CASE REPORT Brain Tumor Res Treat 2025;13(4):164-170 / pISSN 2288-2405 / eISSN 2288-2413
https://doi.org/10.14791/btrt.2025.0029

Check for updates

Erdheim-Chester Disease Mimicking a Malignant Pituitary Stalk Tumor With Ventricular Dissemination: A Case Report

Myungsuk Oh[1], Se Hoon Kim[2,3,4], Eui Hyun Kim[1,3,4]

Departments of [1]Neurosurgery and [2]Pathology, Yonsei University College of Medicine, Seoul, Korea
[3]Pituitary Tumor Center, Severance Hospital, Seoul, Korea
[4]Brain Tumor Center, Severance Hospital, Seoul, Korea

Received July 25, 2025
Revised September 8, 2025
Accepted September 17, 2025

Correspondence
Eui Hyun Kim
Department of Neurosurgery,
Yonsei University College of Medicine,
50-1 Yonsei-ro, Seodaemun-gu,
Seoul 03722, Korea
Tel: +82-2-2228-2150
Fax: +82-2-393-9979
E-mail: euihyunkim@yuhs.ac

Erdheim-Chester disease (ECD) is a rare form of non-Langerhans cell histiocytosis characterized by multi-organ involvement, most commonly affecting the long bones, retroperitoneum, heart, lungs, skin, and central nervous system (CNS). Approximately half of reported cases exhibit CNS involvement, which may affect both intra- and extra-axial compartments. On MRI, ECD typically presents as a strongly enhancing mass lesion, often mimicking neoplastic or infectious conditions. With advances in genetic understanding, ECD is now recognized as a hematologic malignancy of histiocytic origin, driven by mutations in key components of the MAPK signaling pathway. Among these, the *BRAF* mutation is the most frequently observed genetic alteration and often provides a valuable clue for differential diagnosis. However, in cases lacking typical clinical features and the absence of *BRAF* mutation, diagnosis becomes significantly more challenging. We report the case of a 32-year-old man who presented with a pituitary stalk mass and ventricular dissemination, ultimately diagnosed with *BRAF* wild-type ECD harboring a *CSF1R* mutation, which has recently been implicated as a potential driver within the MAPK pathway. A deeper understanding of the molecular pathogenesis of ECD may not only aid in accurate diagnosis but also contribute to improved clinical outcomes.

Keywords *CSF1R*; Erdheim-Chester disease; Histiocytic malignancy; Inflammatory pseudotumor; Pituitary stalk.

INTRODUCTION

A wide range of neoplastic and non-neoplastic disorders can arise in the sellar region. Neoplastic conditions include pituitary neuroendocrine tumor, craniopharyngioma, germinoma, lymphoma, and metastatic tumors. Non-neoplastic diseases encompass inflammatory conditions such as lymphocytic hypophysitis and IgG4-related disease [1]. It is noteworthy that the current World Health Organization (WHO) classification system now designates both Langerhans and non-Langerhans cell histiocytoses as clonal neoplasms, whereas they were previously regarded as inflammatory conditions [2]. Because of the overlapping clinical presentations among these entities, differential diagnosis is critical yet often highly challenging. Diagnosis typically relies on a combination of radiologic studies, serologic markers, and, most importantly, histopathological confirmation through biopsy [1,3,4].

Herein, we present a diagnostically challenging case of Erdheim-Chester disease (ECD) with extensive central nervous system (CNS) involvement.

CASE REPORT

Patient history and examinations

A 32-year-old man presented with polyuria, polydipsia, and a progressively worsening headache over the course of one week. Basal hormone testing revealed a serum cortisol level of 0.3 μg/dL, free T4 level of 0.89 ng/dL, and testosterone level of <2.5 ng/mL. The serum sodium level was 146 mmol/L, and serum osmolality was 309 mOsm/kg, findings consistent with diabetes insipidus. Given the laboratory evidence suggestive of

panhypopituitarism and diabetes insipidus, replacement therapy with corticosteroids and antidiuretic hormone was initiated. Due to suspicion of pituitary hormonal insufficiency, brain CT and MRI were performed, which revealed a sellar and suprasellar mass with strong, homogeneous contrast enhancement. The mass was noted to infiltrate the floor of the third ventricle with dissemination into the lateral ventricles (Fig. 1A). The patient denied any prior history of intracranial masses or relevant medical conditions.

