

# Cardiac involvement in Erdheim-Chester disease: MRI findings and literature revision

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## Abstract

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis, characterized by the involvement of several organs. The lesions may be skeletal or extra-skeletal: in particular, long bones, skin, lungs, and the cardiovascular and the central nervous systems can be affected. In this report, we describe a case of a 34-year-old man, who came to our observation with symptomatic ECD, for a correct assessment of the degree of cardiac involvement through magnetic resonance imaging (MRI).

## Keywords

Erdheim-Chester disease, histiocytosis, non-Langerhans, cardiac magnetic resonance

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## Introduction

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis (1,2) that is characterized by several clinical (3), radiological, and histopathological findings. The highest incidence of the disease occurs at the age of 40 years, with a subtle predominance in men. The histology of ECD is characterized by the presence of lipid-laden histiocytes (“foamy histiocytes”) with surrounding fibrosis. The histiocytes are consistently positive for CD68 and negative for CD1a and S100, and ultrastructural studies show no Birbeck granules in contrast to the findings in Langerhans cell histiocytosis. The pathogenetic mechanisms of the ECD are not well defined, because it is a very rare entity involving a group of chemokine (4) and receptors able to contribute to the cell recruitment, however, there is no evidence on the nature of mono-, oligo-, or polyclonal cells present in the infiltrate. Recent studies have suggested a close relationship of this disease with the mechanism of signal transduction of Ras/Raf/MEK/ERK (5). ECD may present with a typical bone involvement and extra-skeletal manifestations involving the central nervous system, retro-orbital tissue, cardiovascular system, lungs, liver, spleen,

retroperitoneum, and skin. Clinical manifestations include diabetes insipidus if the pituitary gland is affected, dyspnea secondary to pulmonary or cardiac involvement, proptosis, ataxia, rash, fatigue, weight loss, and bone pain. The lack of knowledge of the pathogenic mechanisms results in a lack of a standardized therapy of proven efficacy. The prognosis of ECD in cases with multi-systemic manifestations remains poor, with mortality rates of 60% after 32 months of diagnosis, mainly due to cardiopulmonary causes.

## Case report

A 34-year-old man, affected by ECD, was referred to our department for a correct assessment of the degree of cardiac involvement through cardiac magnetic resonance imaging (MRI). The patient presented with a

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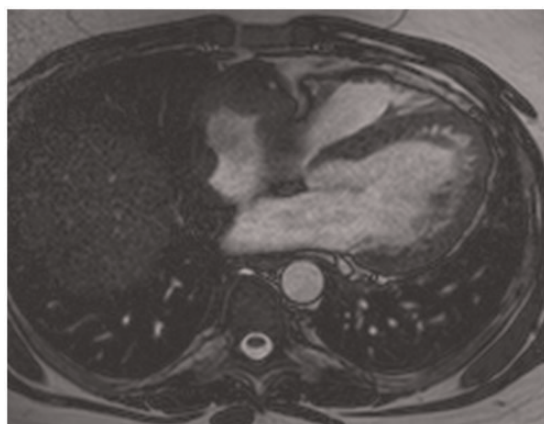
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medical history of bone, retroperitoneal, and orbital involvement, without any cardiac symptoms. The final diagnosis of ECD was obtained from a biopsy of retroperitoneal soft tissue that showed a mononuclear infiltrate consisting of lipid laden, non-Langherans hystiocytes with surrounding fibrosis, lacking Birbeck granules, presenting a BRAF (V600E) mutation. MRI was performed using a superconducting system 1.5 T MR (Gyrosan Intera, Philips Medical System, Best, The Netherlands) with a maximum gradient capability of 30 mT/m and maximum slew rate of 150 mT/ms. MR acquisition was triggered by ECG and included a T1-weighted (T1W) sequence and cine-MR images in the short-axis, and vertical long-axis and horizontal long-axis planes for displaying cardiac contraction. STIR (short time inversion recovery) sequence was obtained to suppress fatty tissue signal. Finally three-dimensional (3D) delayed enhancement 10, 15, and 20 min were acquired after an intravenous injection of Gd-DTPA at a dose of 0.1 mmol/kg. MRI showed a hypointense tissue extending along the ventricular walls and wrapping the free wall of the right atrium. This hypointense tissue also involved the inferior vena cava at the junction with the right atrium, the proximal portion of the ascending aorta, the right coronary artery, and right branch of the pulmonary artery (Figs 1 and 2). Bi-ventricular systolic function was preserved without any alterations of global and segmental kinesis (Fig. 3). A mild mitral insufficiency was found. STIR sequences did not show any area of edema or inflammation. Moreover, the pathological tissue showed mild enhancement after intravenous administration of contrast material (Fig. 4). These findings were consistent with a widespread cardiac involvement in a patient with ECD.

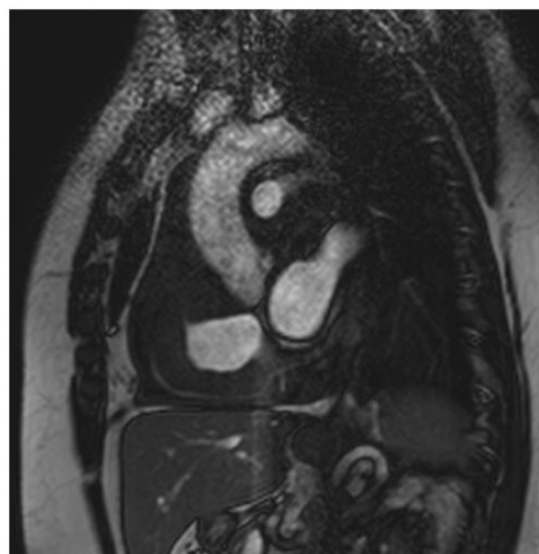


**Fig. 1.** Cardiac MRI cine-balanced fast field echo four-chamber view, showing hypointense tissue surrounding the right coronary artery and extending into the right atrio-ventricular groove.

