

Erdheim - Chester Disease : A Rare Case Report

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ABSTRACT

Erdheim-Chester Disease (ECD) is an extremely rare disorder that can affect many different organs of the body. It is rare form of non-Langerhans-cell histiocytosis. characterized by excessive production and accumulation of specific cells (histiocytes) whose normal function is to fight infections. The histiocytes accumulate in the loose connective tissue of many organs of the body and as a result this tissue becomes thickened, dense and fibrotic. Without successful treatment the disease is debilitating and can result in organ failure. ECD is often described in the medical literature as an extremely rare^[1]. ECD usually presents in adults aged 40-60. In our case report the age of the patient is 26 years. Here we present a case of ECD in a 26 years male patient with progressive course over a period of 4 years developed features suggestive multiorgan involvement (lungs, ear, eye, brain, muscle, skeletal system)

Key words: Erdheim Chester disease; Interferon alpha; Interleukin-1; BRAF

Abbreviations: ECD - Erdheim-Chester Disease

Introduction

Erdheim–Chester disease (also known as Erdheim–Chester syndrome or polyostotic sclerosing histiocytosis) is a rare disease characterized by the abnormal multiplication of a specific type of white blood cells called histiocytes, or tissue macrophages (technically, this disease is termed a non-Langerhans-cell histiocytosis)[1]. Usually, onset is in middle age. The disease involves an infiltration of lipid - laden macrophages, multinucleated giant cells, an inflammatory infiltrate of lymphocytes and histiocytes in the bone marrow, and a generalized sclerosis of the long bones. it was first described in the literature in 1930 by the Austrian pathologist, Jakob Erdheim, and the American pathologist, William Chester [2]. Because it is so rare and because it is not discussed in the common textbooks of medicine, many doctors have never heard of it. It is usually difficult to diagnose. For these reasons, some feel the disease could be under-diagnosed and may not be as rare as thought.

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Case Report

26 years old male, presented with complaints of difficulty in breathing noticed increasing dyspnea on exertion and orthopnea, which has progressively worsened over the past 3 years. He also experienced drooping of eyelid right side with decreased vision since 1 month duration. The drooping of eyelid was insidious in onset, progressive in nature without, diurnal variation. Similar illness – drooping of Right eyelid with double vision 2 years back. There is a history of hearing loss (Rt>Lt), ear pain, ear discharge, headache, bone and joint pain. Giddiness and intermittent tinnitus, difficulty in speech, on and off since 3 years. Patient was on steroid treatment from which he got relief from symptoms for 2 to 3 month. There is no history of fever, vomiting and seizure. On examination pt is oriented and conscious, alert, afebrile, Extra ocular movement - Rt eye restricted in all the direction except abduction, Lt eye-normal in movement in all the direction. Fundus – bilateral papillo-edema present. Pupils – Rt 4mm fixed, Lt 2mm reactive. Vision acuity - Rt 6/12, Lt 6/12. Bilateral conductive deafness present. Motor and Sensor system-normal. CVS, RESPIRATORY, PER-ABDOMEN ON clinical examination –Normal. Investigation-All blood investigations were in normal range. LUMBAR PUNCTURE DONE CSF ANALYSIS SHOWS-GLUCOSE-68, PROTEIN-48, CHLORIDE-126, CELL COUNT-14CELL (All are lymphocyte). PFT SHOWS RESTRICTIVE LUNG DISEASE. CHEST X-ray PA

view- Diffuse bilateral infiltrates present. CSF-Antimyobacterial and anticysternal antibodies negative by ELISA, CSF VDRL - non - reactive, serum RA-negative, serum ANA-negative, Bone marrow Histology - There was complete replacement of the fatty marrow by a variable degree of fibrous tissue and prominent proliferation of foamy histiocytes, including multinucleated forms. AUDIOMETRY - rt profound hearing loss, bilateral middle ear pathology, left moderate conductive hearing loss. CT SCAN BRAIN - There is evidence of T2 hypo intense thick nodular lesion seen along the dorsal aspect of clivus reaching down to sinus and orbital apex, lesion is isotense on TIWI and shows intense homogenous enhancement following in contrast.



Figure 1: Chest –X-ray PA VIEW. Showing Diffuse bilateral infiltrate.

