was normal except for slightly elevated C-reactive protein (0.34 mg/dl), although the white blood cells were within the normal limits, and tumor markers were as follows: soluble interleukin-2 receptor, 594 U/ml (normal, <530 U/ml); carcinoembryonic antigen, 1.2 ng/ml (normal, <5.0 ng/ml); progastrin-releasing peptide, 24.5 pg/ml (normal, <46.0 pg/ml); and cytokeratin 19 fragment, 1.1 ng/ml (normal, <2.3 ng/ml). On echocardiogram the wall of the ascending aorta was thickened, and there was extrinsic compression of the main pulmonary artery, resulting in an antegrade acceleration of the flow velocity in the main pulmonary artery. The ejection fraction

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans histiocytosis characterized by the infiltration of numerous tissues by foamy CD68+/CD1a− histiocytes. Cardiovascular involvement is frequently seen and is one of the common causes of death.1–3 Herein, we describe a patient with ECD involving the heart and thoracic aorta.

A 64-year-old woman with hypertension, dyslipidemia and hypothyroidism presented with heart murmur. Physical examination indicated low-grade fever (37.0–37.5°C) and a systolic murmur without chest pain or back pain. Routine blood testing

Figure 1. (A, B) Computed tomography (CT) angiography performed before treatment showing circumferential soft tissue (asterisk) sheathing the ascending aorta, pulmonary artery, and coronary artery. (C, D) Magnetic resonance imaging showing hyperintense tissue, relative to the soft tissue on T1- and diffusion-weighted sequences. (E, F) On CT angiography after prednisolone therapy, the tumor has vanished completely.
was 67%, and the wall motion was normal. Computed tomography (CT) angiography showed circumferential soft tissue sheathing the ascending aorta, pulmonary artery, and coronary artery as well as pericardial effusion (Figures 1A,B). On magnetic resonance imaging (MRI), the tissue was hyperintense, relative to the soft tissue on T1- and diffusion-weighted sequences (Figures 1C,D). For definitive diagnosis, biopsy of the periaortic tumor was performed under median sternotomy. On routine H&E staining, large foamy (xanthomatous) histiocytes and multinucleated giant cells (up to 2–3 nuclei/cell) were scattered or accumulated in a background of marked fibrosis and lymphoplasmacytic infiltrate lacking neutrophils, eosinophils and epithelioid cells (Figures 2A,B). These histiocytes and giant cells had neither nuclear atypia nor mitotic figures. Rare histiocytes had phagocytosed lymphocytes (emperipolesis). These histological findings were suggestive of an advanced phase of histiocytic proliferative disease. On immunohistochemistry, foamy CD68+/CD1a– histiocytes were observed (Figures 2C,D). These cells were positive for CD163 and Factor XIIIa (Figures 2E,F) and were weakly positive for S100 protein. A diagnosis of ECD was established. Ki-67 labeling index of approximately 5% meant that cell proliferation was detected, and a proliferating cell that had phagocytosed a lymphocyte, known as emperipolesis, was observed (Figure 2G). A BRAF V600E mutation was detected using BRAF V600E mutant-specific antibody (VE1; Figure 2H).

Technetium-99m bone scintigraphy showed symmetrical uptake in the pelvis and the proximal left femur.

Treatmen with 20mg/day prednisolone (PSL) was initiated, given that medical reports on ECD were rare at that time and only a few reports were available for reference.14 Prompt improvement was observed on CT angiography, and the flow velocity in the main pulmonary artery decreased soon thereafter. PSL therapy was continued, and the PSL dose was gradually decreased. Two years later, the cardiovascular tumor had completely vanished on CT angiography (Figures 1E,F). The patient has remained well for 5 years since the start of the PSL therapy.

ECD is a rare form of non-Langerhans cell histiocytosis of unknown etiology that typically involves multiple organ systems, and there is no known effective treatment.5 Given that ECD is rarely seen, delayed and erroneous diagnoses are common. Because diagnosis can take months, clinicians need to be able to recognize ECD. This disease usually manifests between the ages of 40 and 70 years and has a male predominance.6 The clinical manifestations of ECD are non-specific and depend on the affected organ, and range from asymptomatic, clinically indolent, to sometimes life-threatening.7 Any organ system can be involved, but long bone involvement is the first manifestation in half of all patients. The second most commonly involved organ is the cardiovascular system.8–12 Circumferential soft-tissue sheathing of the thoracic and abdominal aorta and its branches, known as “coated aorta”, is the most common abnormality and is present in up to two-thirds of patients. Coronary artery disease inducing myocardial infarction has been described. In the present case, the patient had the typical findings of circumferential lesions sheathing the ascending aorta and main pulmonary artery, and a cardiac lesion surrounding the coronary artery.

A diagnosis of ECD is made on identification of distinctive
histopathological findings in an appropriate clinical and radiologic context. Lesional tissue typically shows the infiltration of foamy histiocytes. On immunohistochemistry, ECD histiocytes are positive for CD68, CD163, and Factor XIIIa and negative for CD1a and Langerin (CD207). S100 protein positivity is rarely observed. In the recent literature, estimates of the \( \text{BRAF} \) V600E mutation frequency in ECD range between 38% and 68%. The present case was also typical for the immunohistochemistry, and a \( \text{BRAF} \) V600E mutation was detected using the specific antibody VE1. Radiographic findings, such as CT angiography, MRI, bone scintigraphy, and positron emission tomography are useful for the diagnosis of this rare entity.

Although treatment for ECD has not been established, the efficacy of interferon (IFN)-\( \alpha \)-2a and pegylated IFN-\( \alpha \) has been described in a recent study. In addition, anti-cytokine-directed therapy such as anakinra, infliximab or tocilizumab, corticosteroids, cytotoxic chemotherapies, radiotherapy, and surgery, have been reported. Although corticosteroids are not considered to be an effective monotherapy in recent consensus guidelines, the present tumor vanished and the patient has remained well without relapse. Further long-term follow-up of this patient will be necessary.

ECD with cardiovascular lesions is rarely seen but can be a life-threatening condition. Thus, clinicians need to be able to recognize and treat this entity.

Grants

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References


