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## Case report

# Erdheim-Chester disease with multisystem involvement evaluated by multimodal imaging: A case report

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## ABSTRACT

Erdheim-Chester disease is a rare, idiopathic, multisystemic non-Langerhans cell histiocytosis. Little is known about the imaging features. Herein, we report a very uncommon case of Erdheim-Chester disease in a 54-year-old woman with multisystem involvement including cardiovascular system, skeleton, retroperitoneum (renal and adrenal infiltration), orbit and pituitary. Multimodal imaging modalities, including computed tomography, magnetic resonance imaging, echocardiography, and bone scintigraphy were used to comprehensively evaluate different organs involvement. Finally, myocardial biopsy results indicated Erdheim-Chester disease. Electrocardiography showed sick sinus syndrome and slowest heart rate of 20 beats/min. The patient underwent permanent pacemaker implantation and had initial treatment with interferon. There were no remarkable changes in right atrial lesion during 9-month follow-up period. Erdheim-Chester disease was a rare entity with a dismal prognosis, especially when there were cardiac and neurological involvement. The present case report aimed to describe and analyze radiological findings of multiple organs involvement of Erdheim-Chester disease with multimodal imaging retrospectively, and being familiar with the imaging features of Erdheim-Chester disease might help prompt and correct diagnosis of this disease in the future.

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Erdheim-Chester disease (ECD) is a rare, idiopathic, systemic non-Langerhans cell histiocytosis, characterized by tissue infiltration by large amount of non-Langerhans foamy histiocytes (CD 68+, CD1a- and S100-) and chronic inflamma-

tion [1]. ECD frequently involves multiple organs and systems including the skeleton (74%), neurologic system (25%~50%), cardiovascular (36%), retroperitoneum (more than 33%), skin (27%), orbit (25%), and pulmonary (18%) [2]. Most of these or-

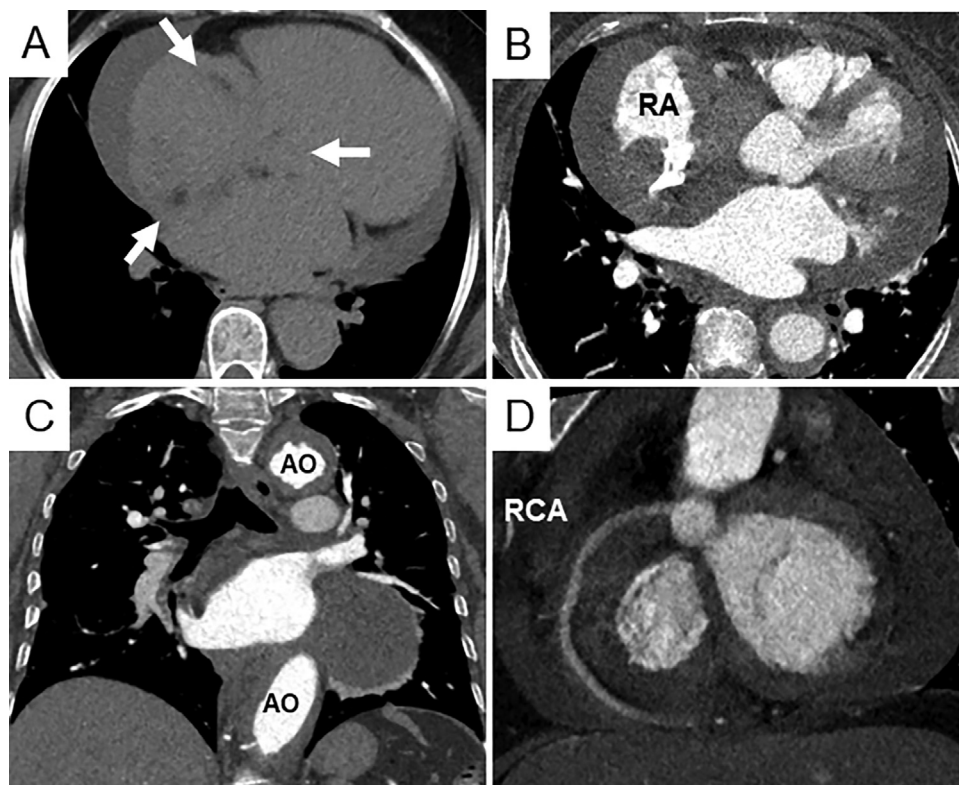
CT, Computed tomography; ECD, Erdheim-Chester disease; MRI, Magnetic resonance imaging; RA, Right atrium; SSFP, Steady state free precession; T1WI, T1 weighted imaging; T2WI, T2 weighted imaging.

