Case Report

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Erdheim–Chester Disease Involving the Biliary System and Mimicking Immunoglobulin G4-Related Disease: A Case Report

면역글로불린 G4 연관 질환과 유사한 담관 침범을 보이는 Erdheim-Chester 병: 증례 보고

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First described in 1930 as a lipoid granulomatosis, Erdheim-Chester disease (ECD) is a rare histiocytosis encompassing a group of disorders caused by overproduction of histiocytes, a subtype of white blood cells. This disease most commonly involves the bones and can affect organs in the abdomen; however, biliary involvement is rarely reported. We report a case of ECD with biliary involvement, which rendered it difficult to radiologically distinguish ECD from immunoglobulin G4-related disease.

Index terms Erdheim-Chester Disease; Histiocytes; Immunoglobulin G4-Related Disease

INTRODUCTION

Erdheim–Chester disease (ECD) is a rare histiocyte proliferative disease with multisystem involvement (1). ECD has a slight male predominance and usually affects adults aged > 40 years (2). It most commonly involves the bones (95%), especially in the lower extremities, and in most patients, extraosseous involvement is found in various organs, leading to a variety of symptoms. Relatively common extraosseous involvement sites are the central nervous

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system (CNS), retroperitoneum, aorta, and orbit (1, 3). Periarticular pain is commonly present; however, patients may be asymptomatic even if ECD involves the bones or other organs. Therefore, ECD treatment depends on the location and extent of organ involvement, and treatment may not be required in mild cases (1).

Skin, breast, lymph node, and solid visceral organ involvement in ECD is extremely rare (3). We report a case of biliary involvement in ECD presenting with multifocal ductal wall thickening with luminal narrowing and mild distal intrahepatic ductal dilatation, which was initially presumed to be an immunoglobulin G4 (IgG4)-related disease. Since ECD can be misdiagnosed without the knowledge of visceral organ involvement, we present rare radiologic features of biliary involvement in ECD.

CASE REPORT

A 61-year-old female presented with persistent right upper abdominal discomfort for a few months. Four years prior, she was diagnosed with central diabetes insipidus (DI), which was associated with a mass in her pituitary stalk detected on MRI (Fig. 1A). She was on desmopressin for treatment. She had no history of smoking or alcohol drinking and prior surgeries. She was admitted to our institution for further evaluation and treatment of the abdominal discomfort and pituitary stalk mass.

