Case Report
Multimodality imaging of spleen involvement in Erdheim-Chester disease mimicking splenic hemangioma: a unique case report

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Abstract: Erdheim-Chester disease (ECD) is a rare and clinically heterogeneous non-Langerhans cell histiocytosis, and its diagnosis relies on established clinical, radiologic, histopathological criteria. ECD can be evaluated by whole-body preoperative imaging methods. Although 18F-FDG PET/CT shows negative findings in some splenic benign or borderline lesions, such as splenic inflammatory myofibroblastic tumors and hemangioendotheliomas, it can provide value in differentiating some malignant diseases, such as hemangiosarcoma and metastases. Here, we report the CT, MRI, and 18F-FDG PET/CT imaging performance of an ECD patient who presented with only spleen involvement. Even though some clinical and radiological descriptions can be found in the literature, ECD reports with only splenic involvement mimicking splenic hemangioma as the first presentation are rare, to the best of our knowledge. Histopathology and molecular analysis of this case confirmed the diagnosis of ECD. Clinicians should pay attention to the possibility of ECD occurrence in the spleen, while negative findings on 18F-FDG PET/CT of the spleen indicated a low risk for high-grade malignant splenic tumors and metastases.

Keywords: Erdheim-Chester disease, spleen, computed tomography, magnetic resonance imaging, 18F-FDG PET/CT, case report

Introduction

Erdheim-Chester disease (ECD) is an uncommon, nongenetic and clinically heterogeneous non-Langerhans cell histiocytosis [1, 2] that was first described under the name “lipogranulomatosis” by Jakob Erdheim and William Chester in 1930 [3], and approximately 1000 cases have been reported to date. The diagnosis relies on established clinical, radiologic, and histological criteria [4]. Theoretically, ECD can affect every organ and tissue. In most cases, it is a multisystemic disorder with a variety of clinical manifestations depending on the location, ranges, and outcome ranging from occult to life-threatening [2, 5, 6]. Only spleen involvement and no involvement of other organs or systems in ECD is rare.

ECD can be effectively evaluated by preoperative imaging, which provides powerful methods to aid in the diagnosis and improvement of prognosis. Here, we report the CT, MRI, and 18F-FDG PET/CT imaging performance of ECD patients with only spleen involvement. To the best of our knowledge, this is the first report of ECD with only spleen involvement with multimodality imaging mimicking splenic hemangioma as the primary presentation.

Case presentation

A 43-year-old man underwent physical examination with no clinical complaint, and a solid mass in the middle and lower part of the spleen was found near the splenic hilum by abdominal ultrasound. The patient had no known family history of hereditary disease, and he was previously healthy. Physical examination and laboratory tests did not reveal any significant abnormalities. Contrast-enhanced CT examination showed irregular splenic morphology and multiple slightly low-density masses near the splenic hilum, with a maximum size of approximately
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5.2 cm × 4.7 cm × 5.8 cm (AP × LR × SI). The lesions showed obvious circumferential enhancement at the arterial phase filling toward the centers of the lesions in the venous phase and reduced enhancement in the delayed phase. The CT attenuation values in the plain scan and enhancement in each phase were 42 HU, 69 HU, 106 HU and 82 HU, respectively (Figure 1). MRI showed multiple nodular non-homogeneous, abnormal signals in the splenic mass with slightly high signal on T1WI, slightly low signal on T2WI, equal-slow signal on DWI, and slightly low signal on ADC images (Figure 2). The patient underwent 18F-FDG PET/CT to further evaluate the lesions (Figure 3). PET/CT images showed an irregular splenic lesion with multiple slightly hypodense loci. The splenic lesions exhibited well-defined borders, and the FDG uptake within the lesions (SUVmax = 3.1) was similar to physiologic uptake in the remaining splenic parenchyma, and there was no abnormal uptake of FDG in the other regions. Splenic hemangioma was considered one possible diagnosis in this case before the surgery, but low-grade malignant or borderline splenic tumors could not be excluded. With the consent of the patient, laparoscopic splenectomy was performed for the purpose of obtaining a definite diagnosis and further exploration.

