MULTIFOCAL LANGERHANS CELL GRANULOMATOSIS (Hand-Schuller-Christian disease)

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A 47-year-old female developed multifocal Langerhans cell granulomatosis (Hand-Schuller-Christian disease) manifesting as papulo-pustular, nodular, crusted and scaly lesions, xanthelasma, ulceration of gingival mucosa with loss of teeth, vaginal granulomatosis, diabetes insipidus, multiple osteolytic bone lesions and honeycombing of the lungs. Skin biopsy confirmed the diagnosis. Treatment with prednisolone 45 mg and methotrexate 2.5 mg daily, led to regression of lesions, reduction of bone pains, partial clearance of lung lesions and osteolytic bone lesions. However, the patient died due to widespread nature of the disease.

Key words : Langerhans cell granulomatosis, Eosinophilic granuloma, Hand-Schuller-Christian disease.

Lichtenstein in 1953 had grouped Letterer-Siwe disease, (an acute or subacute disease affecting very young persons and almost fatal in character), Hand-Schuller-Christian disease (a chronic disseminated disease), and eosinophilic granuloma (a disease restricted usually to the bones), under the common term histiocytosis X.[1] Later, when many cases with intermediate and mixed pictures of the last two disorders were reported, it led to the concept of a uni- and multifocal eosinophilic granulomatosis, and still later to uni- and multifocal Langerhans cell granulomatosis when it was known that the basic defect in all these cases lies in the abnormal proliferation of Langerhans cells.[2]

We observed a case of multifocal Langerhans cell granulomatosis in a 47-year-old female, with the history suggestive of a unifocal origin as eosinophilic granuloma of the lung which later progressed to involve multiple organ systems like the skin, mucous membranes, bones and hypothalamus.

Case Report

A 47-year-old female was admitted with cough, expectoration and breathlessness for the last two years, and anorexia, weight loss, polyuria and polydypsia for the last five months. She had developed painful papulo-pustular and crusted skin lesions for the last 10 days and also had low grade, intermittent pyrexia for 6 days. She had been earlier diagnosed as a case of pulmonary tuberculosis and given antitubercular treatment (ATT). She stopped ATT after 3-4 months on her own, as there was no relief. Old chest X-rays were not available. She did not follow-up in the intervening period. She was cachectic, with 25 Kg weight, low grade fever, tachycardia, mild pallor, and bilateral pitting oedema of feet. There was no icterus, cyanosis, clubbing or lymphadenopathy. Liver was enlarged 5 cm, soft, smooth and non-tender. Chest was clinically clear. Both femurs were tender. Cardio-vascular and CNS were normal. The skin lesions were papulo-pustular, crusted, scaly, erythematous and nodular with discharging sinuses on the scalp, forehead, chest, interscapular region, axillae, thighs and proximal parts of arms. In addition she had xanthelasma, ulceration of gingival mucosa with loss of teeth and vaginal vegetative lesions.

Investigations revealed hemoglobin 9 gm%, ESR 50 mm, normal total and differential leucocyte counts, platelet count 1,25,000/ cmm, 24-hour urinary output three litres, and urine specific gravity 1004. Blood sugar, serum

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creatinine, blood urea, serum cholesterol, liver function tests and urinary protein were normal. X-ray chest showed honeycombing of both lung parenchyma, and thickened horizontal interlobar fissure of the right lung. Skeletal survey revealed multiple osteolytic lesions in both the femurs, tibia, fibula and pelvic bones with pathological fracture of the head of left fibula. Skull X-ray showed erosions of bony sockets and loss of teeth in the mandible. Histopathological examination of skin showed infiltration of the upper dermis with mature histiocytes, plasma cells, occasional neutrophils, a few eosinophils in clusters and occasional multinucleated giant cells, with ulceration and invasion of the epidermis with histiocytes. There were no malignant cells. The picture was consistent with eosinophilic granuloma. Urine concentration test with water deprivation and pitressin injection confirmed pituitary onset diabetes insipidus.[3]

The patient was put on 45 mg prednisolone and methotrexate (MTX) 2.5 mg daily. The skin lesions regressed, bone pains reduced and there was partial clearance of the lung lesions and some resolution of the osteolytic lesions after 4 weeks. The patient however died at home while she was still on MTX 2.5 mg daily and prednisolone 45 mg alternate days, after the initial four weeks.

Comments

Our case had an onset similar to eosinophilic granuloma of the lung, mistakenly diagnosed as pulmonary tuberculosis, which progressed in two years to multiple organ involvement of bones, skin, hypothalamus, gingiva and vagina, with an ultimate fatal outcome. Transitional forms and mixed type of presentations between eosinophilic granuloma and Hand-Schuller-Christian disease suggest a spectrum of the disease process involving abnormal proliferation of Langerhans cells. In a large review of 538 cases of Hand-Schuller-Christian disease, Dolezal and Thomson[4] found 76% of the cases below 10 years of age, 91% below 30 and less than 4% above 50 years. Our case had onset at 47 years.

The multifocal disease is known to respond better to a combination of prednisolone and methotrexate than a combination of prednisolone and vincristine.[3,5] Hepatic, pulmonary and haemopoietic system dysfunction are considered to be poor prognostic signs, while diabetes insipidus, loss of teeth, skin lesions and pathological fractures are not considered life threatening.[6,7] Pulmonary involvement, disseminated nature of the disease and older age were probable causes of death in our case, in spite of the recommended therapy.

References

1. Moschella SL : Diseases of the mononuclear phagocytic system (the so called reticuloendothelial system), in : Dermatology, Second ed, Editors, Moschella SL and Hurley HJ : WB Saunders, Philadelphia, 1985; p 890-999.
2. Gianotti F and Caputo R : Skin ultrastructure in Hand-Schuller-Christian disease, Arch Dermatol, 1969; 100 : 342-349.
3. Lieberman PH : Langerhans cell (eosinophilic) granulomatosis and related syndromes, in : Cecil Textbook of Medicine, Sixteenth ed, Editors, Wyngaarden JB and Smith LH Jr : WB Saunders, Philadelphia, 1985; p 961-963.
4. Dolezal S and Thomson S : Hand-Schuller-Christian disease in a septugenerian, Arch Dermatol, 1978; 114 : 85-87.
5. Jones B, Kung F, Chevalier L et al : Chemotherapy of reticuloendotheliosis; comparison of methotrexate plus prednisolone vs vincristine plus prednisolone, Cancer, 1974; 34 : 1011-1022.
6. Lahey ME : Histiocytosis X—an analysis of prognostic factors, J Pediat, 1975; 87 : 184-189.
7. Nazelof C, Frileux-Herbert F and Cronier-Sachot J : Disseminated histiocytosis X : analysis of prognostic factors based on a retrospective study of 50 cases, Cancer, 1979; 44 : 1824-1838.