A transsphenoidal biopsy of the posterior pituitary gland followed by histological examination revealed dense inflammatory infiltrates suggestive of either an inflammatory condition—such as sarcoidosis, tuberculosis, IgG4-related disease, or lymphohistiocytic disorder—or a neoplastic condition. Immunohistochemical stains for IgG/IgG4, cytokeratin, synaptophysin, and c-kit were negative. Alpha-fetoprotein and beta-human chorionic gonadotropin, tumor markers for germ cell tumors, were also negative. Testing for a *BRAF* mutation, commonly associated with histiocytic disorders, was negative. Under impression of lymphocytic hypophysitis, the patient was discharged on steroid therapy and continued hormone replacement. One month later, follow-up brain MRI showed a reduction in the size of the lesions involving the pituitary gland and third ventricle (Fig. 1B). The patient's condition remained stable on medical therapy; however, his symptoms worsened 3 months after the initial biopsy. Repeat MRI revealed recurrence of the lesions in the pituitary region and third ventricle (Fig. 1C). To remove a larger amount of tissue, a second surgery was planned.

Operation

The tumor was accessed via an endoscopic endonasal approach under the guidance of a neuro-navigation system. The mass had a firm consistency and low vascularity, with dense

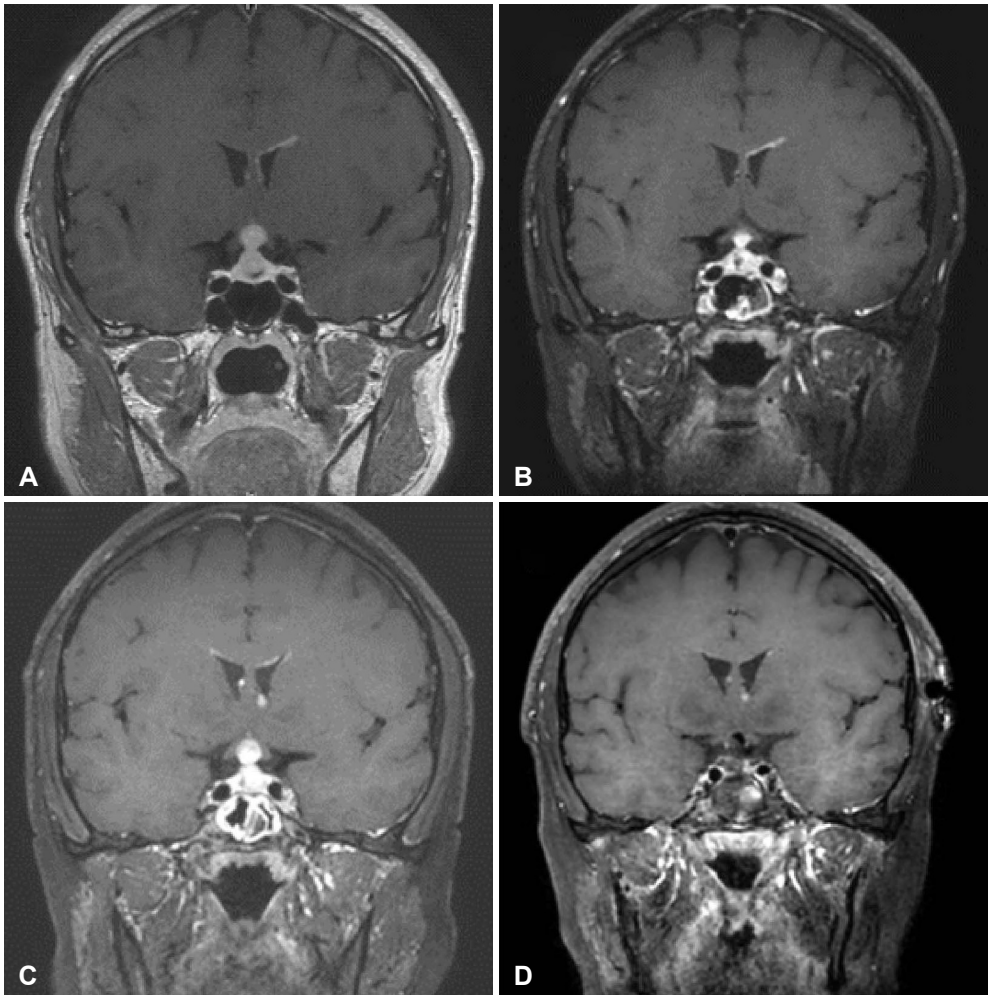

Fig. 1. Serial contrast-enhanced T1-weighted magnetic resonance imaging (MRI). A: Initial MRI at presentation demonstrated an enhancing mass lesion in the sellar and suprasellar regions which mainly involves the pituitary stalk and the floor of the third ventricle, along with multiple enhancing seeding lesions along the ventricular wall. B: Follow-up MRI 1 month after the first transsphenoidal biopsy showed a partial reduction in the size of the mass. C: At 3 months post-biopsy, MRI revealed progression of the lesion. D: MRI obtained after the second transsphenoidal surgery showed that the main sellar and suprasellar mass was completely removed.