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**Fig. 1 – CT demonstrating cardiovascular involvement of Erdheim-Chester disease. (A) Unenhanced CT shows a soft tissue density lesion with inhomogeneous density and unclear boundary that infiltrates RA wall, interatrial septum, and atrioventricular sulcus (arrows) with small pericardial effusion. (B) the lesion is slightly enhanced after administration of contrast agent. (C) shows perivascular infiltration of the aorta, called “coated aorta”. (D) Coronary CT angiography shows that the right coronary artery is encased by the lesion without luminal stenosis. CT, Computed tomography; RA, right atrium; AO, Aorta; RCA, right coronary artery.**

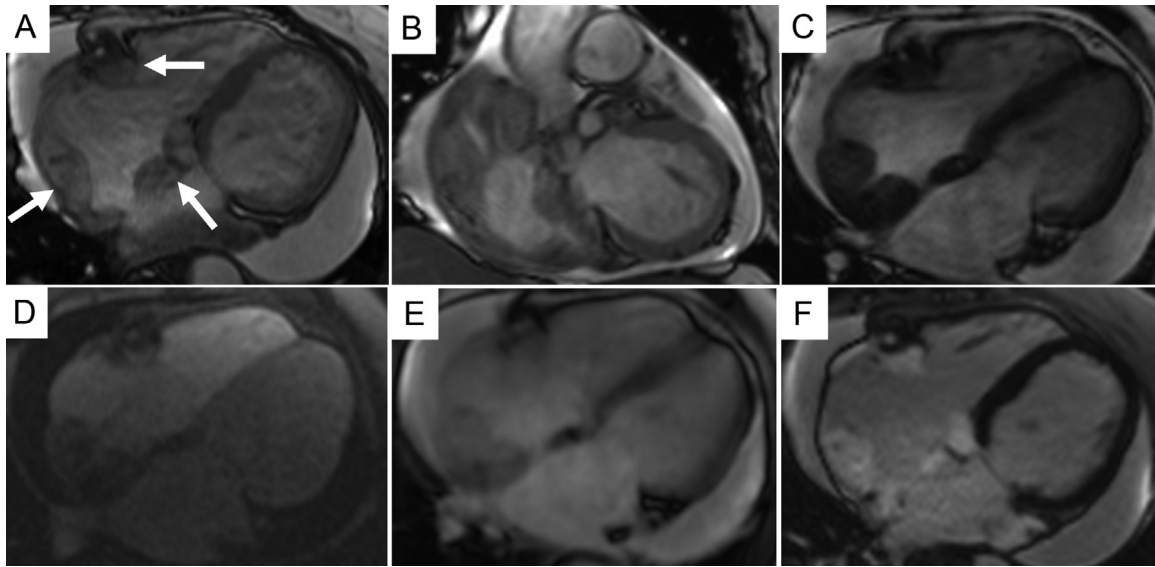
gans and systems were involved in our case, including cardiovascular (right atrium, interatrial septum, and atrioventricular sulcus, aorta, renal artery, and celiac artery), skeleton, retroperitoneum (renal and adrenal infiltration), orbit, and neurologic system (pituitary). A ECD patient with involvement of so many organs has rarely been reported in literature. In general, the ECD patients had poor prognosis. A systematic review ( $n = 448$ ) showed that the median age at death, and mean survival time after diagnosis were 56 years old and 2.3 years, respectively [2]. Estrada-Veras et al. [3] indicated that the patients with cardiac and neurological involvement should be paid special attention due to their association with increased morbidity and mortality. Due to its poor prognosis, early correct diagnosis is necessary for this extremely rare entity. Herein, we presented multimodal images in comprehensively assessing imaging features in each system, and meanwhile we also showed detailed clinical manifestations in this report.