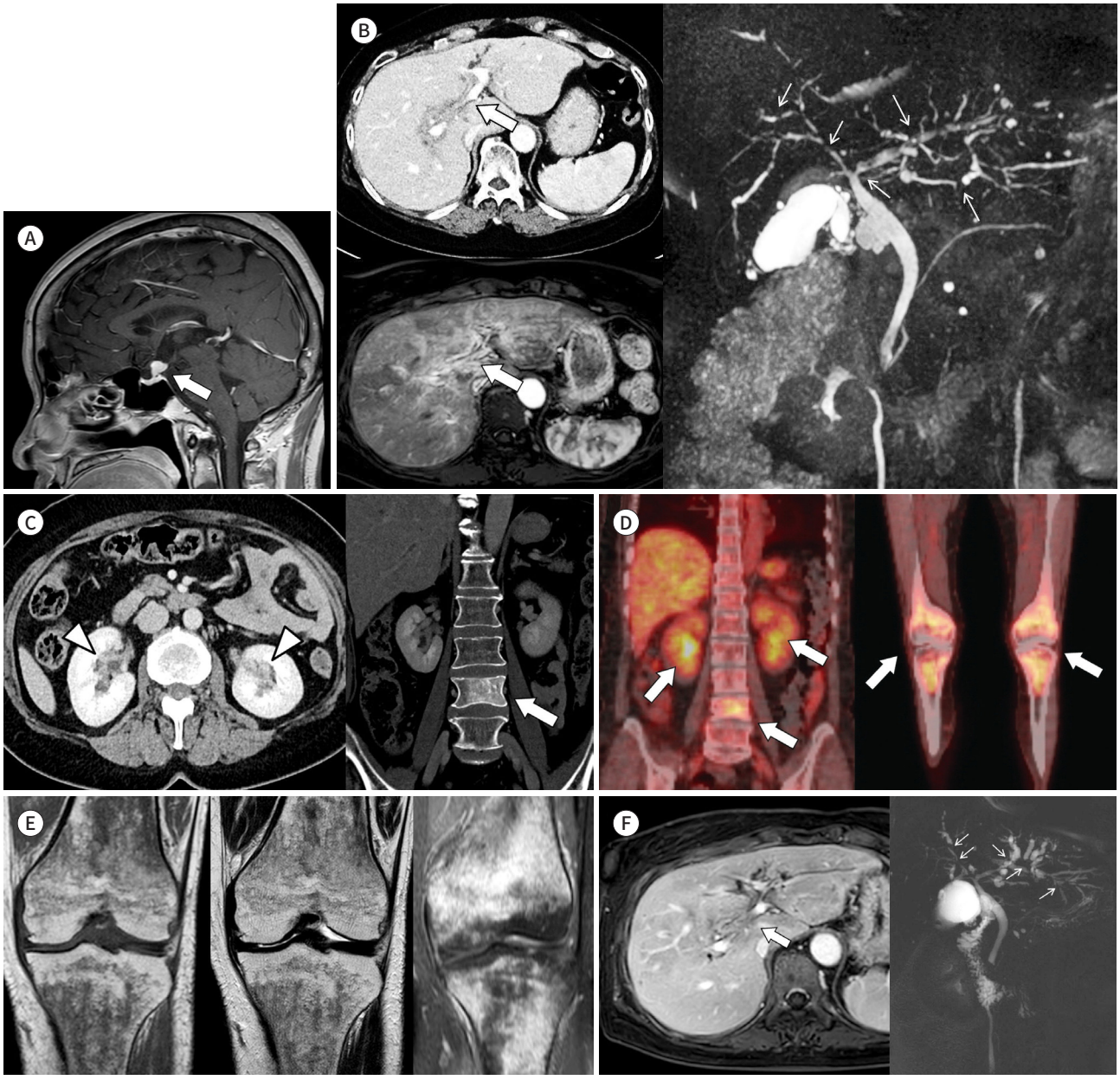
Initial abdominal CT and MR cholangiopancreatography (MRCP) revealed multifocal bile duct wall thickening with strictures and mild ductal dilatation (Fig. 1B). Enhancing soft tissue lesions at both renal pelvis and ill-defined sclerotic lesions at L4 of the vertebral body were also observed on abdominal CT (Fig. 1C).

PET/CT revealed heterogeneously high fluorodeoxyglucose (FDG) uptake in the liver. An increased FDG uptake was also observed in the bilateral renal pelvis, pituitary stalk, L4 vertebral body, and periarticular bones of both knees (Fig. 1D). Knee MRI showed an enhancing lesion with low signal intensity on both T1- and T2-weighted imaging (Fig. 1E), which corresponded to a lesion with high FDG uptake on PET/CT.

Based on the imaging findings, the initial diagnosis was IgG4-related disease with multisystemic involvement. However, serum IgG (1226 mg/dL, normal range: 700–1600 mg/dL) and IgG4 (519 mg/dL, normal range: 30–2010 mg/dL) levels were within the normal range, and the anti-mitochondrial antibody and perinuclear anti-neutrophil cytoplasmic antibodies were negative. Lymphoma was also considered as a differential diagnosis; however, the possibility was thought to be relatively low because of the absence of lymph node enlargement in the abdomen. Therefore, liver and bone biopsies of the L4 vertebral body were performed. Pathologic findings showed foamy histiocytes with small nuclei and surrounding fibrosis, multinucleated giant cells, and Touton giant cells. Immunohistochemical staining was positive for CD68 and BRAF V600E mutations, which was consistent with ECD. IgG and IgG4 counts of the specimen were 11/high-power field (HPF) and 0/HPF, respectively, which were not compatible with IgG4-related disease.

