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# Rare clival localization of an eosinophilic granuloma: illustrative case

Martin E. Weidemeier, MD,[1] Steffen Fleck, MD, PhD,[1] Werner Hosemann, MD, PhD,[2] Silke Vogelgesang, MD, PhD,[3] Karoline Ehlert, MD, PhD,[4] Holger N. Lode, MD, PhD,[4] and Henry W. S. Schroeder, MD, PhD[1]

Departments of [1]Neurosurgery, [2]Otolaryngology, Head & Neck Surgery, and [4]Pediatric Oncology and Hematology, University Medicine Greifswald, Greifswald, Germany; and [3]Institute of Pathology, University Medicine Greifswald, Germany

**BACKGROUND** Eosinophilic granuloma (EG) belongs to the family of Langerhans cell histiocytosis (LCH) and is considered to be a benign disease typically found in children younger than 15 years of age. Here, the authors describe an EG of unusual localization and clinical presentation.

**OBSERVATIONS** The authors report a 9-year-old girl with an EG presenting as an osteolytic lesion of the clivus. After transsphenoidal resection and histological confirmation, adjuvant chemotherapy was initiated. Presenting signs and symptoms were weight loss, episodic grimacing, and moderate ballism-like movements. After a follow-up-period of 32 months, the patient presented with a total resolution of initial symptoms and no further tumor growth.

**LESSONS** Although these lesions are rare, one should consider EG as a differential diagnosis when confronted with osteolytic lesions of the clivus.

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**KEYWORDS** eosinophilic granuloma; cranial; pediatric; neurosurgical treatment; oncology; radiotherapy

Eosinophilic granuloma (EG) belongs to the family of Langerhans cell histiocytosis (LCH) and was described in the 19th century.[1,2] The cause of the disease is still unclear. EG is considered a benign disease that is limited to lung or bone and is typically found in children younger than 15 years of age.[3] We describe an eosinophilic granuloma of unusual localization and clinical presentation. Histopathological workup led to the diagnosis of EG.

## Illustrative Case

### History

A 9-year-old girl presented initially at an outside hospital because of a 3-week course of fatigue and weight loss (3 kg). The parents had noticed new-onset listlessness, grimacing, squinting of the eyes, and sudden elevation of both arms above the head. Other symptoms included evening headaches of unspecific localization and sleep disturbances with moaning and crying. Signs of infection and night sweats were denied. Interestingly, an impaired range of movement at head turns was noticeable, making the patient turn the upper body when the head needed to be rotated. The patient's previous history was uneventful with regular physical and mental development and good grades in school.

### Investigations

Initial magnetic resonance imaging (MRI) showed a space-occupying lesion within the petrous bone and clivus that later was specified as a contrast-enhancing and diffusion-restricted lesion reaching from the apex of the left petrous bone to the clivus and left occipital condyle with close contact to the carotid artery and jugular vein (Fig. 1A–E). Additionally, computed tomography (CT) scanning showed a destructive osteolytic growth pattern, thus suspicious for a chordoma (Fig. 1F–J). However, quite unusual was the obvious infiltration of the surrounding parapharyngeal muscles, which is not observed in chordomas. Full-body MRI showed no further skeletal lesions. A single photon emission computed tomography (SPECT; $^{99}$ $^{m}$Tc/TECEOS) revealed an area of slightly elevated bone metabolism at the left skull base corresponding to the lesion along the physiologically bilateral enhancement at the epiphyseal plates. Subsequent workup, including electrocardiography, electroencephalography, ultrasound of the abdomen, extensive blood tests, lung function, and endocrinological testing was unremarkable except for an elevated neuron-specific enolase level (23 ng/mL).

**ABBREVIATIONS** CT = computed tomography; EG = eosinophilic granuloma; LCH = Langerhans cell histiocytosis; MRI = magnetic resonance imaging; SPECT = single photon emission computed tomography.

