

A case of Erdheim-Chester disease involving the orofacial bones in a child

Moruo Deng

The Affiliated Stomatological Hospital of Southwest Medical University

Hao Deng

Ziyang Central Hospital

Dan Li

The Second Hospital of Hebei Medical University

Minhai Nie

The Affiliated Stomatological Hospital of Southwest Medical University

Jian Wei

Zigong Fourth People's Hospital

Yaoqiang Liu

The Second Hospital of Hebei Medical University

Xuqian Liu

liuxuqian@swmu.edu.cn

The Affiliated Stomatological Hospital of Southwest Medical University

Case Report

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Abstract

Background

Erdheim-Chester disease is an extremely rare non-Langerhans cell histiocytosis characterized by infiltration of foamy histiocytes and multisystem involvement. The disease predominantly affects middle-aged adults, and pediatric cases are exceptionally uncommon. Orofacial bone involvement, particularly extensive maxillary destruction and sclerosis, has rarely been reported in children. We describe a pediatric case of Erdheim-Chester disease with prominent craniofacial skeletal lesions and central nervous system involvement to improve awareness of this unusual presentation.

Case presentation:

A 14-year-old boy presented with a 5-month history of unsteady gait and developmental delay. Physical examination revealed short stature, delayed sexual development, strabismus, and nystagmus. Imaging studies demonstrated multiple enhancing lesions involving the sellar region and cerebellar tentorium, diffuse cerebellar atrophy, and extensive mixed osteolytic and sclerotic lesions of the maxillofacial bones, predominantly affecting the maxilla. Additional findings included pulmonary nodules, pancreatic atrophy, and endocrine abnormalities, including hyperprolactinemia and hypogonadism. Histopathological examination of a maxillary biopsy showed diffuse infiltration of foamy histiocytes that were positive for CD68 and negative for CD1a and S100. Molecular testing identified a BRAF V600E mutation, confirming the diagnosis of Erdheim-Chester disease. The patient received treatment with dabrafenib combined with trametinib. After 10 months of therapy, follow-up imaging demonstrated marked regression of intracranial lesions and pulmonary abnormalities, with overall clinical improvement.

Conclusions

Pediatric Erdheim-Chester disease may present with atypical craniofacial bone lesions and multisystem manifestations, leading to delayed diagnosis. The combination of characteristic histopathological findings and molecular testing is essential for accurate diagnosis. Early targeted therapy with BRAF and mitogen-activated protein kinase kinase inhibitors can achieve significant clinical and radiological improvement in children with BRAF-mutated disease.

Trial registration

Clinical trial number: Not applicable.

Introduction

Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis that has been included in the 2016 (revised) World Health Organization (WHO) Classification of Tumors of the Blood and Lymphoid Tissues and is recognized as a distinct tumor entity of histiocytic and macrophage origin with well-defined histochemical and molecular characteristics.[1] It is primarily characterized by multi-organ infiltration by CD68-positive foam-like histiocytes, accompanied by chronic inflammation and fibrosis, which can lead to organ dysfunction or even failure.[2,3] ECD primarily affects middle-aged and elderly individuals; cases in children are extremely rare (fewer than 30 reported cases).[4] Its clinical presentation is highly heterogeneous, with common involvement of the skeleton (80–95% of patients, presenting as symmetrical osteosclerosis of long bones or atypical bone resorption), the central nervous system (CNS) (20–50%, such as diabetes insipidus and cerebellar ataxia), as well as the cardiovascular, pulmonary, retroperitoneal, and cutaneous systems.[2,4,5] Diagnosis relies on histology (CD68+, CD1a-, S-100- or weakly positive), imaging (e.g., bone scan, FDG PET/CT), and molecular testing (e.g., BRAF V600E mutation, present in approximately 50% of cases)[2,3] Interferon- α is the first-line treatment; BRAF inhibitors (such as dabrafenib) are highly effective in cases with BRAF mutations, and severe cases may be treated with a combination of chemotherapy or surgery.[3] Because the symptoms of ECD are nonspecific, diagnosis is often delayed and requires a multidisciplinary evaluation.[2] This case report describes a 14-year-old male patient who presented with 5 months of unsteady gait, developmental delay, extremely poor oral hygiene, and multisystem involvement (CNS, skeletal, endocrine, and pulmonary). The diagnosis of ECD was confirmed by maxillary biopsy and detection of the BRAF V600E mutation. Unique features of this case include: childhood onset; atypical bone destruction with sclerosis in the maxillofacial bones; extensive CNS involvement (intrasellar and cerebellar); endocrine abnormalities (hyperprolactinemia, low testosterone); a history of smoking (5 years); and rare oral hygiene issues. The extremely poor oral hygiene may be related to the maxillary lesions and systemic inflammation.[4,5] This provides a new perspective on the clinical manifestations of ECD. Through the analysis of this case and the literature, this article explores diagnostic and treatment strategies for ECD.

