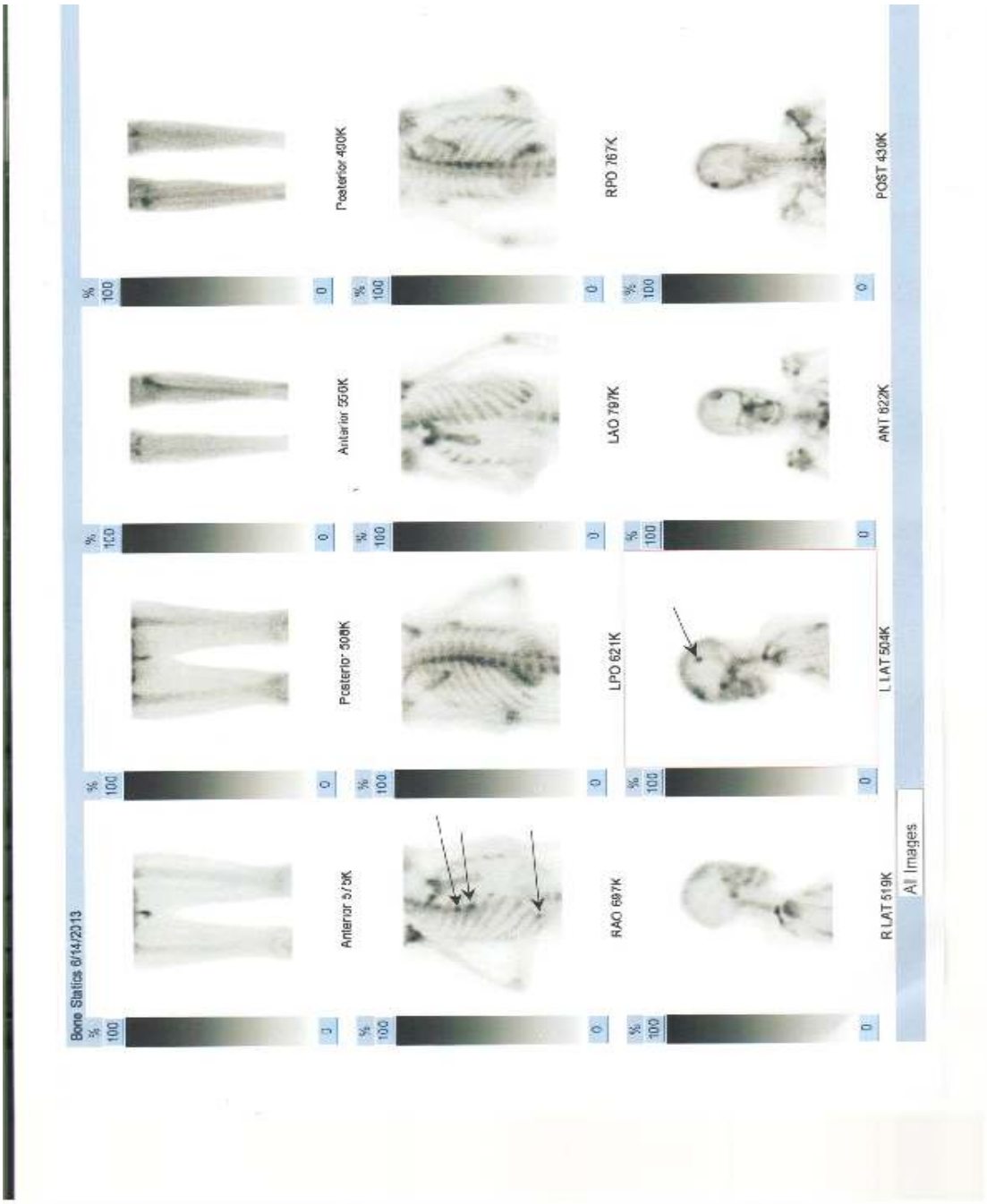

Fig. 2. A technetium-99 m methylene diphosphonate ((99 m)Tc-MDP) bone-scan done showing osteoblastic lesions in the right 4^{th}-6^{th} ribs anteriorly, the right 10^{th} rib antero-laterally and in the left lateral parietal skull

Confirmation of the diagnosis of ECD is actually established by the distinct histological pattern that characterizes the condition which is a mononuclear infiltrate consisting of lipid laden, foamy histiocytes (xanthogranulomatosis) that stain positively for CD68 [4,7,20]. Immunohistochemically, the histiocytes are usually negative for S-100 protein and CD1a, but may occasionally be found weakly positive for S-100 protein. A few Touton-type cells may be seen while ultra structural studies show Birbeck granules in fewer than 20% of histiocytes [4,7,

21]. In our patient a brain biopsy of the left basal ganglia with subsequent histopathological analyses revealed an infiltration of lipid storing macrophages with non- Langerhans' features (CD 68+, CD1a–, S100 –), which is consistent with ECD.

Different treatment modalities have been applied in the management of ECD including use of steroids and irradiation. Currently the first line of management in ECD is the use of Interferon-α / Peginterferon alfa-2a [22-25], with a second line alternatives including the use of Cladribine [26], Vemurafenib [27] Anakinra [28] and Infliximab [29]. Our patient had irradiation of the intracranial mass and was placed on interferon. This patient made some clinical improvement and was discharged for outpatient follow up visits. Patient was hence not treated with the second line drugs like vemurafenib, which is a newly approved BRAF inhibitor, which should be considered for patients with severe and refractory $BRAF^{V600E}$ histiocytoses, particularly when the disease is life-threatening [27].

The prognosis is poor in patients with extra-skeletal involvement. Arnaud et al. [30] reported a one year survival of 96% and a 5 year survival of 68% while Veyssier-Belot [7] reported a mortality rate of 59% in a study involving 37 patients and 3-120 months of follow up with respiratory and cardiac failure being the most common cause of death. Similarly, a mortality rate of 60% was reported by Haroche et al. [31] in patients with cardiovascular involvement. Positron Emission Tomography (PET) and CRP may be useful in monitoring disease activity in ECD, however they were not done in this patient due to cost implication of PET.

4. CONCLUSION

We have reported a rare ECD presenting atypically with a skull and ribs infiltration as depicted by the whole body Technetium-99m methylene diphosphonate ((99 m)Tc-MDP) bone-scan and SPECT/CT.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

All authors hereby declare that a written informed consent was given by the patient and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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