Postoperative pathology showed diffuse hyperplasia of short spindle cells with a single nucleus, short spindle-like cells, irregular morphology that was partially distorted, fine nuclei, partially visible small nucleoli, lightly stained cytoplasm, partially empty and bright, scattered foam-like cells, rare nuclear division, scattered lymphocytes, plasma cells and eosinophilic infiltration. Immunohistochemistry showed LCA/CD45 (++), CD68 (KP1) (++), CD68 (PGM1) (++), MPO (scattered +), S-100 (scattered +), CD1a (-), CD21 (-), CD35 (-), FXIII (-), CD34 (vascular +), CD31 (vascular +), ERG (-), CD8 (scattered +), FVII (+), CD61 (-), CD20 (-), and CD3 (-) (Figure 4A-D). The molecular analysis of histiocytes further revealed the \textit{BRAF} V600E gene mutation (Figure 4E). Combined with histological morphology, immunohistochemistry and molecular analysis, the final diagnosis of splenic ECD was made. The patient exhibited a satisfactory recovery following surgery and has undergone a 12-month follow-up period without experiencing any recurrence or significant complications.

Discussion

Histiocytosis can be classified into three general groups: malignant, Langerhans cell histo-
Figure 2. Magnetic resonance images (MRI) of splenic Erdheim-Chester disease. (A) T1WI transverse image shows an equal-slightly high signal lesion. (B) T2WI transverse image shows a heterogeneous slightly low signal lesion. The lesions showed an equally slow signal on DWI (C) and a slightly low signal on ADC images (D). (E) At the early stage of enhancement, the edge of the lesion showed circumferential enhancement. (F) Uniform enhancement of lesions in the delayed phase.

Figure 3. 18F-FDG PET/CT images of splenic Erdheim-Chester disease. A. The anteroposterior 3-dimensional maximum intensity projection image (MIP) demonstrated no metabolic abnormality in the whole body. B. The transverse images showed that the well-defined lesions had multiple slightly hypodense occupancies, with the largest lesion measuring approximately 4.6 cm in length (long arrows). C. Coronal images showed that the spleen was irregular in shape, and the FDG uptake in the lesion (SUVmax = 3.1) was similar to the physiologic uptake in the remaining splenic parenchyma.
cytosis (LCH), and non-LCH [2]. ECD is a rare and clinically heterogeneous non-LCH that mostly occurs in adults in their fifth and seventh decades of life, with a higher incidence in...
MAP2K1 in approximately 30% of cases, which gene in 57% to 70% of cases and mutations in Mainly, there are the associated with activating the MAPK pathway.

ECD pathogen has been widely improved, with more than Recently, the understanding of ECD pathogen-negative for CD1a, supporting the diagnosis of ECD. Positive staining for MPO and S-100, and completely negative staining for LCA/CD45, CD68 and factor VII, weakly positive for CD1a for ECD, whereas positive S100 is rare [13]. In this case, the patient stained positively for LCA/CD45, CD68, and completely negative for CD1a, supporting the diagnosis of ECD. Recently, the understanding of ECD pathogenesis has been widely improved, with more than 80% of ECD patients having mutations in genes associated with activating the MAPK pathway. Mainly, there the V600E mutation in the BRAF gene in 57% to 70% of cases and mutations in MAP2K1 in approximately 30% of cases, which results in inflammatory histiocytes [14-18]. It is imperative to analyze BRAF V600E mutations for potential therapeutic implications [13].

Imaging methods play crucial roles in the diagnosis of ECD, as well as in the assessment of disease progression. Due to various imaging presentations of ECD, “unusual” may be the norm for ECD. Accurately determining the extent of ECD involvement is important in the clinic and often requires the combination of radiography, CT, MRI, and 18F-FDG PET/CT for the characterization of specific organ involvement. Nikpanah et al. [12] studied the abdominal involvement of 61 ECD patients and found that the commonly affected abdominal organs were the kidneys and seminal vesicles as a result of retroperitoneal infiltration. No infiltration of other adjacent organs in the abdomen was found in our patient by CT and MRI. 18F-FDG PET/CT (vertex-to-toe protocol) is helpful for the evaluation of the extent and the quantification of the severity of ECD, and also improves the detection of lesions that meet the response criteria [2, 6, 19, 20].

Inflammatory cells are well known for their increased glucose uptake, which is enhanced when cytokines are present [21]. Young et al. [2] found that the results of 18F-FDG PET/CT were related to the presence of BRAF mutations, which help in the diagnosis of ECD patients, biopsy guidance, treatment response assessment and disease surveillance. The clinical utility of 18F-fluoride PET/CT in detecting and characterizing bone lesions in the ECD has been highlighted by Caoduro et al. [22]. Wu et al. [23] found that patients with ECD can benefit from 68Ga-DOTA-FAPI-04 PET/CT for evaluating the extent of their disease, guiding biopsy procedures, and monitoring treatment outcomes. The splenic lesion in our case showed slight uptake on PET/CT, similar to physiologic uptake of the remaining splenic parenchyma, which may suggest early diagnosis and a low extent of inflammation. It is recommended to perform organ-specific imaging every 3 months after the initial treatment and up to 6 months once the disease is stable [7, 24].