Case Report

A 14-year-old male patient presented with a 5-month history of unsteady gait. Physical examination revealed a height of 1.3 m, weight of 35 kg, and BMI of 20.71 kg/m². He exhibited developmental delay, and secondary sexual characteristics were not prominent. Neurological examination revealed poor bilateral ocular convergence reflexes, strabismus, nystagmus, and a positive test for ataxia with eyes closed. The patient has a 5-year history of smoking. Cranial MRI revealed multiple abnormally enhanced masses within the sella turcica, bilateral cavernous sinuses, and bilateral tentorium cerebelli, accompanied by diffuse cerebellar atrophy (Fig. 1). Maxillofacial CT showed multiple areas of bone destruction and sclerosis, with the maxilla being the most severely affected (Fig. 2); Laboratory findings: cerebrospinal fluid pressure 220 mmH₂O, urine specific gravity 1.026; serum endocrine panel showed testosterone 0.00 ng/mL, prolactin 65.70 ng/mL, and fasting growth hormone 0.71 ng/mL. PCR testing detected a BRAF V600E mutation (Figure 4). Based on clinical, imaging, and pathological features, the

diagnosis was Erdheim-Chester disease (ECD). A biopsy of the maxilla and surrounding lesions was performed in the Department of Oral and Maxillofacial Surgery; histology revealed diffuse infiltration of foamy histiocytes, consistent with a histiocytic proliferative lesion. Immunohistochemical results: CD68(+), Ki-67(+3%), Vimentin(+); CD1a, CD34, S-100, CKpan, FVIII-R-Ag, HMB45, Melan-A, SATB2, and SF-1 were all negative (Figure 5). After 10 months of treatment with the BRAF inhibitor dabrafenib in combination with the MEK inhibitor trametinib, follow-up MRI and CT scans revealed a marked reduction in the size of the abnormally enhanced masses in the sella turcica region and bilateral tentorium cerebelli, along with a reduction in meningeal thickening; however, localized cerebellar atrophy had progressed compared to previous findings; pulmonary nodules had decreased, interstitial changes had improved; there were no significant changes in pancreatic atrophy, suggesting an overall improvement in the patient's condition. The same patient was previously reported in a Chinese-language radiology case report[6]. The previous report mainly described the imaging findings of the patient.

Discussion

Erdheim-Chester disease (ECD) is a rare non-Langerhans cell histiocytosis classified by the World Health Organization as a myeloid neoplasm. It is primarily characterized by multiorgan infiltration by CD68-positive foam-like histiocytes, accompanied by chronic inflammation and fibrosis, and can lead to organ failure in severe cases.[2,3] This case report describes a 14-year-old male patient who presented with 5 months of unsteady gait, developmental delay, extremely poor oral hygiene, multisystem involvement (central nervous system, skeletal, endocrine, and pulmonary), and a BRAF V600E gene mutation. ECD was confirmed via maxillary biopsy. This discussion focuses on analyzing the clinical characteristics of ECD in children, exploring the differential diagnosis between LCH and ECD as well as the possibility of concurrent cases, and reviewing treatment strategies for ECD based on the latest literature.

1. Clinical features of ECD in children

ECD primarily affects middle-aged and older adults (with most cases occurring between the ages of 40 and 70); it is rare in children. However, an increasing number of cases in children and adolescents have been reported in recent years, suggesting that ECD in childhood is not unheard of, though it is still often misdiagnosed or diagnosed late[7,8] Bone involvement is the most common manifestation and often the initial presentation: typical features include symmetrical sclerosis of the medullary bone or mixed bone destruction in long bones (particularly the femur and tibia), which may present with pain or radiographic abnormalities; in pediatric cases, radiographic findings are more diverse, with involvement of the craniofacial region and jawbones possible, although rare, with several reports already documented. Bone scintigraphy, X-ray, CT, MRI, and PET-CT are complementary in identifying the distribution of lesions[9,10] Children with ECD are more likely to present with central nervous system manifestations (including focal mass lesions, cerebellar and brainstem involvement, and lesions in the meningeal or pituitary regions). Common clinical symptoms include ataxia, optic nerve and ocular motor abnormalities, central diabetes insipidus, and cranial nerve deficits. Additionally, MRI often reveals enhancing lesions, as well as masses in the sella turcica or cavernous sinus[11,12] Endocrine

abnormalities are relatively common (particularly involving the hypothalamic-pituitary axis): Pituitary involvement can lead to hypothalamic/pituitary dysfunction, manifesting as impairment of the gonadal axis (low sex hormone levels), elevated prolactin, reduced growth hormone, or diabetes insipidus (excessive thirst and urination). Therefore, one should be highly vigilant when unexplained developmental delay or abnormal sexual characteristics occur in children or adolescents[11,13] Multisystem involvement: lungs, cardiovascular system, perirenal/retroperitoneal adipose tissue, pancreas, etc. ECD is a multisystem disease; in addition to bone and CNS involvement, it is characterized by pulmonary interstitial changes and small nodules, as well as retroperitoneal fibrotic changes. These manifestations may also be observed in pediatric cases[10,14] Pathological and Molecular Characteristics: Histologically, the cells appear foamy or xanthoma-like (commonly Touton giant cells); the typical immunophenotype is CD68-positive, CD1a-negative, and S100-negative or weakly positive. A significant proportion (approximately half) of cases test positive for the BRAF V600E mutation; molecular testing is crucial for diagnosis and for guiding decisions regarding targeted therapy[8,15]

