Case Report

Erdheim Chester Disease (ECD)

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ABSTRACT

ErdheimChester disease (ECD) is an uncommon aggressive, multisystem form of non-Langerhans' cell histocytosis, which was first reported by Jakob Erdheim and William chester in 1930.The diagnosis of Erdheim-Chester disease, a rare illness, is difficult and requires increased awareness.

We report the case of a 40-year-old woman who initially presented with Complicated urinary tract infection & Acute Kidney injury.Diagnosis was suspected by retro bulbar and radiological findings of the tubular bones. Erdheim-Chester disease diagnosis was confirmed with CD68(+) histiocytes detected by immunohistochemical analysis of orbital tissue.

Key-words : Erdheim Chester Disease (ECD), Non Langerhans' cell histocytosis, Acute kidney injury (AKI)

Introduction :

Erdheim-Chester Disease (ECD) is one of the non-Langerhans cell histiocytosis.[1] (also known as Erdheim Chester syndrome or polyostotic sclerosing histiocytosis). It is a very rare disease. characterized by the abnormal multiplication of a specific type of white blood cells called histiocytes, or tissue macrophages. It was declared a histiocytic neoplasm by the World Health Organization in 2016. Onset typically is in middle age. There are approximately 500 to 550 case reports in the literature.[2,3] Long bone involvement is almost universal in ECD patients and is bilateral and symmetrical in nature. More than 50% of cases have some sort of extra skeletal involvement. This can include kidney, skin, brain and lung involvement, and less frequently retroorbital tissue, pituitary gland and heart involvement is observed.[2] ECD should be suspected by the radiological findings of skeletal system besides the clinical findings of multisystem involvement. Definite diagnosis can be made by CD68(+) CD1a(-) histiocytes seen in biopsy specimen.[4] Treatment should be administered by experienced professionals in ECD.[2]

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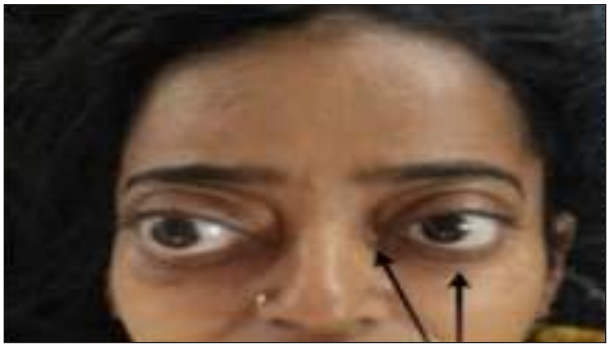
Case Report :

A 40 years old female admitted in Medicine ward for high grade fever with chills, burning micturition and oliguria of 10 days duration. She had altered level of consciousness since 3 days prior to hospitalization. Considering her urine microscopic findings & Impaired renal function (Blood urea, serum creatinine) diagnosis of Urinary tract infection with Acute Renal Failure was entertained & managed conservatively with higher antibiotics. In addition to the presenting symptoms of UTI, she had diffuse continuous bone and articular pain for the last 2 years. She also complained of blurred vision since the same duration.

On clinical examination she was drowsy but arousable. Pulse was100 / min regular, RR- 24 /min, BP- 130/80 mmHg. She had left renal angle tenderness. There was bilateral Proptosis with normal pupils & eye movements ***(Fig. 1).*** She had xanthelasmas like lesions in both periorbital region ***(Fig. 2).*** Systemic examination was within normal limits.

Proptosis



Xanthelesm

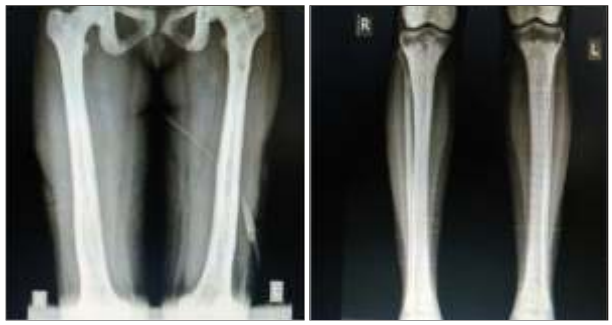
Lab examinations revealed Hb - 6.0 gms%, Total leucocyte count 14000 / mm3, platelet count 93000 / mm3 & MCV 79 fl. On admission serum creatinine was 1.7 mg% that subsequently showed a rising trend 2.6, 3.2 & 3.7 mg% in the initial three days. Serum electrolytes (sodium & potassium) were normal. Total Serum Bilirubin 0.8 mgm%, Serum proteins 4.8 gm% (albumin 1.8 gm% & globulin 3.0 gm %). Urine routine & microscopy showed turbid urine, protein spot 2+ with plenty of pus cells, RBC 10-15 / HPF, No casts. Urine culture showed growth of E.coli sensitive to Piperacillin / Tazobactum. ABG depicted - pH-7.30, pCO2 - 22.9 mm of Hg, HCO3 - 11.5 suggestive of metabolic acidosis.