### Case presentation

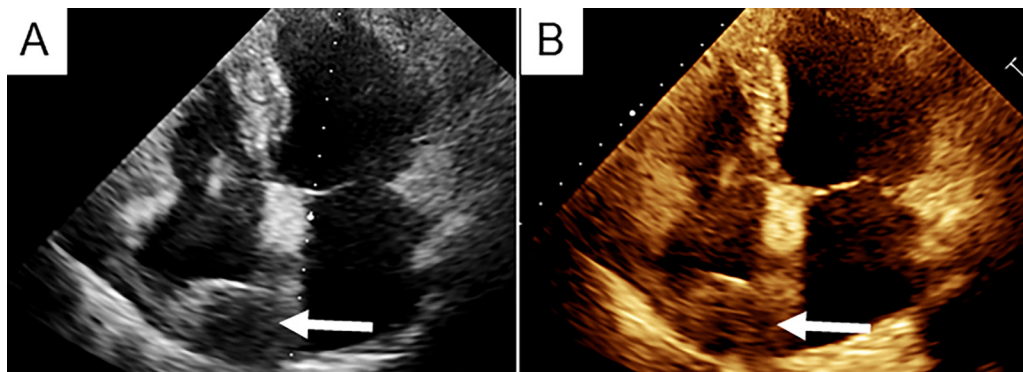
A 54-year-old woman was referred to the emergency department in our institution for complaining of exertional dysp-

nea, palpitation, fatigue, dizziness, and mild pitting edema of lower extremities over the last 4 years. The initial blood pressure was 125/77 mm Hg. She had a medical history of diabetes insipidus, chronic osteomyelitis, well-controlled hypertension and hyperthyroidism. Laboratory examination showed the erythrocyte sedimentation rate (100 mm/h), C-reactive protein (42.4 mg/l), and type B natriuretic peptide (2137 ng/l), interleukin-6 (61.3 pg/ml), white blood cell count ( $15.7 \times 10^9/l$ ), and platelet count ( $653 \times 10^9/l$ ) were significantly elevated. The level of the tumor marker serum carbohydrate antigen-199 (32.93 U/ml) was slightly increased. Her daily urine output was greater than 10,000 ml.

The cardiac computed tomography (CT) showed a soft tissue lesion with inhomogeneous density and unclear boundary that infiltrated right atrium (RA) wall, interatrial septum, and atrioventricular sulcus with small pericardial effusion. The lesion was slightly enhanced after administration of contrast agent. Coronary CT angiography showed that the right coronary artery was encased by the lesion without luminal stenosis. Perivascular infiltration of the aorta, called “coated aorta”, also can be observed (Fig. 1). For further evaluating cardiac function and characterizing the lesion, cardiac magnetic resonance imaging (MRI) and transthoracic echocardiography were performed. The cardiac MRI showed that cardiac lesion was mildly inhomogeneous hypertense on T2-weighted



**Fig. 2 – Cardiac magnetic resonance showing cardiac involvement. An irregularly contoured lesion with infiltrating the right atrium wall, atrioventricular groove and interatrial septum is shown mildly inhomogeneous hypertense on transverse (A, arrows) and coronal (B) T2-weighted bright-blood images, hypointense on cine SSFP image (C); (D), (E), and (F) after administration of contrast agent, the cardiac lesion is gradually and heterogeneously enhanced from first-pass myocardial perfusion to late gadolinium enhancement. SSFP, steady-state free precession.**