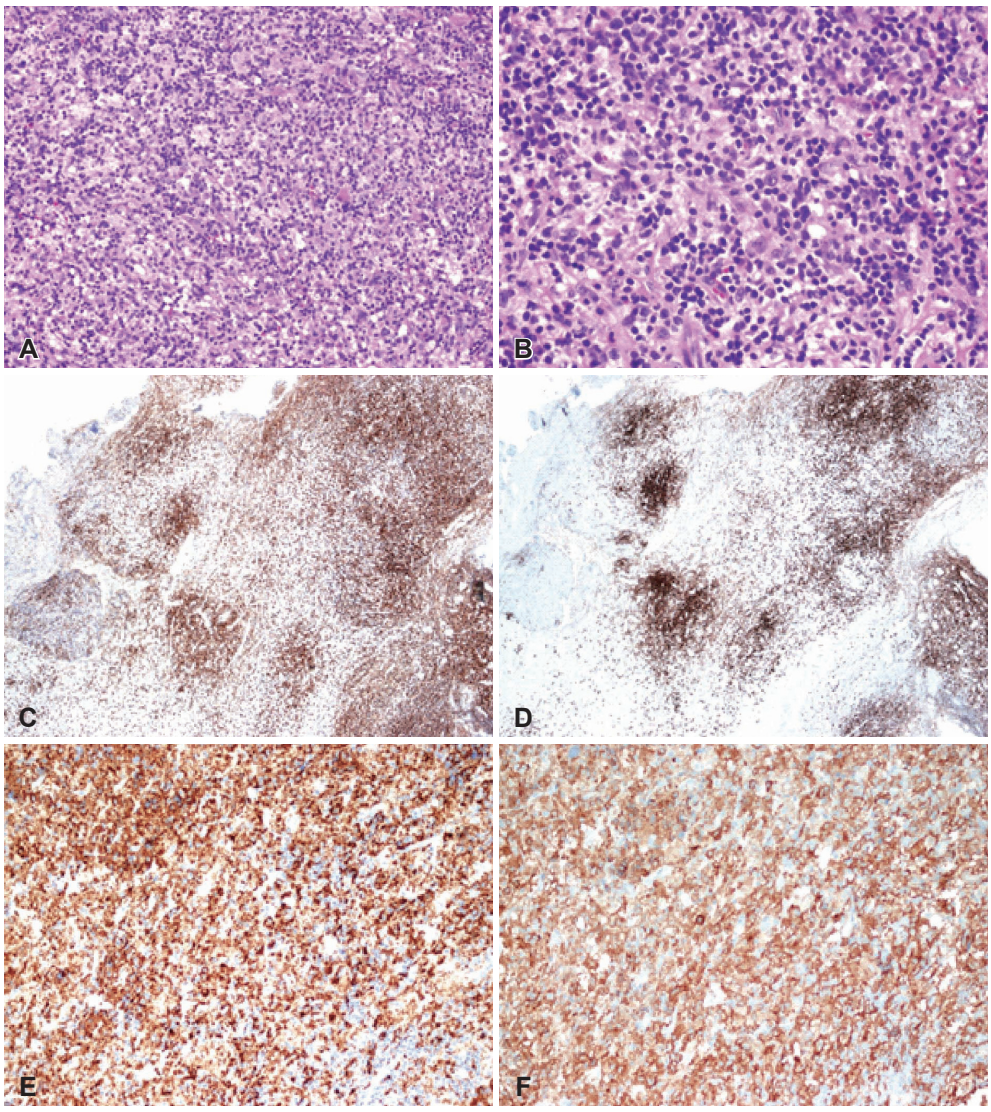

Fig. 2. Histopathologic findings of the mass. A and B: Hematoxylin and eosin (H&E) staining at ×200 and ×400 magnification showed dense inflammatory cell infiltrates. C and D: Immunohistochemical stains showed CD3/CD20 mixed pattern (×40). E and F: CD68 and CD163 immunostaining revealed diffuse infiltration of histiocytes/monocytes showing foamy features (×100).

adhesion to surrounding neurovascular structures including the optic apparatus and the floor of the third ventricle. Gross total removal of the sellar and suprasellar mass was achieved (Fig. 1D), and the skull base defect was reconstructed in a multilayered fashion, reinforced with a nasoseptal flap.