Specificity of pediatric cases: ECD in children is more likely to be characterized by CNS symptoms or endocrine abnormalities than in adults, and craniofacial/maxillofacial primaries, osteolytic destruction, or space-occupying foci have been reported in a relatively high proportion of children. In addition, lesions in childhood may be more aggressive, requiring early molecular and histologic confirmation of the diagnosis in order to start targeted therapy as early as possible[7,11] The present case is a 14-year-old male, which fits the age range for ECD diagnosis in children and adolescents documented in the literature (2.5 to 15 years). Our child was 1.3m tall, developmentally backward, with unremarkable secondary sexual characteristics and low serum testosterone and growth hormone levels. This is highly consistent with neuroendocrine dysfunction (e.g., growth hormone deficiency) resulting from infiltration of the hypothalamic-pituitary axis as noted in the literature. The patient presented with positive strabismus, nystagmus, unsteady walking, and difficulty in standing with eyes closed, which is consistent with the common signs of CNS involvement (cranial nerve deficits, ataxia, and cerebellar syndromes) documented in pediatric ECD. The MRI of the cranium in this case showed multiple abnormally enhanced masses in the saddle and bilateral cavernous sinuses, which was in line with the statistical pattern of "CNS involvement is most common in the saddle and para-saddle regions (50.0%)" in the literature. In this case, the patient was characterized by "multiple bone destruction and osteosclerosis in the maxillofacial region, with the most pronounced involvement of the maxilla". Although different from the most common long bone involvement, extensive osteolysis and osteosclerosis of the maxillofacial bones (including the maxilla, mandible, and frontal bone) in children has been documented in the literature, and this case fits this atypical distribution pattern. At the molecular level, the maxillary biopsy in this case showed a diffuse infiltration of foam-like histiocytes, with immunohistochemical findings such as CD68(+), CD1a(-), and S-100(-), and the PCR test revealed a BRAF V600E mutation. The results were consistent with the typical pathologic and molecular genetic features of ECD in children established in the literature.

2. Differential diagnosis between LCH and ECD

Langerhans cell histiocytosis (LCH) is a clonal proliferative disorder originating from bone marrow precursors and differentiating towards Langerhans/dendritic cells. The lesion cells express CD1a and langerin (CD207), have morphological features of Langerhans cells (e.g., nuclear folding, nuclear grooves), and Birbeck's vesicles can be seen on electron microscopy. Clinical manifestations are diverse and may include single bone disease, skin lesions, pituitary-central neuropathy, or multi-systemic lesions. Several studies have suggested that LCH is a MAPK pathway-driven inflammatory myeloid tumor[16] Erdheim-Chester disease (ECD) belongs to the non-Langerhans histiocytosis spectrum, and its typical histology is infiltration of mature histiocytes, foamy or yellowish tumor-like cytoplasm, and fibrotic or scarring changes. The typical histology is infiltration of mature histiocytes (histiocytes) with foamy or yellowish cytoplasm, fibrosis or scarring, and multisystemic involvement is common in the skeletal, cardiovascular, perirenal, pulmonary, and cerebral/saddle regions. Current classifications place ECD and LCH in different subtypes under group L (Langerhans group). BRAF V600E mutations or other MAPK pathway gene variants are detected in most cases[10,17] Because both can have MAPK pathway-driven variants and can involve the skeleton and central nervous system, there is a possibility of overlap in actual pathologic or imaging features, and careful differentiation is needed. Table 1 summarizes the key points of difference between LCH and ECD (including immunophenotype, morphology, imaging and organ distribution, molecular features, etc.)

Project	LCH	ECD
Immunohistochemistry	CD1a(+),Langerin/CD207(+), S100 ++	CD68(+), CD1a(-), S100-- Sometimes FXIIIa(+)
Morphology	Dendritic/Langerhans-like cells, nuclear grooves, nuclear folding, less foamy changes	Foamy/yellowish tumor-like histiocytes predominate with fibrotic, scarring changes
Patterns of Bone Involvement	Focal osteolytic lesions are common (skull, jaw, metaphysis of long bones, etc.) and may be accompanied by bone pain and localized symptoms of bone lesions	Characteristic symmetric sclerosis of long bones (especially humerus, femoral stem/epiphysis region), jaws/cranium may also be involved but not typically first
Other systemic involvement	Skin, liver, spleen, lungs, and pituitary gland (urolithiasis) are more common	Prefer cardiovascular (periaortic peritoneum), perirenal/retroperitoneal fibrosis, interstitial lung changes, cerebral/saddle infiltration, etc.
Molecular mutagenesis	BRAF V600E is seen in several LCH cases (but at a lower rate than reported in some ECDs).	BRAF V600E is seen in many ECD cases; may also have downstream MAPK pathway gene variants
Prognosis	Good prognosis if focal; poor prognosis if multi-system or high- risk organ involvement	Traditionally poor prognosis (especially for cardiovascular, CNS involvement), but targeted era BRAF inhibitors significantly improve prognosis in a subset of patients

Table 1 Comparison of clinicopathological features between Langerhans cell histiocytosis (LCH) and Erdheim-Chester disease (ECD).