Multiorgan involvement of ECD often necessitates a broad differential diagnosis [25]. In this case, only the spleen was involved, which should be distinguished from splenic hemangioma, lymphoma, hamartoma, and angiosarco-
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Hemangiomas appear iso- or hypodense on CT, with nodular enhancement at the edge in the arterial phase and isodensity in the delayed phase. The T1WI signal of hemangiomas is either hypo- or isointense, while the T2WI signal is heterogeneously hyperintense on MRI. The filling in peripheral nodules in hemangiomas is usually continuous on delayed enhanced scanning [26]. MRI has great value for the diagnosis of primary splenic lymphoma. T1WI shows equal and slightly low signal, and T2WI shows slightly high signal. Splenic lymphoma shows a high signal on the DWI sequence and a low ADC signal, suggesting that the diffusion of the lesion is limited. Enhanced scans show mild enhancement and clearer boundaries. In addition, postenhancement splenic lymphomas may fuse with each other to form a “map-like” lesion often with markedly enlarged retroperitoneal lymph nodes [27]. CT scans of splenic hamartomas show isointense or slightly hypointense masses located within or around the spleen, sometimes with calcification or fatty tissue. In MRI, low signal or mixed low signal is shown in T1WI. To determine whether fat components are present, fat-saturated T2WI should be used. Enhanced scans show diffuse heterogeneous patchy enhancement and no enhancement of fat components [28]. Hemangiosarcoma of the spleen appears on CT scan as a single or multiple hypodense mass with uneven density and poorly defined borders, often accompanied by cystic changes, calcification, and hemorrhage. MRI shows a slightly low signal in T1WI, a high signal in T2WI, and a low signal in T2WI in the presence of chronic bleeding and iron-containing hemoglobin deposition. CT enhanced scan shows mild or obvious inhomogeneous ring enhancement in the arterial phase and progressive enhancement in the portal and delayed phases, which is similar to hemangioma, but its irregular enhancement is more obvious than hemangioma. Some hemangiosarcomas may have liver and other distant metastases [29].

The treatment of ECD is chosen based on a patient’s phenotype, severity, and risk status, while spontaneous regression is rare [4, 13]. The prognosis for ECD used to be poor, with an overall survival rate of almost 2.3 years after diagnosis [30]. There is currently no standardized treatment for ECD, and the prognosis of this condition is closely linked to the degree of multisystem involvement [31]. Notably, cardiovascular and central nervous system manifestations are associated with the most unfavorable prognosis [7]. The application of kinase inhibitor therapies has revolutionized the treatment of many ECD patients since 2012, including the BRAF inhibitors vemurafenib and dabrafenib and the MEK inhibitors cobimetinib and trametinib [32, 33]. The efficacy of targeted therapies in ECD is robust; however, Haroche et al. [4] suggest only using them if the disease exhibits severe manifestations, as there may be serious adverse effects and unknown long-term effects. Compared to targeted therapies, interferon-based regimens usually have a slower and partial therapeutic response, and there are several adverse effects associated with the medication, including depression and fatigue in nearly 50% of patients [4, 34]. Splenic hemangiomia was considered one possible diagnosis in this patient before the surgery; however, some low-grade malignant or borderline potential splenic tumors, such as inflammatory myofibroblastic tumor, hemangioendothelioma, and sclerosing angiomatoid nodular transformation, could not be excluded. Therefore, tumor resection surgery was the first choice rather than embolization of splenic arterial branches. After surgical excision treatment, the prognosis of our patient was good.

Conclusion

In summary, ECD is a rare histiocytic proliferative disease with multisystem and multiorgan involvement, so only splenic involvement is rare. The application of multimodality imaging methods provides strong support for the diagnosis, efficacy assessment and follow-up of ECD. The lesion in our patient showed slight uptake on PET/CT in the splenic lesion, and involvement of other systems were excluded, especially skeletal involvement. Although 18F-FDG PET/CT showed negative findings in the splenic lesion, it warded off the risk for more serious disease, such as splenic hemangiosarcoma or lymphoma or spleen metastases. Clinicians should be aware of the possibility of ECD occurrence in the spleen considering the findings in multiple imaging methods.

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Disclosure of conflict of interest

None.

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