Pathological examination

Immunohistochemical staining demonstrated a mixed CD3/CD20 pattern, with 20% of Ki-67 labeling index. CD68 and CD163 staining revealed diffuse infiltration of foamy histiocytes/monocytes containing both macro- and microvesicles. Staining for c-kit, Langerin, and BRAF was negative (Fig. 2). To exclude the possibility of lymphoma, a T-cell receptor (TCR) gene rearrangement test was performed, which was negative for TCR gamma, beta, and delta chain gene rearrangements. Additionally, there was no evidence of a clonal B-cell population or rearrangement of the immunoglobulin heavy chain, kappa light chain, or lambda light chain genes. A positron emission tomography scan was negative for any other systemic malignancies (Fig. 3A). Collectively, these findings were suggestive of inflammatory hypophysitis, with differential considerations including Langerhans cell histiocytosis and Rosai-Dorfman-Destombes disease. Among these possibilities, the pathological features were considered to be most suggestive of ECD. However, a whole-body bone scan, performed to evaluate for osteosclerosis, was negative—an imaging result that is inconsistent with classic ECD (Fig. 3B).

Exclusion of infectious conditions

As none of the findings aligned with a single neoplastic dis-

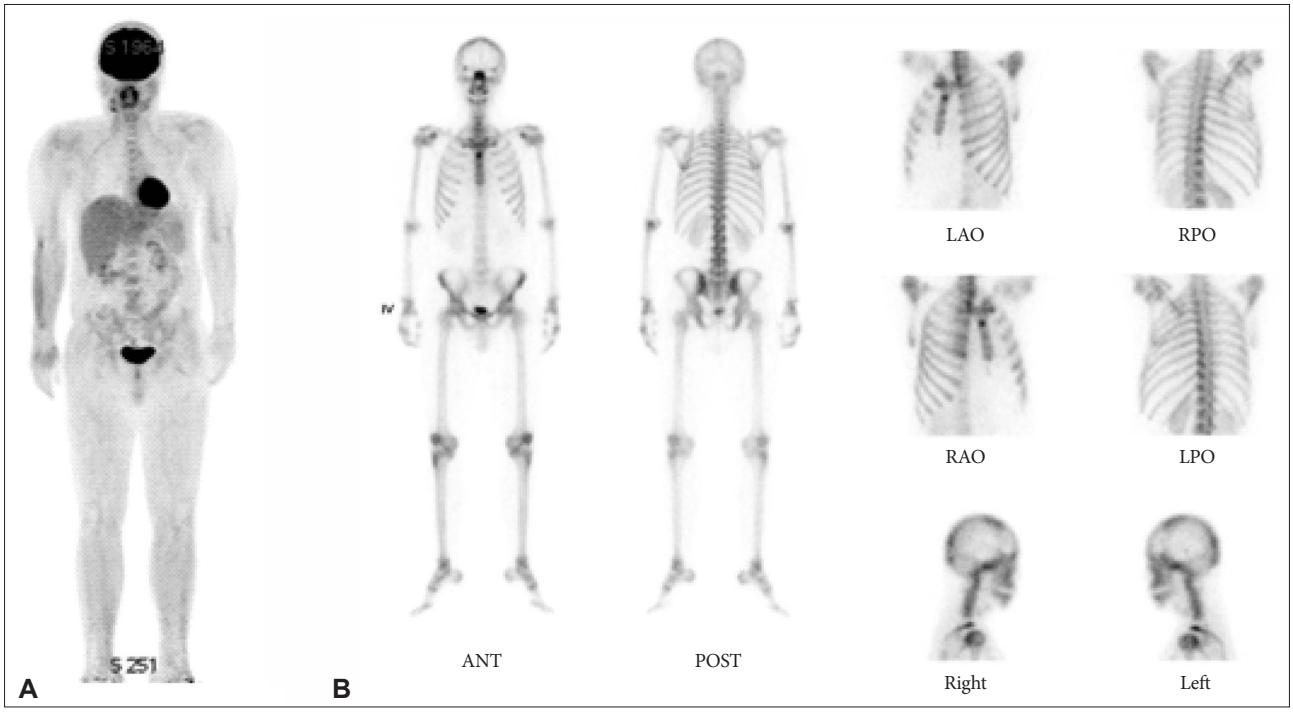

Fig. 3. Positron emission tomography (PET)-CT and whole-body bone scan. A: There was no significant abnormal uptake on PET/CT. B: Whole-body bone scan showed no definite osteosclerotic or hypermetabolic lesion. LAO, left anterior oblique; RPO, right posterior oblique; RAO, right anterior oblique; LPO, left posterior oblique.

