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Cardiac and cerebral involvement in Erdheim-Chester disease

Kalp ve beyin tutulumlu Erdheim-Chester hastalığı

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Abstract

Erdheim-Chester disease (ECD) is a rare non-Langerhans form of systemic histiocytosis of unknown etiology that progresses with multiple organ involvement. It is characterized by a xanthomatous infiltration showing positive staining with CD68 and negative staining with CD1a in tissues. We report a 62 year-old case complaining of malodor, in the brain magnetic resonance imaging of whom a mass was found at the clivus and leptomeningeal involvement was determined. The accompanying intracardiac mass was excised and the case was diagnosed histopathologically as ECD. We present the unusual clinical symptoms along with histopathologic and radiodiagnostic findings and discuss the differential diagnosis of this rare disease.

Keywords: Erdheim-Chester disease, magnetic resonance imaging, cardiac involvement, neurological signs.

Öz

Erdheim-Chester hastalığı (ECD) etyolojisi bilinmeyen, multipl organ tutulumu ile seyreden, sistemik histiyositozisin nadir bir non-Langerhans formudur. Dokularda CD68 ile pozitif ve CD1a ile negatif boyanma gösteren ksantomatöz infiltrasyon ile karekterizedir. Bu makalede 62 yaşında kötü koku alma şikayeti ile başvuran ve beyin manyetik rezonans görüntüleme tetkikinde klivusta kitle ve leptomeningeal tutulum saptanan ve eşlik eden intrakardiyak kitle eksizyonu sonucu histopatolojik tanısı ECD ile uyumlu bulunan bir olgu bildirilmektedir. Olgunun sıra dışı belirtileri, histopatolojik ve radyodiagnostik bulguları eşliğinde sunulmakta ve bu nadir hastalığın ayırıcı tanısı tartışılmaktadır.

Anahtar Sözcükler: *Erdheim-Chester hastalığı, manyetik rezonans görüntüleme, kardiyak tutulum, nörolojik bulgular.*

Introduction

Erdheim-Chester disease (ECD) is a rare non-Langerhans form of systemic histiyocytosis. The disease is characterized by its multi-organ involvement of heart, lungs, musculoskeletal, gastrointestinal and central nervous system (1). Neurological involvement is observed in less than % 50 of the patients who are diagnosed as ECD (2). Cerebellar and pyramidal syndromes were the most frequent clinical manifestations, but seizures, headaches, neuropsychiatric manifestations or cognitive impairment, sensory disturbances, cranial nerve paralysis or asymptomatic lesions were also reported. Hypothalamic pituitary axis, brain parenchyma, orbita and meninges of the brain are involved frequently whereas meninges of the spine and bony spinal column are involved less frequently (2).

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The inflammatory response which consists lipid foamy macrophages, multinuclear giant cells and lymphocytes, were observed in the histopathological tissue sections. Histiocytes of ECD are positive for CD68 but not for S-100 protein and CD1a (3,4).

Case Report

A 62-year-old man was referred to our clinic with a complaint of unpleasant smell lasting for 3 months. He was smelling unpleasant odors while the others around him did not. Also he has experienced a loss of interest to his surroundings and has become indifferent for a few seconds during those attacks of misperception of smell. He has been found dysarthtric and ataxic at his neurological examination. In his routine laboratory work-up, erythrocyte sedimentation rate and C-reactive protein were elevated and electroencephalography was normal. Magnetic resonance imaging (MRI) detected a mass lesion at clivus which has signaled T1 heterogenous hypointense, T2 heterogenous isointense. That mass has shown enhancement to contrast

gadolinium and it has also elevated the optic nerve. Another mass lesion which has leptomeningeal involvement and which has shown enhancement to contrast gadolinium, was detected aside by left tentorium. Bilateral chronic cerebellar infarct lesions were also detected (Figure-1a,b,c).

