

Case study

TECHNETIUM-MDP BONE SCAN/SPECT CT FINDINGS IN ERDHEIM-CHESTER DISEASE; A CASE REPORT OF SKULL AND RIBS INVOLVEMENT.

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.

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.

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 ($2.15 \times 10^9/L$) with low neutrophils ($1.02 \times 10^9/L$) and lymphocytes ($0.80 \times 10^9/L$) count but high basophils ($7.42 \times 10^9/L$). There was also an associated low red cell count ($3.04 \times 10^{12}/L$), high MCV (114.1 FL), MCH (41.4pg) and MCHC (36.3g/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 4th-6th ribs anteriorly, the right 10th 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 was then discharged to follow up with the medical team including rehabilitative therapies like speech therapy.

DISCUSSION

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) It is documented to be more common between the 5th and 7th decades of life with a mean age of 53-54 years [5-7] and slight male predominance (7-8). 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 infiltration of multiple organ systems (skin, lung, bone, heart, central nervous system, pituitary, retroperitoneum, (retro-) orbital tissue) by xantogranulomatous lipid-laden histiocytes (2). A variety of general and non specific symptoms may accompany ECD 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.

Cardinal in the establishment of the presence of ECD includes radiological and histological criteria. The initial step towards a diagnosis of ECD is either 99mTc 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).

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.

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.

REFERENCES

1. Chester W. U^{ber} lipoidgranulomatose. Virchows Arch A Pathol Anat Histopathol 1930; 279:561–602.
2. Roei D Mazor, Mirra Manevich-Mazor and Yehuda Shoenfeld, Erdheim-Chester Disease: a comprehensive review of the literature Orphanet Journal of Rare Diseases 2013, 8:137
3. Haroche J, Arnaud L, Amoura Z: Erdheim-Chester disease. Curr Opin Rheumatol 2012, 24:53–59.
4. Trifon J. Spyridonidis · Costas Giannakenas Panagiota Barla · Dimitrios J. Apostolopoulos Erdheim–Chester disease: a rare syndrome with a characteristic bone scintigraphy pattern Ann Nucl Med (2008) 22:323–326
5. Volpicelli ER, Doyle L, Annes JP, Murray MF, Jacobsen E, Murphy GF, Saavedra AP: Erdheim-Chester disease presenting with cutaneous involvement: a case report and literature review. J Cutan Pathol 2011, 38:280–285
6. Al-Quran S., Reith J., Bradley J : Erdheim-Chester Disease: case report, PCR-based analysis of clonality and review of literature. *Mod Pathol*, 2002, 15: 666-672.

- 105 7. Veyssier-Belot C, Cacoub P, Caparros-Lefebvre D, Wechsler J, Brun B, Remy M, et al : Erdheim-Chester disease.
106 Clinical and radiologic characteristics of 59 cases. *Medicine* 1996, 75:157–169.
107
- 108 8. Drier A, Haroche J, Savatovsky J, Godeneche G, Dormont D, Chiras J, et.al : Cerebral, facial, and orbital
109 involvement in Erdheim-Chester disease: CT and MR imaging findings. *Radiology* 2010,
110 255:586–594.
111
- 112 9. Petrikowski GC, W. Tim McGaw, Erdheim-Chester disease of the jaws: Literature review and case report *Oral*
113 *Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:389-98)
114
- 115 10. Tran TA, Fabre M, Pariente D, Craiu I, Haroche J, Charlotte F et al : Erdheim-Chester disease in childhood: a
116 challenging diagnosis and treatment. *J Pediatr Hematol Oncol* 2009, 31:782–786.
117
- 118 11. Allen TC, Chevez-Barrios P, Shetlar DJ, Cagle PT: Pulmonary and ophthalmic involvement with Erdheim-Chester
119 disease: a case report and review of the literature. *Arch Pathol Lab Med* 2004, 128:1428–1431.
120
- 121 12. Mills JA, Gonzalez RG, Jaffe R: Case records of the Massachusetts General Hospital. Case 25–2008. A 43-year-
122 old man with fatigue and lesions in the pituitary and cerebellum. *N Engl J Med* 2008, 359:736–747
123
- 124 13. Dion E, Graef C, Miquel A, Haroche J, Wechsler B, Amoura Z et al : Bone involvement in Erdheim-Chester
125 disease: imaging findings including periostitis and partial epiphyseal involvement. *Radiology* 2006, 238:632–639.
126
- 127 14. Zanglis A, Valsamaki P, Fountos G.Erdheim-Chester disease: symmetric uptake in the (99m)Tc-MDP bone scan.
128 *Hell J Nucl Med.* 2008 Sep-Dec;11(3):164-7.
129