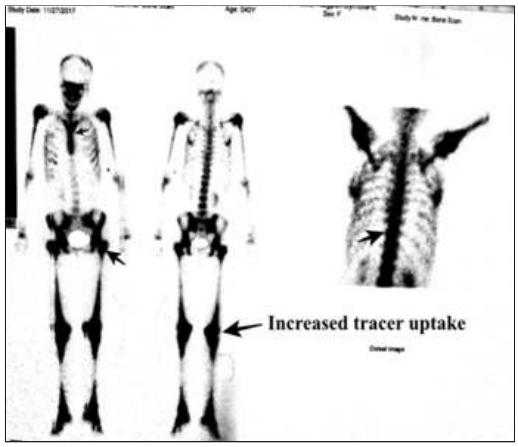
Antibiotics, Blood Transfusion and supportive treatment was given. She regained consciousness, her infection was controlled, urine output improved & renal function improved progressively over a period of 2 weeks; she did not required dialysis. Ultrasound of abdomen showed moderate hepatomegaly with left hydroureter with mild hydronephrosis.

Thereafter evaluation for her bilateral proptosis, bony pains, skin lesions & renal problem was done. Her Thyroid profile was normal & negative for Anti microsomal antibody (6.0) (normal < 34). C - reactive protein (CRP), was increased - 8.89 ? Mg / dL, rheumatoid factor (RF), and anti-cyclic citrullinated peptides (anti-CCP) were negative.

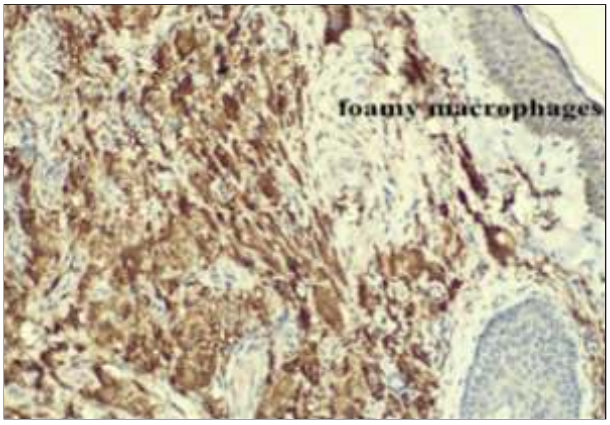
Fundus examination revealed C:D ratio- 0.3:1, clear media, macula showing diffuse circular and other ill defined hypopigmented patches involving entire macula & FRwas absent. Other findings were bony hyperpigmented blackish spicules in macula and inferotemporal quadrant with multiple hypopigmented tiny lesions in inferior quadrant. All the findings were suggestive of bilateral proptosis with macular dystrophy.

Chest X-ray was normal. Skeletal imaging of long bones showed diffuse metaphysical and diaphysial sclerosis of both femur, tibia &humerus with cortical thickening suggestive of systemic disease. ***(Fig. 3 A, B, C)*** So she was subjected to Skeletal scintigraphy which revealed diffusely increased tracer uptake involving bilateral humerus, sacroiliac joints, femurs and tibia suggestive of widespread bone.

