Case Report
Olgu Sunumu

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Erdheim Chester disease: A case with cutaneous involvement

Erdheim Chester hastalığı: Deri tutulumu olan bir olgu

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Abstract

Erdheim-Chester disease (ECD) is a rare multisystem disease characterized by the proliferation of non-Langerhans histiocytes. It is characterized by excessive production and accumulation of histiocytes in multiple tissues and organs. Sites of involvement may include long bones, skin, eyes, lungs, brain, pituitary gland, and additional tissues and organs. The disease course varies depending on the organ and degree of involvement. In this case report, we presented the case of a 54-year-old female patient diagnosed with ECD, manifesting with squamous, enduring plaque lesions on the skin.
Keywords: Erdheim Chester disease, skin, immunosuppressant, BRAF

Öz

Erdheim-Chester hastalığı (ECH) Langerhans hücre dışı histositlerin proliferasyonu ile seyreden nadir bir multisistem hastalığıdır. Birden fazla doku ve organda aşırı histiyosit üretimi ve birikimi ile karakterizedir. Tutulum bölgeleri arasında uzun kemikler, deri, göz, akciğerler, beyin, hipofiz bezi ve/veya ek doku ve organlar yer alabilir. Hastalık seyri organ tutulumu ve tutulum derecesine bağlı olarak değişkenlik gösterir. Bu olgu raporunda, deride skuamöz endüre plak lezyonlarla seyreden ECH tanısı konmuş 54 yaşında bir kadın olguyu ele aldık.
Anahtar Kelimeler: Erdheim Chester hastalığı, deri, immünosüpresan, BRAF

Introduction

Erdheim Chester disease (ECD) is a rare non-Langerhans histiocytic multisystemic disorder characterized by infiltration of tissues with foamy histiocytes. The mean age of diagnosis is 40 to 60 years old, with male predominance. Although the etiology is unclear, somatic mutations in the *BRAF* gene are suspected to have a role in the pathogenesis. Cangi et al.[1], in their study, showed that BRAFV600E mutation is present in all the patients diagnosed with ECD.

Here, we presented a patient who was diagnosed with ECD based on skin findings.

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Case Report

A 54-year-old female patient presented to the outpatient neurology clinic with a complaint of severe headache and redness in both eyes for 3 months. After a short-term follow-up, she developed binary vision, unilateral deafness, and scaly, erythematous indurated plaques on her face (Figure 1A). In ocular examination, papilledema was detected, and otolaryngological examination showed sensorineural hearing loss. Laboratory tests showed only mild normocytic anemia. Her serologic and autoimmune tests were negative. Neither diffusion defect nor cranial mass was detected in her cranial magnetic resonance imaging (MRI). A lumbar puncture was done following cranial imaging, and the results were normal. There was no pathology in the computerized tomography (CT) of the abdomen and thorax. Skeletal scintigraphy did not show any pathology in osseous tissues. The skin biopsy showed non-Langerhans cell type histiocytic infiltration composed of foamy cells (Figure 2A). Immunohistochemical (IHC) staining was positive for CD68 (Figure 2B) and CD163 (Figure 2C) and negative for CD1a (Figure 2D). With those findings, the patient was diagnosed with ECD. The patient's BRAF mutation analysis was negative. The patient was started on 100 mg/day methylprednisolone and 2 gr/day mycophenolate mofetil treatment with topical clobetasol propionate twice a day. After one month, significant regression was observed in the patient's skin lesions and eye complaints (Figure 1B).

Discussion

ECD is a rare disease with multiple system involvement. Tissue infiltration was characterized by foamy histiocytes with fibrosis. IHC staining is positive for CD68 and CD163 and negative for CD1a and Langerin. S100 is usually negative but can be weakly positive. In our case, histopathology from skin lesions showed infiltration of foamy histiocytes, which were positive for CD68 and negative for CD1a. Apart from histopathological features, radiological findings are also important for diagnosis[2]. Osteosclerotic lesions, especially in distal extremities, are nearly always present in ECD cases[3]. Therefore, one of the most common initial symptoms in patients diagnosed with ECD is pain in the distal extremities. In our case, the patient had no symptoms in the musculoskeletal system. Cutaneous involvement is seen in 20-30% of ECD patients. The most common form of involvement is xanthelasma-like lesions in the head and neck region, especially in the periorbital region[4]. In addition, granuloma ring-like lesions and panniculitis-like involvement may also be seen[5]. Our patient had erythematous indurated plaque lesions on her face. Unlike the commonly encountered skin manifestations in the literature, facial squamous indurated papules and plaque lesions are less frequently observed in ECD patients. Therefore, albeit rare, ECD skin involvement should be included in the differential diagnosis of a patient with facial plaque lesions.

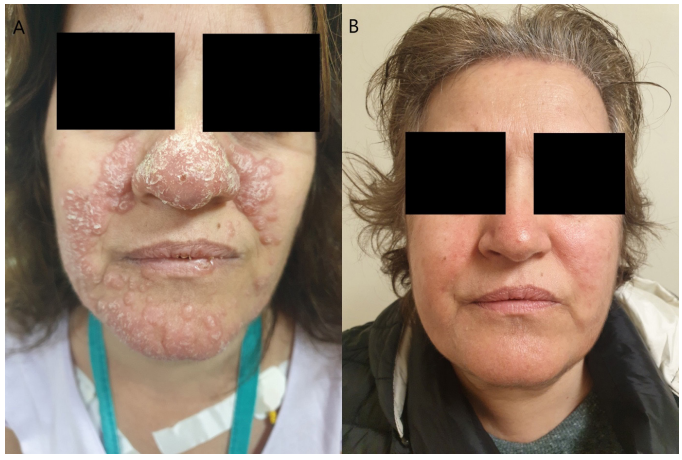

Figure 1. (A, B) Scaly, erythematous, infiltrated papules and plaques on the face of a patient with Erdheim-Chester disease **(A)** and regression of lesions after treatment **(B)**