2.1 Immunomarker aspects

The histiocytes of LCH (Langerhans cell histiocytosis) and ECD (Erdheim-Chester disease) differ significantly in their immunophenotype. This reflects their different cellular lineages: LCH lesion cells originate from Langerhans' dendritic cells and are typically positive for CD1a and Langerin (CD207), and S-100 protein is also commonly expressed. In contrast, ECD is a non-Langerhans histiocytosis with infiltrating histiocytes showing a macrophage-like phenotype: the classical immunological hallmark is CD68 positivity, while CD1a and S-100 are negative[18]. In addition, Birbeck's granules (reticulated vesicles characteristic of Langerhans cells) were seen ultrastructurally in the cells of LCH tissues,

whereas this feature was not present in the cells of ECD lesions[19]¶Thus, immunohistochemistry makes it possible to distinguish between two types of histiocytic hyperplasia and indicate their cellular origin: Langerhans cell-like (LCH) versus macrophage-like (ECD)[20]¶This case was diagnosed by virtue of typical ataxia, saddle zone involvement, macrophage-like immunophenotype (CD68+/CD1a-/S100-) and BRAF V600E mutation testing.

2.2 In morphology and molecular biology

Histomorphologically, the characteristic cells of LCH (i.e., abnormally proliferating Langerhans cells) usually have irregular nuclear shapes, appearing as distinct nuclear grooves or nuclear folds, and have pale and slightly eosinophilic cytoplasm[19]¶The lesions are often richly infiltrated with eosinophils and other inflammatory cells, which is one of the reasons why LCH is also called “eosinophilic granuloma”[19]¶In contrast, the histiocytes of ECD show a mature macrophage-like pattern, typically with foamy, lipid-rich cytoplasm, sometimes forming Touton-type giant cells, and significant fibrotic or scar-like changes are common in the stroma of the lesion[18]¶These morphological differences, together with the immunophenotype, support the conclusion that LCH belongs to the dendritic cell lineage while ECD belongs to the macrophage lineage.

Molecularly, however, they have something in common: the vast majority of LCH and ECD cases have activating mutations in the RAS-RAF-MEK-ERK pathway. The BRAF V600E mutation is detected in about half of these cases[15]¶¶The remaining patients may have mutations in MAP2K1, KRAS, NRAS and others[18,21]¶This common molecular feature suggests that the two intersect in pathogenesis. It has been found that identical BRAF V600E mutations can be detected in different lesions in patients with LCH and ECD coexisting, which implies that the proliferation of these two types of cells may originate from the same mutation or early common precursor cells[21]¶Therefore, although immunophenotyping and histology clearly distinguish LCH from ECD, molecular evidence suggests that they belong to clonal hyperplasia under the same disease spectrum, suggesting that both phenotypic differences and common tumorigenic pathways should be taken into account when classifying them. The immunohistochemical results of the pathologic biopsy in this case showed that the histiocytes were strongly positive for CD68 and negative for CD1a and S-100 markers[18]¶This immunophenotype is highly consistent with ECD and supports a histiocytosis of non-Langerhans cell origin. In the case of LCH, there should be at least CD1a or Langerin expression[19]¶This case did not fit the immunophenotype of LCH. In this case, a diffuse foamy histiocytic infiltration with typical Touton-type multinucleated giant cells and significant focal interstitial fibrosis was observed in the pathologic biopsy, and the morphology showed mature macrophage-like features, with the absence of nucleated furrowed Langerhans' cells and large numbers of eosinophils, which are common in LCH[19]¶The combination of a strong CD68-positive, CD1a- and S-100-negative immunophenotype definitively excluded LCH, which is characterized by infiltration of nucleus pulposus histiocytes and eosinophils. The combination of the child's clinical and imaging findings, as well as the PCR-confirmed BRAF V600E mutation, favored the diagnosis of Erdheim-Chester disease, and ultimately, the combination of endocrine defects and central nervous system imaging findings, which were highly consistent with childhood ECD, ruled out LCH with a

similar clinical presentation, suggesting that the histiocyte profile was attributable to a non-Langerhans cell-type clonal hyperplasia. clonal hyperplasia. Erdheim-Chester disease.