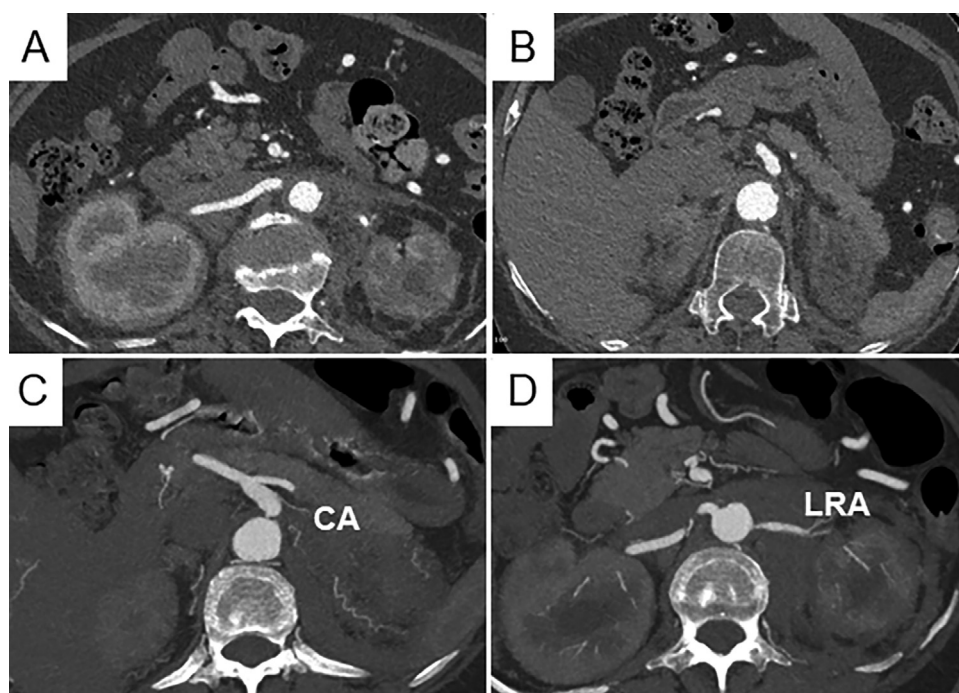


**Fig. 3 – Echocardiography showing cardiac involvement. (A) Echocardiography shows a mass on right atrium wall (arrow); (B) and the mass is enhanced after contrast agent injection.**

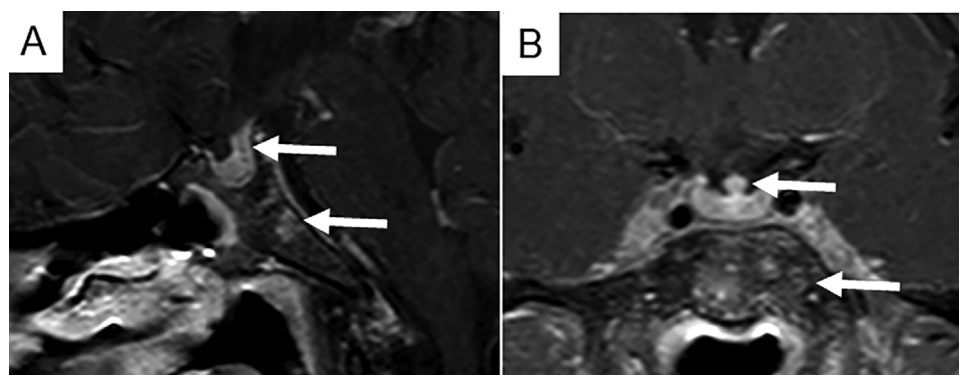
bright-blood images and hypointense on cine steady state free precession (SSFP) image. After gadolinium administration, the cardiac lesion was gradually and heterogeneously enhanced from first-pass myocardial perfusion to late gadolinium enhancement (Fig. 2). Echocardiography demonstrated a hypoechoic mass on the RV wall with enhancement after contrast agent injection (Fig. 3). The patient had normal global left ventricular systolic function with an ejection fraction of 63%.

The abdominal CT scan showed soft tissue density lesion with irregular contour and mild enhancement that involved retroperitoneal organs (bilateral adrenal glands and kidneys) and fat gap. Due to the infiltration of perirenal fat and fascia, it had a “hairy kidney” appearance. Meanwhile, mild hydronephrosis was observed in the left kidney. In addition,

we found vascular involvement of the retroperitoneum, presented with severe stenosis of the proximal segment of celiac artery and left renal artery (Fig. 4). Sella turcica MRI was used to determine whether diabetes insipidus was caused by pituitary affection, and the MRI revealed thickening and homogeneous enhancement of pituitary stalk with patch enhancement in clivus (Fig. 5). Furthermore, laboratory examinations for tuberculosis, pituitary function (adrenocorticotropic hormone, luteinizing hormone, and follicle-stimulating hormone), adrenal function (morning serum cortisol), thyroid function, and immune diseases were all negative. The biopsy of retroperitoneal or cardiac lesion has not yet been performed due to the poor physical condition of the patient. Eventually, the patient was managed conservatively with diuretics and antihypertensive drugs. After three weeks of conserva-



**Fig. 4 – Computed tomography demonstrating retroperitoneal infiltration of Erdheim-Chester disease. (A) and (B) show infiltration in bilateral kidneys (“hairy kidney”), adrenal glands, and retroperitoneal fat gap; meanwhile, there is mild hydronephrosis in the left kidney. (C) and (D) reveal the severe stenosis of the proximal of celiac artery and left renal artery. CA, celiac artery; LRA, left renal artery.**