ease entity, further differential diagnosis was pursued to evaluate for rare infectious conditions. Blood cultures were negative, and testing for human immunodeficiency virus was also negative. Serologic tests, including the Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin tests, were positive. Based on a review of the patient's medical history—information not disclosed during the initial evaluation—it was confirmed that he had been diagnosed with syphilis 8 years earlier and had been treated with intramuscular penicillin at that time. Analysis of cerebrospinal fluid (CSF) revealed a protein level of 54.8 mg/dL, a neutrophil count of 15/μL, and a glucose level of 58 mg/dL. The CSF VDRL test was negative, while the fluorescent treponemal antibody absorption test was positive. Based on a clinical impression of neurosyphilis, the patient received intravenous penicillin G (24 million IU/day) for 14 days. However, follow-up brain MRI after completion of antibiotic therapy showed no radiological improvement. At 3 months, MRI revealed further disease progression, including extensive ventricular dissemination involving the sellar and suprasellar regions and the cerebellum (Fig. 4A-C). Following the exclusion of neurosyphilis, immunosuppressive pulse therapy with cyclophosphamide was initiated for a suspected intractable inflammatory condition. Despite undergoing three CSF diversion procedures due to ventricular obstruction, the patient's neurological condition continued to deteriorate.

Diagnosis of Erdheim-Chester disease

As the patient failed to respond to immunosuppressive therapy, the possibility of histiocytosis was revisited. Through a multidisciplinary team approach, targeted gene panel sequencing was performed and identified an activating mutation of *CSF1R* gene (NM_005211.3:c.1648_1659delTGGAAGATCTAC; p.Trp550_Ile553del). Given that this mutation has been previously reported in several cases of ECD, a final diagnosis of *BRAF* wild-type ECD was established [5,6]. As an interim measure, whole-brain radiotherapy (WBRT) was initiated because initiation of interferon-alpha (IFN-α) therapy was delayed due to institutional approval and drug preparation processes [7,8]. Following WBRT, the patient showed clinical improvement, and follow-up MRI demonstrated marked reductions in the size and extent of the mass lesions (Fig. 4D-F). After initiation of IFN-α therapy, the patient continued to improve symptomatically. However, 1 week after the first IFN-α injection, the patient suffered sudden cardiac arrest and expired [9]. The exact cause of death could not be determined, as no autopsy was performed.

DISCUSSION

Most sellar space-occupying lesions are pituitary adenomas; however, a wide range of other neoplastic and non-neoplastic conditions, including infections, inflammatory diseases, and