3. Treatment and prognosis

3.1 Overview of treatment principles

Erdheim-Chester disease (ECD) is a rare multisystemic histiocytic proliferative disorder. Recent advances in molecular biology have revealed the presence of MAPK/ERK pathway-driven mutations in a large number of cases (especially BRAF V600E), which has led to a shift in treatment strategy from empirical conventional chemotherapy to individualized therapy based on molecular targets. The latest international consensus suggests that most patients require systemic therapy at the time of diagnosis, except for asymptomatic, non-vital organ solitary lesions that can be observed[13,22]

3.2 Medication options

3.2.1 BRAF inhibitor

BRAF inhibitors (darafenib) have become the preferred or prioritized systemic therapy for patients with detectable BRAF V600E, with multiple studies and case series demonstrating significant clinical efficacy and improved organ function. Long-term follow-up studies and multicenter reviews have demonstrated durable responses with BRAF inhibitors, but attention should be paid to the management of toxicities (e.g., skin reactions, photosensitization, joint or muscle pain, and liver function abnormalities)[23,24] When CNS involvement is present, the literature suggests that darafenib may have advantages in intracerebral distribution and treatment of CNS lesions, and that combining it with an MEK inhibitor (e.g., trametinib) enhances efficacy and reduces the risk of resistance and side effects (cardiac, dermal, and endocrine toxicity are concerns with the combination). Therefore, darafenib is often preferred in cases with extensive CNS involvement. Significant efficacy of darafenib has also been reported in pediatric cases[25]

3.2.2 MEK inhibitor

In patients who are BRAF-negative but have downstream MAPK pathway mutations (e.g., MAP2K/MAPK, etc.), MEK inhibitors (trametinib) are used for targeted therapy or in combination with other agents. MEK inhibitors have also shown efficacy in some BRAF mutation-negative cases[26,27]

3.2.3 Traditional therapy

Prior to the popularity of molecularly targeted drugs, interferon-alpha (IFN-alpha) was a common first-line treatment for ECD and was used for long-term control of the disease in some patients, but it has limited efficacy in patients with multiorgan critically ill disease and is more problematic to tolerate. Chemotherapeutic agents, immunosuppressants, or anti-inflammatory drugs (IL-1) can be used as

alternatives when other treatments are not available. Overall, targeted therapies have significantly improved the prognosis of patients with gene-driven mutations, making them the first choice for[27,28]

3.3 Treatment of this case

In this case, BRAF V600E-positive with significant CNS (saddle region, cavernous sinus, cerebellar vermis and cerebellar atrophy) and multisystemic involvement, systemic therapy based on BRAF inhibitors is preferred according to the international consensus and a large number of case reports. The use of dabrafenib in this case in combination with trametinib is in line with current practice and clinical trials, which often prioritize dabrafenib, especially in the setting of CNS involvement or the need for better brain penetration. Literature and case reports have shown that dabrafenib in combination with trametinib or dabrafenib alone can lead to significant clinical improvement in pediatric and adult ECD cases with CNS involvement[29,30] After 10 months of treatment with dabrafenib in combination with trametinib, MRIs of the patient showed a significant reduction in the size of the abnormally enhancing lesions in the saddle region and bilateral cerebellar tegmentum, a reduction in meningeal thickening, and a reduction in the size of the pulmonary nodules, suggesting that this regimen produced a significant efficacy on the central system lesions and the pulmonary lesions; the overall efficacy is consistent with the efficacy of BRAF/MEK inhibitors in multi-system ECDs as reported in the literature[27,29]

3.4 Prognostic influences and overall prognostic trends

Traditionally, the prognosis of ECD is considered to be poor, and the mortality rate is particularly high in patients with cardiac, macrovascular, or CNS involvement. However, in the last decade, since the advent of targeted therapy, BRAF/MEK inhibitors have significantly improved the survival and quality of life of some BRAF V600E-positive patients, and several long-term follow-up studies have shown that patients receiving BRAF inhibitors have a longer period of disease control. Overall, the prognosis of BRAF V600E-positive patients who are able to receive targeted therapies has improved significantly. The treatment of ECD has fundamentally changed in the era of molecular targeting: BRAF inhibitors in combination with MEK inhibitors (trametinib, etc.) are the first choice for BRAF V600E-positive patients with symptomatic or vital organ involvement, significantly improving clinical symptoms and altering the prognosis of patients. Conventional therapies (IFN- α , etc.) are still used in some cases or as alternative treatments. Successful individual cases have been reported in pediatric cases despite limited information, and the present case of dabrafenib combined with trametinib achieved significant imaging improvement after 10 months of treatment, which is in line with current evidence-based and empirically supported strategies. Long-term follow-up and multidisciplinary management are essential to maintain efficacy and manage toxicity[13,23,29].