The patient was initially treated with a corticosteroid for 5 months and her serum total bilirubin level decreased from 4.7 mg/dL to 1.2 mg/dL; however, follow-up MRCP showed aggravated bile duct wall thickening and intrahepatic bile duct dilatation (Fig. 1F). Thus, her treat-

Fig. 1. Erdheim-Chester disease involving biliary tree in a 61-year-old female.
A. Contrast-enhanced sagittal T1-weighted image shows an enhanced mass (arrow) in the pituitary stalk.
B. Contrast-enhanced axial CT (upper left) and contrast-enhanced axial MR images (lower left) show multifocal bile duct wall thickening (arrows) with stricture and dilatation of the intrahepatic bile duct. Three-dimensional MR cholangiopancreatography image (right) shows a multifocal stricture and dilatation of the intrahepatic bile duct (thin arrows).
C. Contrast-enhanced axial CT image (left) shows soft tissue infiltration involving the bilateral renal pelvis (arrowheads). Coronal CT image (right) shows patchy sclerotic lesion at the L4 vertebral body without bony destruction (arrow).
D. Fluorodeoxyglucose PET/CT scan shows increased fluorodeoxyglucose uptake in both renal pelvis, L4 vertebral body, and both knees (arrows).
E. Coronal T1- (left) and T2-weighted images (middle) show multifocal patchy hypointense lesions with strong enhancement on contrast-enhanced coronal fat-suppressed T1-weighted imaging (right).
F. Contrast-enhanced axial MR (left) and three-dimensional MR cholangiopancreatography (right) images after 8 months show aggravated bile duct wall thickening (arrow), multifocal stricture, and dilatation of the intrahepatic bile duct (thin arrows).



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ment regimen was revised to interferon treatment. After interferon treatment initiation, follow-up CT and MRCP showed no significant change and laboratory test results were normal.

This study was approved by the Institutional Review Board of our hospital (IRB No. 4-2021-1077). The requirement for informed consent was waived.

DISCUSSION

Histiocytoses are rare diseases characterized by the accumulation and/or proliferation of histiocytes in various tissues and were previously categorized according to their origin: Langerhans cells or non-Langerhans cells (1). However, they have recently been classified into five groups based on the histology, phenotype, molecular alterations, and clinical and imaging characteristics: 1) Langerhans-related, 2) cutaneous and mucocutaneous, 3) malignant histiocytosis, 4) Rosai–Dorfman disease, and 5) hemophagocytic lymphohistiocytosis and macrophage activation syndrome (4, 5). According to the recently revised classification of the Histiocyte Society in 2016, ECD is now classified as a Langerhans-related group, which was first described as a lipoid granulomatosis in 1930 (1, 4). In immunohistochemical studies, ECD expresses CD68, which is a histiocytic marker, and is negative for CD1a (1). Recently, the BRAF V600E mutation, which is an activating mutation of the proto-oncogene BRAF, was discovered in ECD patients and detected in approximately 54% of ECD cases (6).

The symptoms of ECD vary depending on the organ involvement. The most common sites of organ involvement are the long bones, especially at the metaphysis and diaphysis of the lower extremities, which manifests as periarticular pain (1). The typical radiologic finding appears as patchy long bone medullary osteosclerosis in the metadiaphyseal area with epiphyseal sparing; additionally, this characteristic imaging finding helps differentiate ECD from Langerhans cell histiocytosis (LCH), whose osseous involvement shows an osteolytic appearance (1, 3). Other common sites of extraosseous involvement are the CNS and orbit, which present with central DI and bilateral exophthalmos, respectively (3). Retroperitoneal involvement of ECD is also common and manifests as a retroperitoneal mass, which is usually asymptomatic; however, it occasionally causes stenosis of the renal vessels or the collecting system (1). A typical radiologic finding of renal involvement of ECD is perirenal fat infiltration with a spiculated appearance, called the “hairy kidney sign.” Another finding of renal involvement of ECD is soft tissue enhancement involving the renal pelvis, which was observed in our case (3, 7). Although uncommon, lung involvement is significantly associated with increased morbidity and mortality and most commonly presents with interstitial processes characterized by inter- and intra-lobular septal thickening (1, 3).