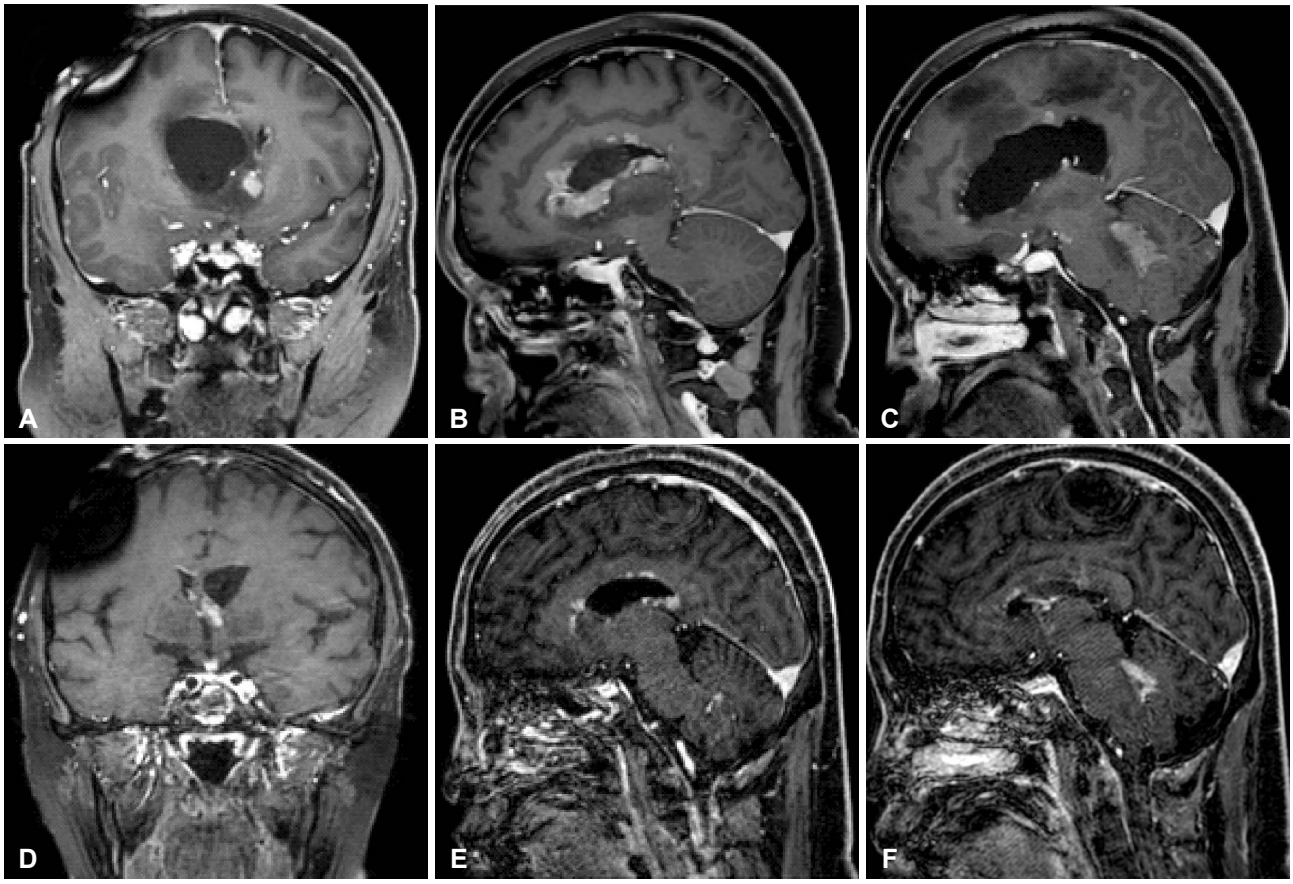

Fig. 4. Contrast-enhanced T1-weighted MRI findings following treatment interventions. MRI performed after ventriculoperitoneal shunt placement and intravenous antibiotic therapy demonstrated persistent enhancing lesions. A: Coronal view showing an enhancing lesion in the sellar and suprasellar region. B: Sagittal view demonstrating enhancement along the ventricular lining. C: Sagittal view showing an enhancing lesion in the cerebellum. D-F: Follow-up MRI after whole-brain radiotherapy revealed a marked reduction in overall disease burden.

various forms of histiocytosis, must also be considered in the differential diagnosis [1]. While initial clinical suspicion should be based on symptoms such as headache, dizziness, visual impairment, or signs of diabetes insipidus, MRI remains the most informative imaging modality for identifying and characterizing sellar lesions. A thorough review of the patient's medication history and any prior infectious diseases is also essential. For suspected systemic diseases such as histiocytosis, evaluation of extracranial involvement is necessary. In patients with a history of cancer, measurements of tumor markers, such as CEA, CA-125, CA-19.9, and PSA are helpful for exclusion of metastasis. Measurement of serum IgG4 is one of the most essential tests for evaluation of IgG4-related hypophysitis. CSF analysis with cytology, flow cytometry, immunohistochemistry, microscopy, and culture can be helpful for evaluation of infectious conditions such as tuberculosis and neurosyphilis [4].

Biopsy is strongly recommended if the diagnosis remains unclear after the best possible non-invasive evaluation. Tissue for histopathological examination can be obtained using a transcranial or transnasal transsphenoidal approach. Many study findings indicate biopsy should be performed when patients exhibit clear radiological, clinical, or endocrinological deterioration, or when lesions progress with an accompanying anterior pituitary deficiency [10,11].

Given the diagnostic complexity of this case, a multidisciplinary team approach was essential in reaching a final diagnosis. Discussion included the implications of the 2016 WHO classification, which expanded the category of miscellaneous primary CNS tumors to include lymphomas and histiocytoses. In addition, attention was given to the role of molecular analysis of the PI3K-AKT and MAPK pathways, which are increasingly recognized as central to the diagnosis and treatment of histiocytic disorders [12,13]. Based on this evolving understanding, we proceeded with comprehensive gene panel sequencing to identify potential mutations in these pathways.

ECD is a rare form of non-Langerhans cell histiocytosis that involves multiple organs, most commonly the long bones, retroperitoneum, heart, lungs, skin, and CNS [14]. Approximately half of all reported ECD cases exhibit CNS involvement, affecting both intra-axial and extra-axial compartments [15]. On MRI, CNS lesions in ECD often present with high signal intensity and contrast enhancement, resembling neoplastic or

Table 1. Summary of clinical, pathological, and molecular findings used for the diagnosis of Erdheim–Chester disease