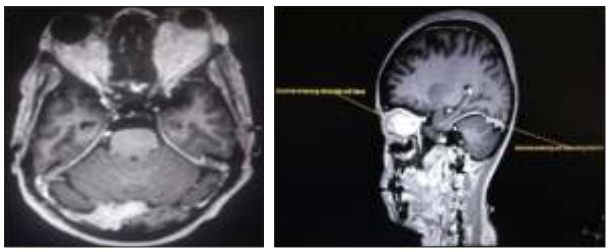


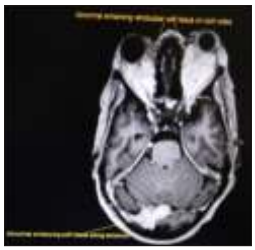


Skin biopsy from lesion around eyes showed epidermal flattening of rete ridges,dermis showed focal collection of histiocytes with foamy cytoplasm. The histopathologic findings were compatible with diagnosis of non-Langerhans' cell histocytosis. Lesional tissue demonstrates infiltration of typically foamy or lipid-laden histiocytes with admixed or surrounding osteonecrosis with fibrosis. ***(Fig. 5)***



MRI brain showed abnormal heterogenously enhancing thickening of meninges along tentorium and posterior falx, measuring 5.1×3.8×2.5 cm in midline and along right tentorium. Brain parenchyma did not show any focal signal changes. ***(Fig. 6 A, B)***





On MRI of orbit diffuse retrobulbar soft tissue noted on both sides in the intraconal compartment, enhancing both optic nerves on both sides. All these imaging features are secondary to intracranial & retrobulbar involvement in Erdheim chester disease. ***(Fig. 6 C)***

On immune histochemical (IHC) staining, the histiocytes had plentiful pale staining and foamy cytoplasm and were positive for Cd68. (4 + score) which is pathognomonic for non Langerhans cell histiocytes. Staining for S-100 reaction was non immunogenic.

Considering her clinical features, Skeletal imaging findings, MRI Brain& Orbit, diagnosis of Erdheim chester disease was entertained & confirmed by CD68 positive IHC marker. She was treated conservatively for her Pyelonephritis & AKI which improved over a period of 15 days. She was discharged from hospital &is under follow up. No specific management was given to her basic problem of Erdheim chester disease.

Discussion :

ECD is a rare incurable disease till date with multisystem involvement with some infiltrative predominance in the bones of the lower and upper extremities, orbit, and CNS, and the disease is aggressively related to the site of infiltration. The etiology of ECD is unknown but it is thought to be either a reactive or neoplastic disorder. Recent findings of mutations in the BRAF proto-oncogene in > 50% of ECD cases clearly add further complexity to the pathophysiology of ECD. In the present case we tried to emphasize multisystem involvement, predominantly skeletal, brain &renal involvement[2,5].

The ECD is slightly more frequent in males. M:F 1.5:1.2 & is most often diagnosed during 6th decade[1]. Our case was 38 yrs old female.

The diagnosis is usually challenging due to the rarity of the disease and clinical overlapping with many other conditions. The diagnosis in our case study was made based on characteristic features including clinical pictures of skeletal pain, skin lesions, and radiological findings including bilateral symmetric increased tracer uptake on 99 mTc bone scintigraphy affecting the periarticular regions of the long bones, in addition to bone X-rays displaying bilateral and symmetric cortical osteosclerosis of the long bones. The definitive diagnosis was confirmed by the histological findings of infiltration of tissues with histiocytes and fibrosis and IHC staining of histocytes positive for CD68 and negative for CD1a, S100.

Our case presented for her bony pains 2 years after her initiation of complains . The rarity and variable presentation of this disease usually leads to delayed

diagnosis and to high morbidity and mortality rates from associated complications[6] which occurred in our case.

In extra skeletal localizations of the disease, the retroperitoneal involvement is by far the most frequent (30-50%); however retroperitoneal infiltration is most often asymptomatic and is occasionally manifested by lower lumbar pain, problems with urination and proteinuria with or without renal function impairment[7]. Our patient had no retroperitoneal infiltration but Complicated UTI & AKI.

The involvement of central nervous system is also relatively frequent and causes intracerebral or intramedullary lesions. Clinical manifestations are clearly dependent on the anatomical localization of the lesion. Our case had involvement of soft tissue orbit and thickening of meninges, brain parenchyma was not involved.[7]

Pulmonary infiltration is less common. Pulmonary involvement was not present in our case.

The effective treatment options are limited with a growing promise with BRAF inhibitor, and the goal of treatment for the time being is to prolong the life expectancy and maintain a high quality of life [2,8]

Statement of Ethics :

Informed consent was obtained and the case study has been approved by the department's committee on human research.

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