ECD treatment depends on the site and extent of organ involvement. The therapeutic options include close observation in mild disease and interferon therapy or chemotherapy in advanced disease. Surgical intervention may be helpful for local symptomatic diseases, such as hydronephrosis because of a retroperitoneal mass or neurological symptoms due to CNS involvement (1, 3). For patients with ECD with a positive BRAF-V600E mutation who have cardiac/neurologic disease or end-organ dysfunction, BRAF inhibitor therapy, such as vemurafenib or dabrafenib, should be implemented as first-line therapy (5).

The biliary involvement of ECD is not well-known, and only a few cases have been reported

(8). Gundling et al. (8) reported that the biliary manifestation of ECD presented with periductal fibrosis, resulting in upstream intrahepatic bile duct dilatation, mimicking Klatskin's tumor. In our case, multifocal bile duct wall thickening with stricture and dilatation was observed on both CT and MRCP, which is suggestive of primary sclerosing cholangitis or IgG4-related sclerosing cholangitis (9). Because our patient showed soft tissue infiltration in both renal pelvis, which is also a characteristic radiologic feature of renal involvement in IgG4-related disease, the findings in the biliary system findings were initially thought to be IgG4-related sclerosing cholangitis. Although rare, biliary tract involvement of LCH manifests as periductal fibrosis which shows radiologic findings similar to those of biliary involvement of ECD (1).

PET/CT is valuable for the evaluation of the extent and severity of ECD. A high FDG uptake is observed in organs where ECD is involved, allowing for accurate detection of the extent of disease, even in asymptomatic lesions. As the degree of FDG uptake reduction reflects the therapeutic effect, PET/CT can also help assess the treatment response (10).

Although there is a difference in the frequency, ECD can involve any organ, resulting in asymptomatic lesions to organ dysfunction. Such involvement in the skeleton, retroperitoneum, and CNS is well-known and has characteristic radiologic findings. However, biliary system involvement in ECD is rare and can lead to misdiagnosis. Due to the low incidence of ECD and the fact that visceral organ involvement in ECD is rare, clinicians and radiologists are not familiar with the biliary manifestation of ECD. This case report presents a CT and MRCP image of ECD involvement in the biliary system, which mimicked IgG4-related sclerosing cholangitis due to similar radiologic findings and the patient's multi-organ lesions.

Author Contributions

Conceptualization, C.Y.E.; data curation, H.H.G., C.Y.E., P.J.; supervision, C.Y.E., P.J., K.Y.E.; validation, C.Y.E.; writing—original draft, H.H.G.; and writing—review & editing, C.Y.E.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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면역글로불린 G4 연관 질환과 유사한 담관 침범을 보이는 Erdheim-Chester 병: 증례 보고

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Erdheim–Chester 병은 희귀한 조직구증으로, 백혈구의 아형인 조직구의 과잉 생산으로 인한 질병 중 하나이며, 1930년에 처음 기술되었다. Erdheim–Chester 병은 가장 흔하게는 뼈를 침범하고, 복부의 다른 모든 기관을 침범할 수 있지만 담도 침범의 증례는 매우 드물게 보고된다. 이에 저자는 영상의학적으로 면역글로불린 G4 연관 질환과 구별하기 어려웠던 Erdheim-Chester 질환의 담도 침범 사례를 보고하고자 한다.

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