Abbreviations

Abbreviation	Full term
ECD	Erdheim-Chester disease
CNS	Central nervous system
CT	Computed tomography
MRI	Magnetic resonance imaging
PCR	Polymerase chain reaction
BRAF	B-Raf proto-oncogene, serine/threonine kinase
MEK	Mitogen-activated protein kinase kinase
CD68	Cluster of differentiation 68
CD1a	Cluster of differentiation 1a
LCH	Langerhans cell histiocytosis
BMI	Body mass index
FDG PET/CT	Fluorodeoxyglucose positron emission tomography/computed tomography

Declarations

Dual Publication

Some portion of the results/data/figures in this manuscript have been published or are under consideration for publication elsewhere. The present manuscript reports the same patient who was previously described in a Chinese-language case report [6]. The previous publication and the present manuscript concern the same underlying clinical case; therefore, some clinical information, diagnostic findings, imaging findings, pathological findings, and treatment history may overlap. The previous publication has been fully acknowledged and cited in the present manuscript. The present manuscript is submitted with transparent disclosure of the previous report, and no previously published material has been presented as new without appropriate acknowledgment. We leave the assessment of any potential overlap to the Editor.

Third Party Material

All of the material is owned by the authors and/or no permissions are required.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of The Second Hospital of Hebei Medical University. Written informed consent to participate and for publication of this case report and the accompanying images was obtained from the patient's parent/legal guardian. All procedures performed in this study

were conducted in accordance with the ethical standards of the institutional research committee and with the Declaration of Helsinki and its later amendments.

Trial registration

Clinical trial number: Not applicable.

Consent for publication

Written informed consent for publication of this case report and the accompanying images was obtained from the patient's parent/legal guardian.

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Competing interests

No, I declare that the authors have no competing interests as defined by Discover, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

Author contributions

MD wrote the original draft of the manuscript, reviewed and edited the manuscript, and conducted the literature review. HD performed data analysis and interpretation. DL was responsible for data curation and clinical data collection. MN conducted the literature review and data interpretation. JW was responsible for clinical data collection and data interpretation. YL was responsible for clinical data collection, supervision, and critical revision of the manuscript. XL was responsible for clinical data collection, study coordination, supervision, and critical revision of the manuscript. All authors read and approved the final manuscript.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data are not publicly available due to ethical restrictions and patient privacy concerns.