Category	Findings
Clinical manifestations	- Symmetric diaphyseal and metaphyseal osteosclerosis in the legs detected by positron emission tomography (PET) scan and/or - Dense infiltration of perinephric fat ("hairy kidneys") on CT scan, periaortic sheathing ("coated aorta") on CT scan, right atrium pseudo–tumor on MRI, xanthelasma, exophthalmos
Pathological features	Infiltration by foamy CD68(+), CD163(+), Factor XIIIa(+), CD1a(–), and Langerin(–) with fibrosis, sometimes with Touton giant cells
Molecular features	- *BRAF*^{V600E} mutation, or - Activating mutation in the MAPK pathway, such as *KRAS*, *NRAS*, *MAP2K1*, *ARAF*, *MAP3K1*, or - Gene fusion activating the MAPK pathway, or - Activating mutation in *CSF1R*

infectious lesions. Clinically, patients may present with symptoms related to infiltrative disease, such as diabetes insipidus, seizures, cognitive impairment, and headache [16]. The diagnosis of ECD relies on a combination of clinical presentation, radiologic findings, and histopathologic confirmation [17]. Unlike Langerhans cell histiocytosis, which is more commonly diagnosed in children, ECD predominantly affects adults [12]. While ECD can involve virtually any organ, long-bone osteosclerosis remains its most frequent manifestation [18]. Additional characteristic imaging findings include perirenal fat infiltration ("hairy kidney") and aortic sheathing ("coated aorta") on CT. Right atrial pseudotumors may be seen on cardiac MRI, and xanthelasma, particularly in the eyelids or periorbital regions, is a classic dermatologic feature [12].

The diagnosis of ECD is based on a combination of characteristic clinical manifestations, radiologic findings, and histopathological features obtained through biopsy. ECD lesions typically show infiltration by foamy histiocytes, often accompanied by surrounding fibrosis or xanthogranulomatous changes. More recently, the identification of molecular alterations, particularly the *BRAF*^{V600E} mutation, as well as other mutations within the MAPK signaling pathway—including *KRAS*, *NRAS*, *MAP2K1*, *ARAF*, and *MAP3K1*—has become a key diagnostic criterion, especially in cases lacking classic clinical or histological features [13]. Moreover, ECD can also be diagnosed when MAPK pathway-activating gene fusions or *CSF1R* mutations are detected in histiocytic tissue samples (Table 1).

Traditional treatments for ECD have included glucocorticoids, cytotoxic agents, bisphosphonates, INF-α, and, in select cases, double autologous hematopoietic stem cell transplantation. In 2011, Arnaud et al. [19] reported that IFN-α therapy was associated with improved survival in patients with ECD. Subsequently, the discovery of the *BRAF*^{V600E} mutation in a significant subset of ECD patients led to the use of vemurafenib, a BRAF inhibitor, which has demonstrated improved survival outcomes in mutation-positive individuals [20]. More recently, in 2019, Diamond et al. [7] reported the efficacy of cobimetinib, an oral MEK1/2 inhibitor, in patients with ECD harboring various MAPK pathway mutations, including *ARAF*, *BRAF*, *RAF1*, *NRAS*, *KRAS*, *MAP2K1* (MEK1), and *MAP2K2* (MEK2).

In summary, this case highlights the value of molecular profiling, the clinical significance of *CSF1R* mutations, and the importance of an early multidisciplinary approach in the diagnosis and management of ECD. Because differential diagnosis for mass-forming lesions in the sellar and suprasellar regions always includes malignant conditions, biopsy is strongly recommended in cases with aggressive clinical features or uncertain diagnosis. Even if the clinical manifestation is not typical for CNS histiocytosis, detection of molecular alterations in disease-specific pathways can facilitate the diagnosis of these rare conditions, which are often associated with poor outcomes.

Ethics Statement

The Institutional Review Board of Severance Hospital exempted informed consent due to its retrospective nature and minimal risk for harm to the patient (4-2025-0637), and this report was conducted according to the guidelines of the Declaration of Helsinki for biomedical research.

Availability of Data and Material

The datasets generated or analyzed during the study are not publicly available due to confidentiality agreements but are available from the corresponding author on reasonable request.

ORCID iDs

Myungsuk Oh https://orcid.org/0009-0009-9666-9238
Se Hoon Kim https://orcid.org/0000-0001-7516-7372
Eui Hyun Kim https://orcid.org/0000-0002-2523-7122

Author Contributions

Conceptualization: Eui Hyun Kim. Data curation: Myungsuk Oh. Formal analysis: Myungsuk Oh. Investigation: all authors. Methodology: Myungsuk Oh, Eui Hyun Kim. Project administration: Eui Hyun Kim. Resources: Eui Hyun Kim. Supervision: Eui Hyun Kim. Validation: Eui Hyun Kim. Visualization: Myungsuk Oh, Eui Hyun Kim. Writing—original draft: Myungsuk Oh. Writing—review & editing: Eui Hyun Kim.

