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Case Report

Dr.Shaheen Master, Dr.Mayur Shah
Consultant pediatrician ,babamemorial hospital Dindoli
Consultant pediatrician Navsari

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ABSTRACT
ECD was first described as " lipoid granulomatose " by JakobErdheim's student William Chester (1930).ECD predominantly involves the musculoskeletal system. In about half of the patients, retroperitoneum, cardiovascular system, lungs, orbits, and CNS are involved. Involvement of skin, testis, breast, and gastrointestinal system has also been infrequently reported. In ECD, involvement of lymph nodes, liver, spleen, or axial skeleton is unusual, which is common in Langerhans cell histiocytosis (LCHClinical presentation can vary from asymptomatic tissue infiltration, bony pains to multiorgan failure.

I. INTRODUCTION

Here we report a rare case of non-Langerhans cell histiocytosis, Erdheim Chester disease (ECD). Very few cases have been reported in the literature in paediatrics. This disease is characterized by the abnormal multiplication of specific type of white blood cells called histiocytes or tissue macrophages. The disease affects patients of middle age and rarely adolescent age group.

II. CASE REPORT

A 10 years old female child presented with macrocephaly with fever and convulsion in December'16. MRI showed patchy meningitis with narrowing aqueduct. She was then treated for meningitis. Patient was readmitted in July'17 with similar complaint, and VP shunt was put as non-communicating hydrocephalus had developed. In February'18, due to recurrent nature of disease, Biopsy of Brain was done which on histopathological examination showed xanthomatous infiltration of tissues with histiocytes and BRAF gene mutation was positive, which was confirmative of ECD. PET–CT showed multiple bony sclerosing sites involving long bones of lower limbs, lumbosacral vertebra without any soft tissue lesion involvement. Patient has taken 3 cycles of LENALIDOMIDE (Thalidomide analogue and immunomodulator with antineoplastic properties) and Dexamethasone, with a close follow up, with a plan to repeat PET-CT.

III. DISCUSSION

ECD was first described as "lipoid granulomatose" by JakobErdheim's student William Chester (1930). The term ECD was first coined by Jaffe HL[1]. ECD predominantly involves the musculoskeletal system. In about half of the patients, retroperitoneum, cardiovascular system, lungs, orbits, and CNS are involved. Involvement of skin, testis, breast, and gastrointestinal system has also been infrequently reported. In ECD, involvement of lymph nodes, liver, spleen, or axial skeleton is unusual, which is common in Langerhans cell histiocytosis (LCH)[2].

Clinical presentation can vary from asymptomatic tissue infiltration, bony pains to multiorgan failure. ECD presents commonly with skeletal symptoms, diabetes insipidus (DI), neurological, and constitutional symptoms.

Bone involvement occurs in about 96% of the cases. ECD classically involves appendicular long bones, especially the distal femur, proximal tibia, and fibula, and less commonly the ulna, radius, and humerus. The most common presenting symptom is persistent bone pain (50% of patients) in lower limbs, especially around knees and ankles. The typical radiological features include bilateral symmetric medullary sclerosis and cortical thickening of the metadiaphysis with epiphysial sparing. Bone scans show intense bilateral, symmetric metadiaphysial tracer uptake. These radiological findings are considered pathognomonic of ECD. These findings are also seen in Gaucher's, Niemann-Pick's, and Fabry's disease. Cranial bone involvement has been infrequently reported, but were seen in 80% of the cases analyzed by Aurelie et al. as osteosclerosis of the maxillary and sphenoid sinuses. This was seen as thickened bone on CT and hypointense signal on T1 and T2w MRI images.[3] In addition to sclerotic lesions, lytic lesions have also been described infrequently.

Retroperitoneal involvement occurs in about two-third, as infiltration and fibrosis of the adrenal glands, kidneys, renal arteries, ureters, and surrounding anatomical spaces. One-third of the patients can have abdominal pain, ureteral

obstruction with hydronephrosis/chronic renal failure, and renal artery stenosis causing renovascular hypertension. On CT scans, this is seen as perirenal infiltration extending through the fat of para-renal spaces (hairy kidney appearance).

In the cardiopulmonary system, pseudo tumoral infiltration of the lung, can lead to dyspnoea. Involvement of pericardium may be complicated by cardiac tamponade. "Coated aorta" is a frequent cardiovascular finding[4]. Central nervous system involvement can cause cerebellar and pyramidal syndromes, headache, seizure, cognitive impairment, cranial nerve palsies and sensory disturbances[5]. Infiltration of pituitary gland leads to diabetes insipidus and rarely hyperprolactinaemia and gonadotropin insufficiency. If other parts are infiltrated it leads to intracranial hypertension, exophthalmos, papilledema, adrenal insufficiency, xenthelesmas and skin lesions. Involvement of renal arteries can lead to renovascular hypertension. Pseudo retroperitoneal fibrosis can cause bilateral hydronephrosis.

Recent studies have identified a high prevalence of the BRAF V600E mutation in patients with ECD. This gene is known to participate in oncogene-induced senescence [6]. This disease is of unknown aetiology, due to reactive or neoplastic pathology. Elevated level of interferon-alpha (IFN-alpha), interleukin7, IL-12, and monocyte chemo attractant protein 1 and decrease levels of IL 4. Mutation in BRAF – proto oncogene occur in >50% of cases. Hallmark histological finding is xanthomatous infiltration of tissues with histiocytes.

Various treatment option are available, but very few data on paediatrics is available. Drugs like pegylated IFN- alpha, Infliximab and vemurafenib (Targeted drug for BRAF gene mutation) can be used. Our patient is treated with Lenalidomide along with steroids. In our patient due to affordability issues, we are still working on procuring vemurafenib. Prognosis is considered poor with CNS involvement [7][8].

IV. CONCLUSION

A 10-year-old female child had presented with fever and convulsion, treated for meningitis. Her radiological and histopathological features were consistent with ECD. Thus, ECD should be considered as a differential diagnosis in patients presenting with nonspecific/diverse features of multiorgan involvement and bony pain. This also highlights diagnostic delay and the importance of musculoskeletal imaging in the diagnosis ECD.

Over the last 10 years, ECD cases have been reported with increasing number as it is has became better characterized. The increase in the number of case reports would provided basis for early diagnosis, further research into the etiology and therapy of ECD. ECD being multisystem disease, multidisciplinary approach would help in better patient care and management.

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