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Figures

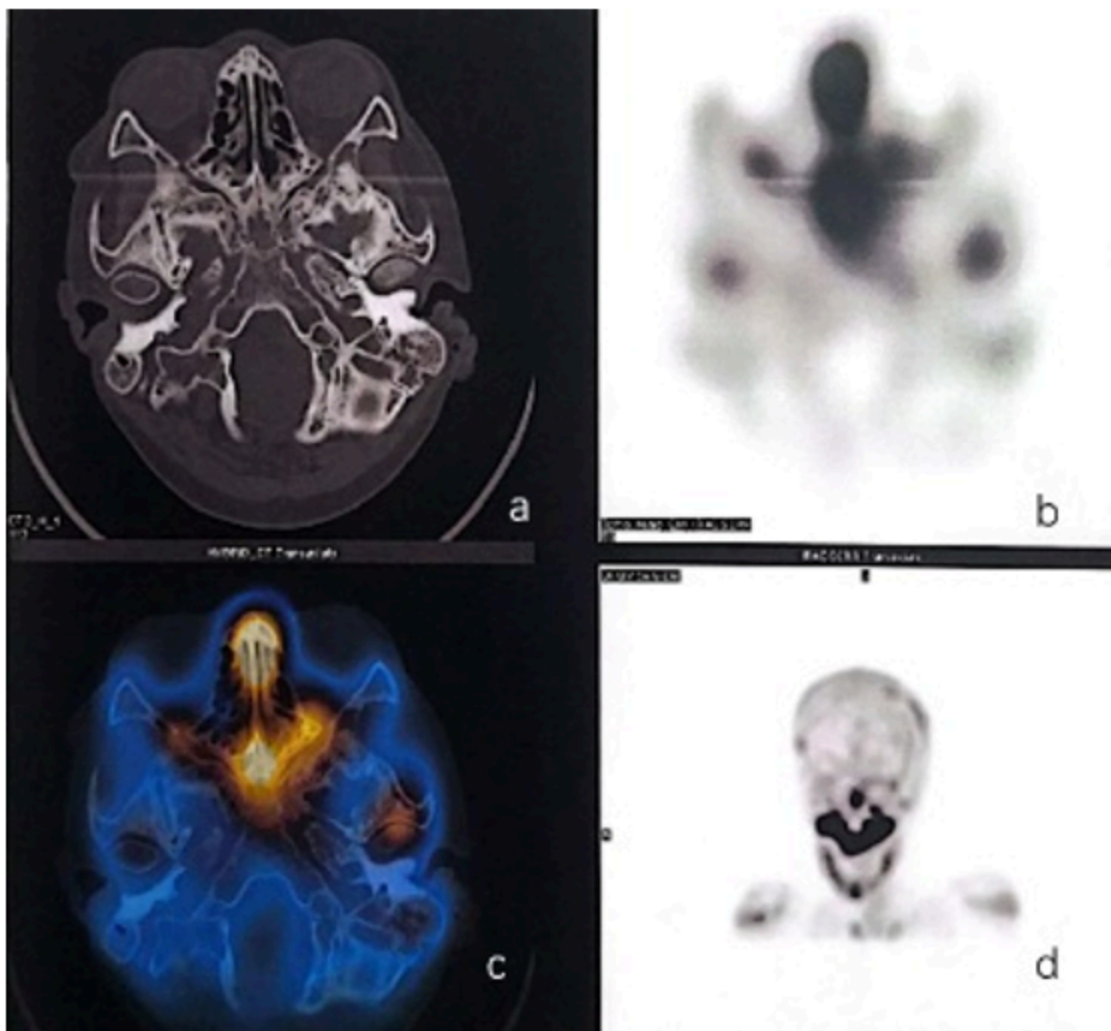


Figure 1

Cranial MRI shows multiple abnormally enhanced masses within the sella turcica, bilateral cavernous sinuses, and bilateral tentorium cerebelli, accompanied by diffuse cerebellar atrophy



Figure 2

Axial CT scan of the maxillofacial region in bone window mode shows widespread bone abnormalities in the maxilla, zygomatic bones, and skull base, characterized by coexisting bone destruction and sclerosis. The maxilla is most significantly affected, with disorganized trabecular bone structure and localized patchy areas of high density, suggesting abnormal bone metabolism and an infiltrative lesion.

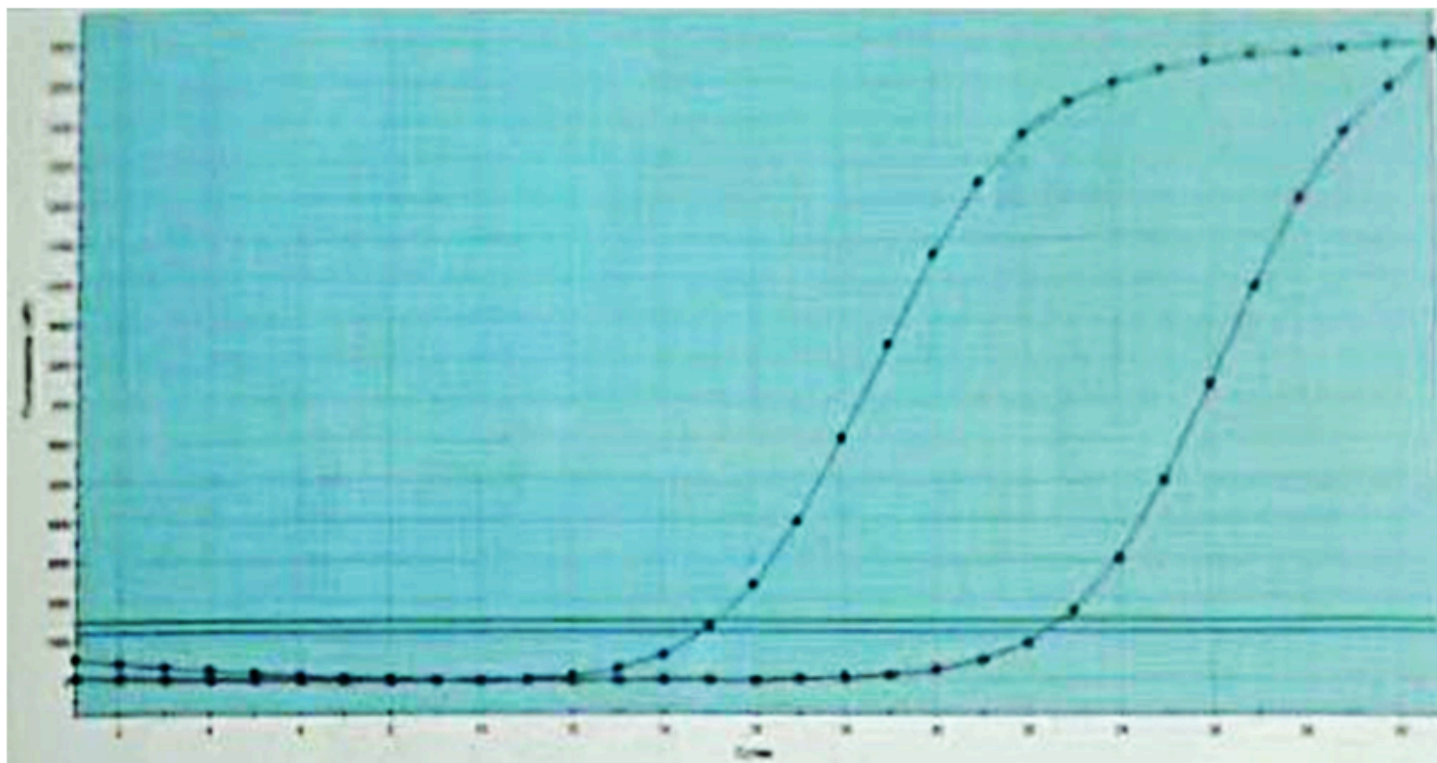


Figure 3

PCR results show a typical S-shaped amplification curve in the mutant lane, whereas the wild-type lane exhibits delayed amplification or no significant amplification, suggesting a positive BRAF V600E mutation.