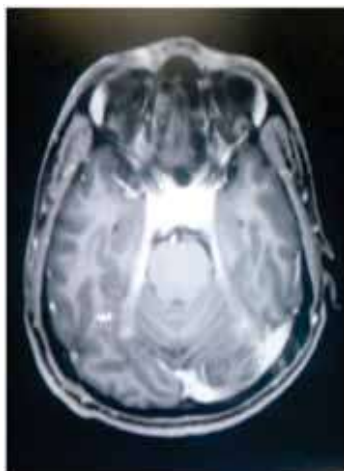


Figure 2: MRI done in year 2010 Imaging feature are suggestive of Pachymeningitis involving sellar parasellar orbital apex and clivus.



Figure 3: MRI done in year 2014 Imaging shows Nodular Thickening and Enhancement of the skull base Pachymeninges.

Discussion

Erdheim-Chester disease (ECD), a non-Langerhans form of histiocytosis, is a multisystemic disease characterized by various manifestations such as skeletal involvement with bone pain, exophthalmoses, diabetes insipidus, renal impairment and central nervous system (CNS) and/or cardiovascular involvement [1,4,10]. Prevalence is unknown. More than 500 cases (<15 pediatric) have been reported since 1930. ECD usually presents in adults aged 40-60 with a 3:1 male to female ratio[4]. Clinical course varies from asymptomatic to multisystemic, life-threatening forms. The pathognomonic feature of ECD is osteosclerosis of the long bones manifesting as bone pain, mainly affecting the distal lower limbs (50% of cases). Pituitary gland infiltration leads to diabetes insipidus and rarely hyperprolactinemia and gonadotropin insufficiency [11]. Constitutional symptoms include fever, weakness and weight loss [5]. Infiltrations in other organs can lead to intracranial hypertension, exophthalmos, papilledema, adrenal insufficiency, xanthelasmas and papulonodular skin lesions. CNS involvement can cause cerebellar and pyramidal syndromes, headaches, seizures, cognitive impairment, cranial nerve palsies and sensory disturbances [6,10]. A frequent cardiovascular involvement is the “coated aorta”. Renal arteries can also be involved, leading to reno-vascular hypertension. Pericardial involvement may be complicated by a tamponade. Pseudo-tumoral infiltration of the right atrium is also seen. Dyspnea, due to lung infiltration, has been reported. Pseudo retroperitoneal fibrosis is sometimes complicated by bilateral hydronephrosis. Etiology is unknown but it is thought to be either a reactive or neoplastic disorder. Elevated levels of interferon-alpha (IFN-alpha), interleukin (IL)-7, IL-12, monocyte chemo attractant protein-1 and decreased levels of IL-4 found in

ECD patients support an associated systemic immune Th-1 oriented perturbation [9,12]. Recent findings of mutations in the BRAF proto-oncogene in > 50% of ECD cases clearly add further complexity to the pathophysiology of ECD [7].

The hallmark histological finding is the xanthogranulomatous or xanthomatous infiltration of tissues with spumous histiocytes. Immunohistochemical staining of a biopsy sample is CD68-positive and CD1a-negative [3 5].

Bone x-rays usually display bilateral and symmetric cortical osteosclerosis of the long bones, while technetium 99m bone scintigraphy shows almost constantly evidence of symmetric and abnormally strong labelling of the distal ends of the long bones of the lower limbs (and sometimes the upper limbs) [8]. Abdominal CT scan may show a “hairy kidney” appearance (in 50%) which can be biopsied. Differential diagnosis includes Langerhans’ cell histiocytosis, Rosai-Dorfman disease, Takayasu arteritis, Wegener’s granulomatosis, primary hypophysitis, chronic recurrent multifocal osteomyelitis (see these terms), malignancies, neurosarcoidosis, mycobacterial infections and metabolic disorders.

First line treatment is the administration of standard or pegylated IFN-alpha for all forms of ECD with higher doses (9 million units, 3 times per week) required on a long-term basis for those with CNS and cardiac localizations (if well tolerated) [13]. Bisphosphonates may be given to alleviate bone pain. Cladribine can be given to those with orbital involvement that have been resistant to other forms of treatment. Anakinra can improve symptoms of mild forms of ECD in patients where IFN-alpha was ineffective. Recently, infliximab and vemurafenib have been used with some success, this latter drug seeming very promising for patients with a BRAFV600 mutation. PET scans are recommended for the assessment of disease activity. ECD has a variable prognosis but is overall poorer in those with CNS involvement. Before IFN-alpha, the mean survival after diagnosis was 19.2 months. Nowadays, with IFN-alpha treatments, the mortality rate is only 26%, and 5-year survival is 68%.

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