- 130 15. Núñez, Rodolfo; Tronco, Gene G.; Rini, Josephine N. M; Hofman, Joshua; Amoashiy, Michel; Bhuiya, Tawfiqul et
131 al. Radionuclide Bone Imaging in Erdheim-Chester Disease Clinical Nuclear Medicine:
- 132 16. Gotthardt M, Welcke U, Brandt D, Tontsch D, Barth PJ, Schaefer J et al : The role of bone scintigraphy in
133 patients with Erdheim-Chester disease. Clin Nucl Med 2000, 25:414–420.
- 134
- 135 17. Drier A, Haroche J, Savatovsky J, Godeneche G, Dormont D, Chiras J et al : Cerebral, facial, and orbital
136 involvement in Erdheim-Chester disease: CT and MR imaging findings. Radiology 2010, 255:586–594.
- 137
- 138 18. Myoung-Shin Kim, Chae-Hwa Kim, Seok-Joo Choi, Chong-Hyun Won, Sung-Eun Chang, Mi-Woo Lee, Jee et al:
139 CASE REPORT Erdheim-Chester Disease (Ann Dermatol 22(4) 439~443, 2010)
- 140
- 141 19. Ajit D. Dinkar, Anita Spadigam, Sharad Sahai, PITAL Oral radiographic and clinico-pathologic presentation of
142 Erdheim-Chester disease: A case report Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;103:e79-e85)
- 143
- 144 20. Sheu SY, Wenzel RR, Kersting C, Merten R, Otterbach F, Schmid KW. Erdheim–Chester disease: case report with
145 multisystem manifestations, including testes, and lymph nodes, and a review of literature. J Clin Pathol 2004;
146 57:1225–8.
- 147
- 148 21. Dion E, Graef C, Haroche J, Renard-Penna R, Cluzel P, Wechsler B, et al. Imaging of thoracoabdominal
149 involvement in Erdheim–Chester disease. AJR 2004; 183:1253–60.
- 150
- 151 22. Arnaud L, Hervier B, Neel A, Hamidou MA, Kahn JE, Wechsler B, et al: CNS involvement and treatment with
152 interferon-alpha are independent prognostic factors in Erdheim-Chester disease: a multicenter survival analysis of
153 53 patients. Blood 2011, 117:2778–2782.
- 154

- 155 23. Haroche J, Amoura Z, Trad SG, Wechsler B, Cluzel P, Grenier PA et al : Variability in the efficacy of interferon-
156 alpha in Erdheim-Chester disease by patient and site of involvement: results in eight patients. Arthritis Rheum
157 2006, 54:3330–3336
158
- 159 24. Suzuki HI, Hosoya N, Miyagawa K, Ota S, Nakashima H, Makita N et al: Erdheim-Chester disease: multisystem
160 involvement and management with interferon-alpha. Leuk Res 2010, 34:e21–24.
161
- 162 25. Hervier B, Arnaud L, Charlotte F, Wechsler B, Piette JC, Amoura Z et al: Treatment of Erdheim-Chester disease
163 with long-term high-dose interferon-alpha. Semin Arthritis Rheum 2012, 41:907–913
164
- 165 26. Myra C, Sloper L, Tighe PJ, McIntosh RS, Stevens SE, Gregson RH et al: Treatment of Erdheim-Chester disease
166 with cladribine: a rational approach. Br J Ophthalmol 2004, 88:844–847.
167
- 168 27. Haroche J, Cohen-Aubart F, Emile JF, Arnaud L, Maksud P, Charlotte F et al: Dramatic efficacy of vemurafenib in
169 both multisystemic and refractory Erdheim-Chester disease and Langerhans cell histiocytosis harboring the BRAF
170 V600Emutation. Blood 2013, 121:1495–1500.
171
- 172 28. Aouba A, Georgin-Lavialle S, Pagnoux C, Martin Silva N, Renand A, Galateau-Salle F, et al: Rationale and efficacy
173 of interleukin-1 targeting in Erdheim-Chester disease. Blood 2010, 116:4070–4076.
174
- 175 29. Dagna L, Corti A, Langheim S, Guglielmi B, De Cobelli F, Doglioni C et al: Tumor necrosis factor alpha as a master
176 regulator of inflammation in Erdheim-Chester disease: rationale for the treatment of patients with infliximab. J Clin
177 Oncol 2012, 30:e286–290.
178
- 179 30. Arnaud L, Hervier B, Neel A, Hamidou MA, Kahn JE, Wechsler B, et al: CNS involvement and treatment with
180 interferon-alpha are independent prognostic factors in Erdheim-Chester disease: a multicenter survival analysis of
181 53 patients. Blood 2011, 117:2778–2782