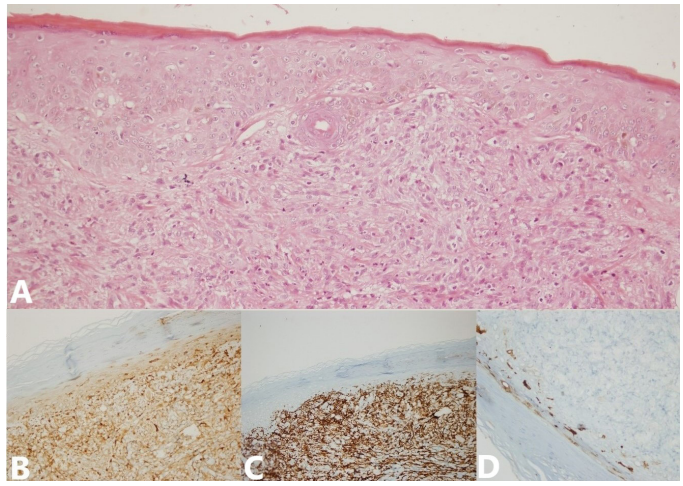

Figure 2. (A-D) Dermal infiltration of foamy histiocytes (H& E, x200) **(A)** and positive immunohistochemical staining for CD68 **(B)**, CD163 **(C)**, and negative for CD1a, respectively **(D)**

Pulmonary manifestations of ECD include interlobular septal thickening, centrilobular opacities, and ground-glass opacities[6]. Chest X-ray is usually normal. However, high-resolution CT usually detects parenchymal involvement in lung tissues. In our patient, there were no symptoms regarding pulmonary involvement. Cardiovascular system manifestations result from histiocytic infiltration surrounding large vessel walls and periaortitis, giving the appearance of a "coated aorta" on imaging, and is the most common type of cardiovascular involvement. However, our patient showed no cardiovascular symptoms related to ECD.

Endocrine system involvement, especially pituitary involvement and related endocrinopathies, most commonly central diabetes insipidus, may be seen in ECD. Also, diabetes insipidus may be present years before the diagnosis of ECD[7,8]. Endocrine tests and cranial MRI imaging did not reveal any pathology in our patient. Exophthalmos, vision loss, and oculomotor nerve palsy may be observed secondary to ocular involvement in patients with ECD[3,9]. Our patient also had ocular involvement and complained of binary vision.

For aiding in diagnosis and defining the extent of the disease, based on the consensus established by Goyal et al.[10], fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT of the entire body, including distal extremities, is recommended for all cases. If FDG-PET is not feasible, imaging of the chest, abdomen, and pelvis with contrast-enhanced CT and imaging of the lower extremities (CT, MRI, or Tc-99 bone scan) can be performed. In addition, brain MRI with

gadolinium is recommended for all patients to check the nervous system[10]. Laboratory studies are conducted to assess kidney function, cytopenias, and inflammatory markers (C-reactive protein). Due to the high prevalence of associated myeloid neoplasms in patients with ECD, especially in the context of otherwise unexplained cytopenias, cytosis, or monocytosis, a bone marrow biopsy should be considered[10].

A lesional biopsy should be performed to confirm the diagnosis of ECD and determine the BRAF mutational status since the BRAF mutation status is crucial for selecting treatment[10].

The treatment plan is determined based on the patient's overall health, severity of symptoms, organ involvement, and genetic characteristics. Due to the rarity of ECD, there is no clear standard protocol for treatment. However, treatment typically aims to reduce inflammation and control the progression of the disease. Patients with minimal symptoms can only be followed up. Systemic corticosteroids and radiation therapy can be used to alleviate acute symptoms, but they are not recommended as monotherapy for ECD. In patients diagnosed with ECD who test positive for the BRAF-V600E mutation and have cardiac/neurological disease or end-organ dysfunction, treatment with a BRAF inhibitor such as vemurafenib or dabrafenib should be applied as the first-line therapy. When access to targeted therapy is not available, treatment with IFN-α, anakinra, or cladribine may be preferred in patients with pronounced systemic involvement[10].

Our patient, who tested negative for BRAF, was initiated on systemic steroid therapy to alleviate acute symptoms. Mycophenolate mofetil was added to the treatment to facilitate the prompt discontinuation of systemic steroid therapy. Our patient also received topical clobetasol propionate treatment and showed improvement in both systemic and cutaneous symptoms during follow-up.

Although ECD is a rare disease, its multisystemic involvement requires a multidisciplinary approach to diagnosis and treatment. In addition to clinical findings, histopathologic and IHC findings are essential in the diagnosis of ECD.

Ethics

Informed Consent: Informed consent was obtained from the patient for the publication of his data on any medical platform accessible to the public.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.N.Y., T.A., Concept: S.N.Y., G.G., A.M.Ö., T.A., Y.D., Z.K., Design: S.N.Y., G.G., T.A., Y.D., İ.S., Ö.A.Ü., Z.K., Data Collection or Processing: S.N.Y., G.G., A.M.Ö., T.A., Y.D., İ.S., Ö.A.Ü., Z.K., Analysis or Interpretation: S.N.Y., G.G., A.M.Ö., Y.D., İ.S., Ö.A.Ü., Z.K., Literature Search: S.N.Y., G.G., Ö.A.Ü., Writing: S.N.Y.

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