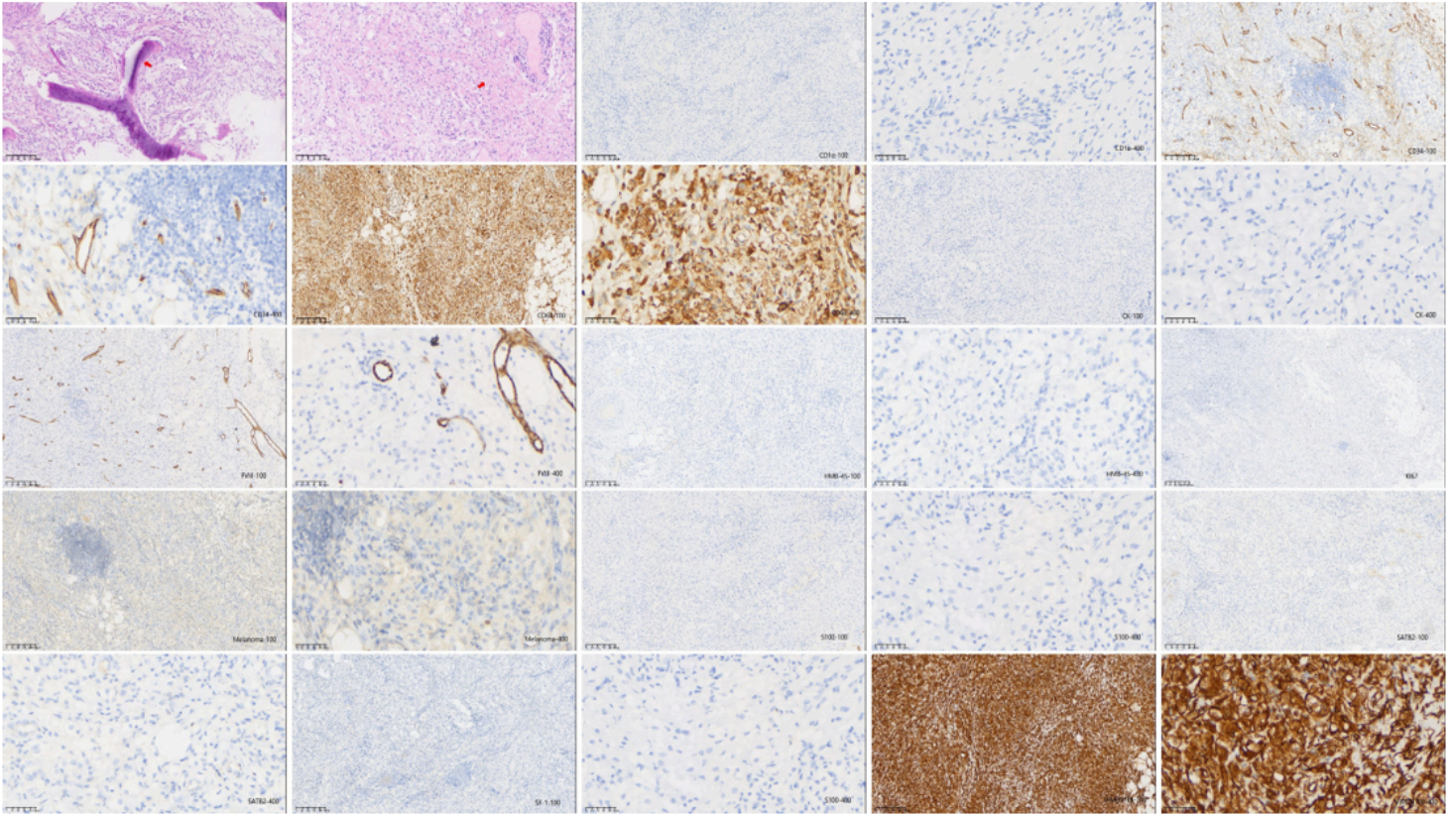


Figure 4

HE staining of the maxillary lesion tissue reveals diffuse infiltration of numerous foamy histiocytes (indicated by white arrows) against a fibrous stroma background (indicated by red arrows), a morphology consistent with a histiocytic proliferative lesion. Immunohistochemical results showed: histiocyte markers CD68 (+), Vimentin (+), and a Ki-67 proliferation index of approximately 3%; Langerhans cell-associated markers CD1a (-) and S-100 (-); epithelial markers CKpan, vascular endothelial markers CD34 (-) and FVIII-R-Ag (-), melanocyte-associated markers HMB45 (-) and Melan-A (-), osteogenic marker SATB2 (-), and endocrine-associated marker SF-1 (-). These findings support the diagnosis of a non-Langerhans cell histiocytic proliferative disorder.