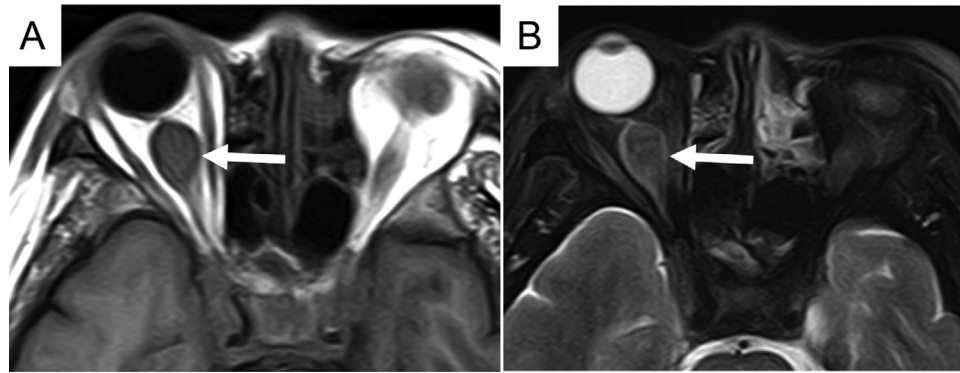


**Fig. 5 – Sella turcica magnetic resonance imaging demonstrating pituitary gland and clivus involvement. Thickening and enhanced of pituitary stalk and patch enhancement area in clivus (arrows) in sagittal (A) and coronal position (B).**

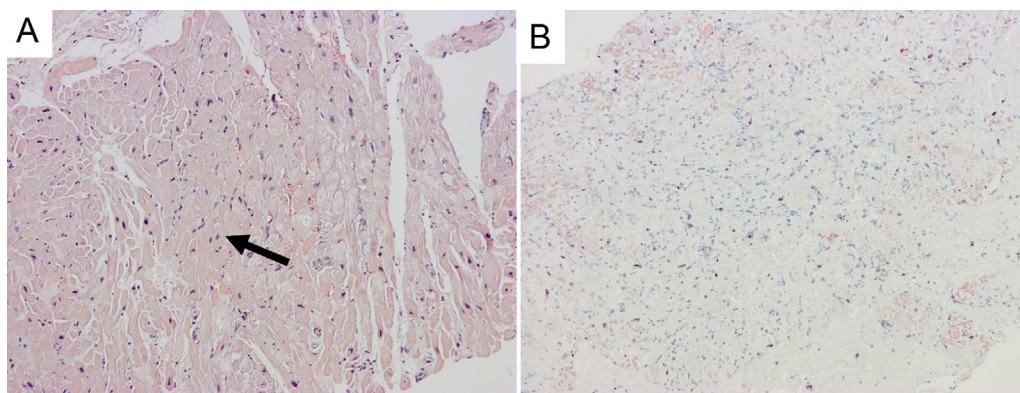
tive treatment, the symptoms of the patient were relieved and asked to be discharged from the hospital.

Recently, the patient was referred to cardiology clinic, owing to the aforementioned symptoms aggravation and new symptoms occurrence (abdominal distention and syncope). The follow-up cardiac CT demonstrated disease progression due to the increased extent of lesion infiltration in the right adrenal gland, right kidney, and retroperitoneal fat gap when compared with images in first admission. Brain MRI showed a right retrobulbar mass with isointense signal on T1 weighted imaging (T1WI) and slightly hypointense signal on T2 weighted imaging (T2WI) (Fig. 6). Bone scintigra-

phy showed increased radiotracer uptake in skull and bilateral symmetric long bones of extremities, especially in the distal femur and proximal tibia. Electrocardiography showed sick sinus syndrome and slowest heart rate of 20 beats/min. Finally, the patient underwent permanent artificial pacemaker implantation. In order to confirm the diagnosis, the patient underwent myocardial biopsy of the right atrium. Histopathology revealed infiltration characterized by large amount of non-Langerhans foamy histiocytes (CD 68+, CD1a-, S100-, and Langerin-) and inflammation cells (Fig. 7), which is a distinctive histopathological feature of ECD. The genomic evaluation revealed that BRAF<sup>V600E</sup> mutation was negative. The patient



**Fig. 6 – Brain magnetic resonance imaging demonstrating a right intraconal lesion. A right intraconal lesion (arrows) with isointense signal on T1-weighted image (A) and slightly hypointense signal on T2-weighted image (B).**



**Fig. 7 – Histopathology findings. (A) Hematoxylin and eosin stain for myocardial biopsy specimen shows foamy macrophages (arrow, original magnification  $\times 200$ ); (B) immunohistochemistry shows that histiocytes are strongly positive for CD68 protein (original magnification  $\times 200$ ).**

had initial treatment with interferon after discharge with regular follow-up. There were no remarkable changes in right atrial lesion during 9-month follow-up period.