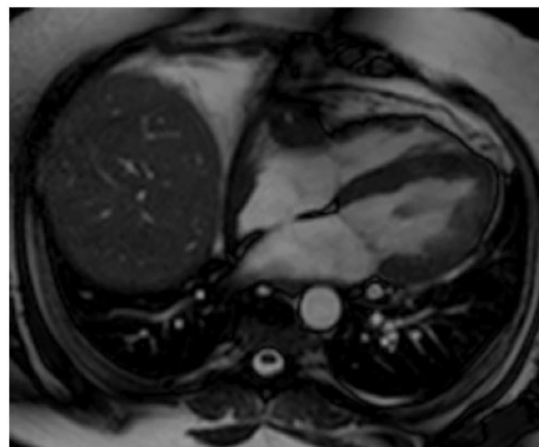
The patient also showed involvement of both kidneys that were surrounded by an inhomogeneous tissue that was hypointense to the contiguous structures on T2-weighted (T2W) MR images, showing mild contrast enhancement on postcontrast T1W MR sequence (Fig. 5a and b).

## Discussion

ECD affects the cardiovascular system in 75% of patients (6). Pericardial infiltration (7) is the most



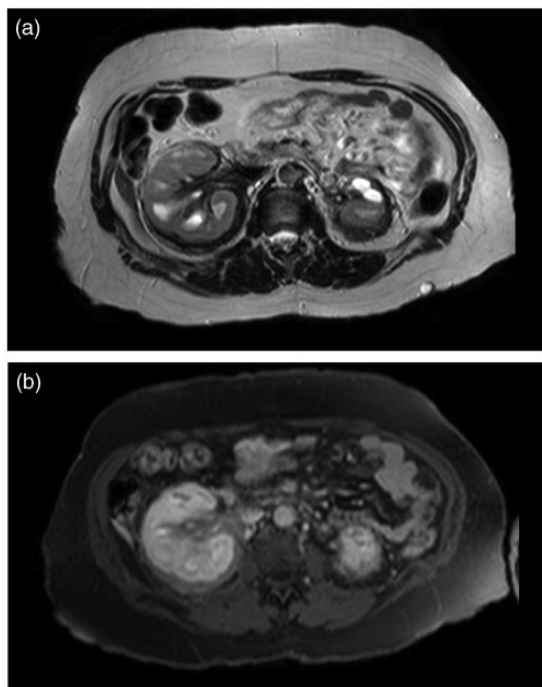
**Fig. 2.** Cardiac MRI cine-balanced fast field echo sagittal view, showing extensive hypointense tissue surrounding the ascending aorta and the right ventricular chamber.



**Fig. 3.** Cine video clip showing the involvement of the right coronary artery surrounded by the extensive hypointense tissue and extending through the atrio-ventricular groove, with preserved right ventricular motion.



**Fig. 4.** Axial postcontrast T1W MR image showing mild enhancement of the hypointense tissue, surrounding the right coronary artery.



**Fig. 5.** Axial T2W (a) and postcontrast T1W MR (b) images showing involvement of both kidneys that were surrounded by an extensive inhomogeneous tissue, which was hypointense to the contiguous structures on T2W images, showing mild contrast enhancement on axial postcontrast T1W images.

frequent cardiac manifestation, giving rise to a variety of symptoms and in some cases resulting in cardiac tamponade (8). Myocardial structures (9), such as atrial and ventricular walls, coronary sulcus, and interatrial septum can also be affected (10); pseudotumoral infiltration of the right atrium is a rather

common event. The valvular involvement can cause aortic and mitral regurgitation. Perivascular infiltration of the aorta (“coated aorta”) can also be observed (11): fibrosis can extend from the ascending aorta to the iliac bifurcation or it can be limited to the thoracic or abdominal portion. The infiltration, that is more frequently peri-advential, appears isointense to muscle on T1 and T2 MR sequences. The left common carotid artery, left subclavian artery, pulmonary trunk, coronary arteries (12), and other abdominal vessels can be affected as well. Cardiac MRI is a necessary tool for a correct assessment of ECD. This technique, allows a precise definition of localization and extension of the fibrotic involvement. An accurate evaluation of the cardiovascular system (13) is mandatory because if affected by ECD, the prognosis will get worse. In nearly 60% of cases death occurs because of cardiovascular complications (14) such as severe arrhythmias, cardiomyopathies, myocardial infarction, valve insufficiency, and cardiac tamponade.

Differential diagnosis of ECD includes cardiac lymphoma (15) and angiosarcoma (16); in our case, the presence of mild contrast enhancement on T1W MR sequence together with the presence on pathology findings of a mononuclear infiltrate consisting of lipid laden, non-Langerhans histiocytes with surrounding fibrosis, lacking Birbeck granules, allowed the correct final diagnosis of ECD, with unusual cardiac involvement.

In conclusion, this report describes a rare case of ECD with cardiovascular and kidney involvement, correctly assessed by MRI.

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