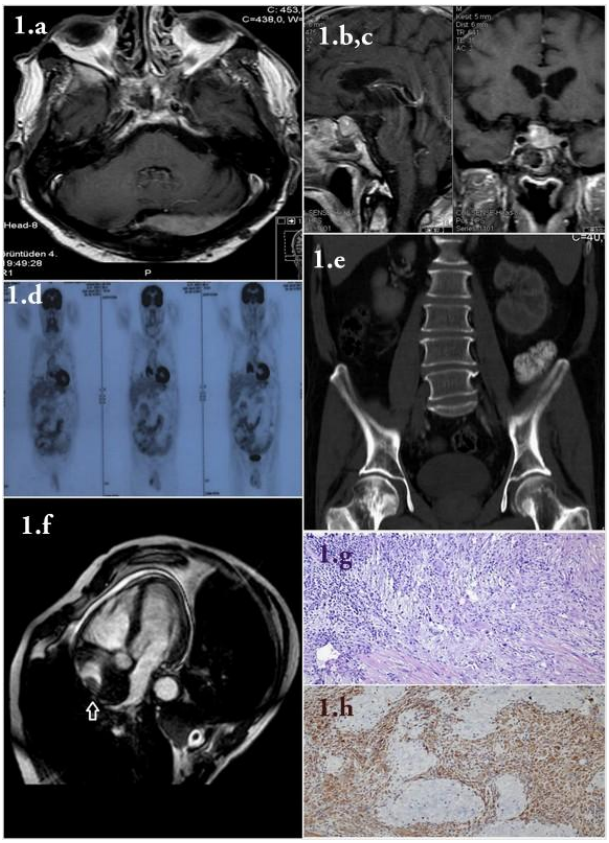

Figure-1.a. The leptomeningeal involvement showing the contrast involvement in left tentorium neighborhood in the axial plane that belongs to contrast enchanced cranial MRI examination. **b,c.** The mass lesion that shows on the clivus of sagittal and coronal plane post-contrast staining, and elevating the right optic nerve, according to constrast enchanced cranial MRI examination. **d.** F-18 FDG whole body PET/CT examination shows, on the clivus and left porterior tenrorial area, leptomeningeal region and right atrium, hypermetabolic appearance and hypermetabolic diffuse sclerotic appearance on the diaphysis-metaphysis areas. **e.** Coronal multiplanar reconstruction computed tomography (CT) shows multiple vertebral body and bilateral proxymal femur cortical thickening and meduller sclerotic lesions. **f.** Cardiac magnetic resonance imaging shows a mass lesion at the right atrium and interatrial septal thickening. **g.** Diffuse chronic lymphohisitocytic inflammation between the muscle fibers in myocardium (H&E x100). **h.** Immunohistochemically CD 68a marker specific for monocytes/macrophages, stained strongly the histiocytes, the intervening muscle fibers in myocardium were not stained (H&E x200).

Following the oncology consultation of the patient, F-18 FDG whole body positron emission tomography/ computed tomography (PET/CT) were planned and it detected hypermetabolic activities both at clivus and at the lemptomeningeal region of the left posterior tentorium. In addition to the intense hypermetabolic activity of the right atrium, both upper and lower extremites of diaphysiometaphysier regions of the long bones and corpus vertebra of T2, L2 have shown heterogenous hypermetabolic diffuse sclerotic appearance (Figure-1d). Besides, the abdominal CT scan has revealed cortical thickening and medullar sclerosis at the bones of vertebrae, pelvis and femur (Figure-1e). At ecocardigraphy, an infiltrative mass lesion was detected at the superior wall of the right atrium which has lied down through the interatrial septal region. Cardiac MRI findings revealed a mass lesion at the right atrium and interatrial septal thickening (Figure-1f). So far with the findings of the patient, curative radiotherapy was applied to the intracranial mass. The patient needed to have a surgery, because right atrial mass carried risk for pulmonary embolism. In the course of coronary angiography as a part of preoperative procedure, a critical stenosis detected in the left anterior descending artery. The infiltrative mass that was localized both in the right atrium including its anterior wall and interatrial septum was excised. Coranary bypass grafting was simultaneously performed. The excised material was evaluated histopathologically.

Macroscopically, the excised material was in multiple fragments and the largest fragment was measured 3.5x2.5x2 cm in dimension. The specimen was rubbery in consistency and had heterogeneous yellow beige color. Microscopically, there was a prominent, diffuse inflammatory infiltration within the myocardium. The infiltrate was composed of mainly histiocytes and the lymphocytes were also scattered in it (Figure-1g). The histiocytes had either pale eosinophilic cytoplasm or foamy in appearance. Immunohistochemically, the histiocytes were diffusely positive for CD 68 and there was rare S-100 positivity (Figure-1h). CD 1a was consistently negative. Myocardial cells were actin and desmin positive. The morphological appearance along with clinical, radiological and immunohistochemical findings was interpreted as ECD.

Discussion

ECD is a rare non-Langerhans form of systemic histiocytosis. The disease was first described in 1930 by the American cardiologist Adam Chester while he has been completing a fellowship in pathology (5). The diagnosis is based on characteristic radiographical and histological features. Bilateral symmetrical osteosclerosis affecting the metaphysis and diaphysis of the long bones are considered almost pathognomonic (6).

Bone pain is the most frequent symptom observed due to bone involvement. However clinical findings were

observed related to exoftalmia, xanthelasma, interstitial lung disease and also urethral, cardiac and brain involvement (1). Neurological disorders are associated with central nervous system infiltration with lipid foamy histiocytes. The presented case had clivus involvement and so far that localized involvement has not been reported in the literature before. Central nervous system lesions are most frequently appear at cerebellum, pons as well as along with the hemispheres, hypothalamus, pituitary gland, brain stem, duramater, spinal cord, falx cerebri and orbital involvement can also ocur (7,8). Neurological presentation in histiocytosis can show up with dysfunction of neuroendocrinological findings (central diabetes insipitus, hypopituitarism, delayed puberty), cerebellar ataxia and seizure due to parenchymal infiltration; aceptic meningitis and typical migraine headaches due to meningeal involvement; pseudobulbar palsy and progressive cerebellar syndrome and loss of cognitive functions due to neurodegenrative involvement (4).

Histopathological differential diagnoses include other histiocytic diseases and chronic inflammatory processes. The patient had no previous or current history and findings of any infectious disease involving the heart. For histiocytic diseases, langerhans cell histiocytosis and Rosai Dorfman disease may be considered. Langerhans cells are arranged in nests an intermingled with leucocytes including eosinophil and neutrophil leucocytes. Additionally, langerhans cells are CD 1a and S 100 positive (9). The histiocytes in Rosai Dorfman disease typically have multiple nuclei and engulfed lymphocytes in their cytoplasm (4).

In follow-up, 2/3 of the patients are lost within three years because of the pulmonary, renal or cardiac problems. The cardiac involvement in ECD is frequently seen as pericardial infiltration, right atrial dysfuction and sypmtomatic valve disease. According to the recent studies, cardiac complications are the reasons of 30% - 60% of deaths in ECD (10).

Establishing an early diagnosis is important in order to start disease-modulating treatment, which may improve prognosis and survival. There is not any standard therapeutic procedure in ECD. Corticosteroids, chemotherapy, radiation therapy, interferon and cyclosporin can be used for its therapy. The extent of the organ involvement and the early response to chemotherapy may be useful prognostic indicators (4).

ECD is a multi-organ involved disease and needs multidisciplinary approaches for its clinical and therapeutical aspects.

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