## Discussion

ECD was a rare multisystem disorder of xanthomatous infiltration by non-Langerhans cell histiocytosis, with a slightly male predominance (62.3%) and the median age at diagnosis was 52.8 years [2]. Underlying etiology of ECD remains uncertain. Recent findings suggested that ECD was a rare clonal disorder, driven by mutations of the mitogen-activated protein kinase/extracellular signal-regulated kinase pathway, with a high frequency of BRAF<sup>V600E</sup> mutation (in >50% of cases), in which chronic inflammation environment was considered as an important mediator of ECD pathogenesis [1].

The diagnosis of ECD is based on supported histopathological findings with appropriate clinical manifestations and radiographic context. The clinical manifestations mainly depended on the affected organs. In our case, the patient mainly presented with cardiac tamponade or right heart failure (exertional dyspnea, fatigue and lower extremity

pitting edema), sick sinus syndrome (syncope, palpitation and dizziness), diabetes insipidus symptoms (polyuria) due to heart (myocardium and pericardium) and pituitary involvement. Retroperitoneal involvement was often asymptomatic in previous literature [2]. However, abdominal distention in our case may be explained by retroperitoneal infiltration. In addition, the secondary systemic hypertension can be caused by renovascular involvement [4,5]. Not only renovascular involvement but also periaortic or other vascular infiltration was found in our case, which may be risk factors for hypertension. Radiology is essential for diagnosing and managing ECD. Therefore, to make a correct diagnosis, consensus guidelines indicated that all patients with suspicion of ECD needed to conduct CT (chest, abdomen, and pelvis), positron emission tomography/computed tomography scan, brain and cardiac MRI. In addition, other radiological examinations could be selected according to clinical symptoms or signs [1]. Cardiovascular involvement is common in ECD patients and it is associated with a worse prognosis [6]. A contrast-enhanced cardiac MRI is optimal to evaluate the extent of myocardial and pericardial infiltration, tissue characterization of the lesion, and ventricular dysfunction. Differential diagnosis for ECD with involvement of the heart mainly includes primary cardiac lymphoma and angiosarcoma. Differentiating ECD

from primary cardiac lymphoma is challenging. The primary cardiac lymphoma can be hypointense on T1WI and hyperintense on T2WI, but it often demonstrates heterogeneous signal with mildly homogenous or heterogeneous contrast enhancement [7]. In our report, cardiac lesion was gradually and heterogeneously intensified from first-pass myocardial perfusion to late gadolinium enhancement and presented finally significant enhancement on late gadolinium enhancement. The pattern of enhancement may be useful in diagnosis and differential diagnosis of ECD. Additionally, angiosarcomas with irregular cauliflower formation often involve free wall of the right atrium and are mostly heterogeneous due to the content of hemorrhage, vessels, or necrosis. After contrast media administration, angiosarcomas typically show marked heterogeneous or rim enhancement [8].

Treatment of ECD has yet to be fully established. Consensus guidelines indicated that initiation of therapy was recommended for all patients, except for those patients who were asymptomatic, and interferon was the most commonly prescribed therapy according to literature [1]. A prospective and multicenter study with 53 ECD patients confirmed that interferon significantly improved overall survival [9]. For BRAF-positive patients, vemurafenib, as an inhibitor of mutated BRAF, was effective with evidence of dramatic clinical and radiographic improvement [10]. Our report also support the view that the patients with ECD need specific treatment for etiology rather than observation or only symptomatic treatment because of disease deterioration over time in our patient. Due to lacking BRAF<sup>V600E</sup> mutation, our patient had initial treatment with interferon and regular follow-up.

## Conclusion

In conclusion, this report shows a rare case of ECD with multisystem involvement, comprehensively assessed by multimodal imaging. Be familiar with the imaging and clinical features of ECD is essential for prompt and correct diagnosis and management of this disease.

## Ethical approval

The present report was approved by the Ethics Committee of the West China Hospital in Sichuan University.

## Patient consent

Written informed consent was obtained from the patient for the publication of this case report.

## Declaration of Competing Interest

The authors have declared that no competing interests exist.

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