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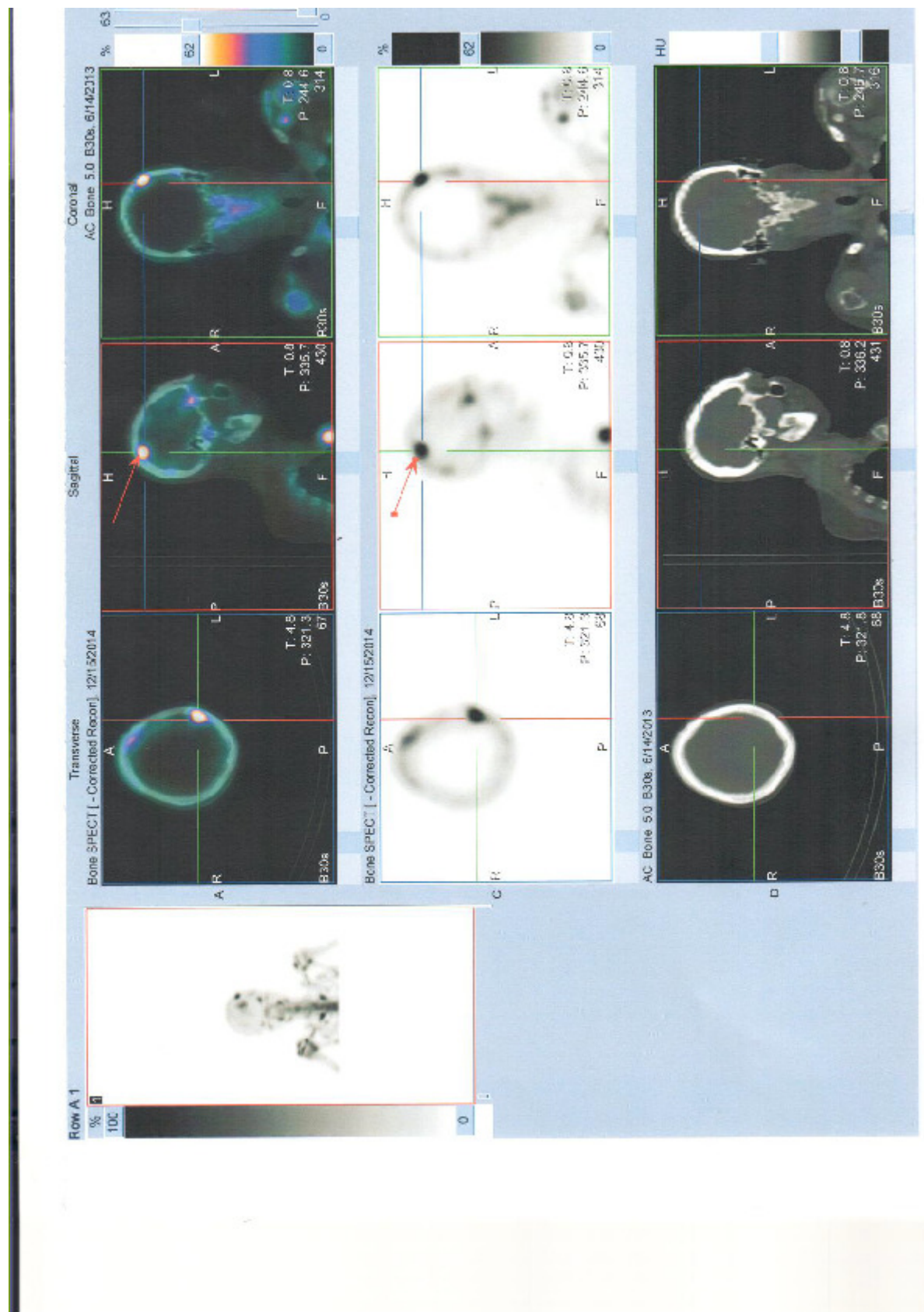
183 31. Haroche J, Amoura Z, Dion E, Wechsler B, Costedoat- Chalumeau N, Cacoub P, et al. Cardiovascular
184 involvement, an overlooked feature of Erdheim–Chester disease: report of 6 new cases and a literature review.
185 Medicine 2004; 83:371–92

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187 **FIGURE LEGENDS**

188 **FIGURE 1.**

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



192 **FIGURE 2.**

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

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