Conflicts of Interest

Se Hoon Kim, a contributing editor of the *Brain Tumor Research and Treatment*, was not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Funding Statement

None

Acknowledgments

None

REFERENCES

1. Catford S, Wang YY, Wong R. Pituitary stalk lesions: systematic review and clinical guidance. Clin Endocrinol (Oxf) 2016;85:507-21.
2. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, et al. The 5th edition of the World Health Organization classification of haematolymphoid tumours: myeloid and histiocytic/dendritic neoplasms. Leukemia 2022;36:1703-19.
3. Cohen Aubart F, Idbaih A, Emile JF, Amoura Z, Abdel-Wahab O, Durham BH, et al. Histiocytosis and the nervous system: from diagnosis to targeted therapies. Neuro Oncol 2021;23:1433-46.
4. Glezer A, Paraiba DB, Bronstein MD. Rare sellar lesions. Endocrinol Metab Clin North Am 2008;37:195-211.
5. Abeykoon JP, Lasho TL, Dasari S, Rech KL, Ranatunga WK, Manske MK, et al. Sustained, complete response to pexidartinib in a patient with CSF1R-mutated Erdheim-Chester disease. Am J Hematol 2022;97:293-302.
6. Durham BH, Lopez Rodrigo E, Picarsic J, Abramson D, Rotemberg V, De Munck S, et al. Activating mutations in CSF1R and additional receptor tyrosine kinases in histiocytic neoplasms. Nat Med 2019;25:1839-42.
7. Diamond EL, Durham BH, Ulaner GA, Drill E, Buthorn J, Ki M, et al. Efficacy of MEK inhibition in patients with histiocytic neoplasms. Nature 2019;567:521-4.
8. Miller RC, Villà S, Kamer S, Pasquier D, Poortmans P, Micke O, et al. Palliative treatment of Erdheim-Chester disease with radiotherapy: a rare cancer network study. Radiother Oncol 2006;80:323-6.
9. Christophi GP, Sharma Y, Farhan Q, Jain U, Walker T, Sayuk GS, et al. Erdheim-Chester disease presenting with histiocytic colitis and cytokine storm. J Gastrointestin Liver Dis 2017;26:183-7.
10. Beni-Adani L, Sainte-Rose C, Zerah M, Brunelle F, Constantini S, Renier D, et al. Surgical implications of the thickened pituitary stalk accompanied by central diabetes insipidus. J Neurosurg 2005;103(2 Suppl):142-7.
11. Jian F, Bian L, Sun S, Yang J, Chen X, Chen Y, et al. Surgical biopsies in patients with central diabetes insipidus and thickened pituitary stalks. Endocrine 2014;47:325-35.
12. Haroche J, Cohen-Aubart F, Amoura Z. Erdheim-Chester disease. Blood 2020;135:1311-8.
13. Ozkaya N, Rosenblum MK, Durham BH, Pichardo JD, Abdel-Wahab O, Hameed MR, et al. The histopathology of Erdheim-Chester disease: a comprehensive review of a molecularly characterized cohort. Mod Pathol 2018;31:581-97.
14. Chester W. [Over lipoid granulomatosis]. Virchows Arch path Anat 1930;279:561-602. German
15. Cavalli G, Guglielmi B, Berti A, Campochiaro C, Sabbadini MG, Dagna L. The multifaceted clinical presentations and manifestations of Erdheim-Chester disease: comprehensive review of the literature and of 10 new cases. Ann Rheum Dis 2013;72:1691-5.
16. Drier A, Haroche J, Savatovsky J, Godenèche G, Dormont D, Chiras J, et al. Cerebral, facial, and orbital involvement in Erdheim-Chester disease: CT and MR imaging findings. Radiology 2010;255:586-94.
17. Kovacs K, Bilbao JM, Fornasier VL, Horvath E. Pituitary pathology in Erdheim-Chester disease. Endocr Pathol 2004;15:159-66.
18. Estrada-Veras JI, O'Brien KJ, Boyd LC, Dave RH, Durham B, Xi L, et al. The clinical spectrum of Erdheim-Chester disease: an observational cohort study. Blood Adv 2017;1:357-66.
19. Arnaud L, Hervier B, Néel A, Hamidou MA, Kahn JE, Wechsler B, et al. CNS involvement and treatment with interferon-α are independent prognostic factors in Erdheim-Chester disease: a multicenter survival analysis of 53 patients. Blood 2011;117:2778-82.
20. Haroche J, Cohen-Aubart F, Emile JF, Arnaud L, Maksud P, Charlotte F, et al. Dramatic efficacy of vemurafenib in both multisystemic and refractory Erdheim-Chester disease and Langerhans cell histiocytosis harboring the BRAF V600E mutation. Blood 2013;121:1495-500.