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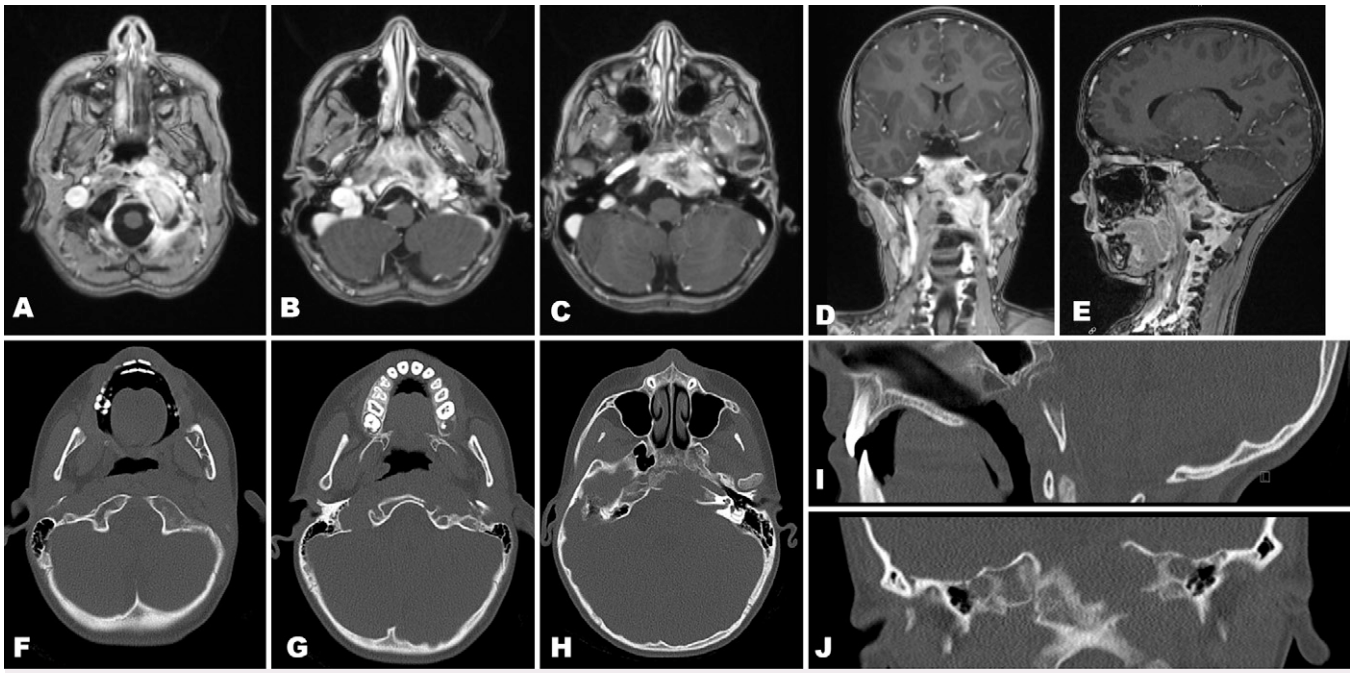


**FIG. 1.** Preoperative axial (**A–C**), coronal (**D**), and sagittal (**E**) contrast-enhanced T1-weighted MRI showing an enhancing lesion involving the left petrous bone and clivus. Note the infiltration of the adjacent muscles. Preoperative axial (**F–H**), sagittal (**I**), and coronal (**J**) CT scans showing an osteolytic lesion involving the left petrous and clival bone.

## Surgery

The patient was referred to our hospital for surgery. In collaboration with our ear, nose, and throat department, we were able to achieve near-total resection of the bony part of the lesion via an endoscopic endonasal approach (Fig. 2). The infiltrated muscles were not resected. To achieve this, we used navigation guidance, neuromonitoring of the lower cranial nerve group, and Doppler ultrasound. Resection was performed using sharp curettage dissection. A high-speed drill was applied to remove the adjacent bone. For closure, we used periumbilical subcutaneous fat tissue and covered the situs with a nasoseptal flap that was crafted at the beginning of the procedure along with a reverse flap.

## Postoperative Course

The postoperative course was uneventful, with no signs of cerebrospinal fluid leak or infection and regular wound healing. Histopathological workup of the frozen section was initially inconclusive, not ruling out a chordoma. The final histopathology with immunohistochemical staining revealed intense expression of CD1a and a Ki-67 index of 10% (Fig. 3). No reaction to the antibody clone HMB45 was noted, and next to the tumor cells $CD3^+$ T-lymphocytes and a few $CD20^+$ B-lymphocytes were seen in the specimen. Concluding the histopathological workup, an osseus LCH in the form of an EG was diagnosed.

Considering its localization and extent of resection (Fig. 4), adjuvant 6-week therapy was recommended according to the LCH-REG-DE-2013 protocol (German registry for LCH in childhood), with vinblastine (6 mg/$m^2$ intravenous) and prednisone (20 mg twice a day by mouth) given and started 9 days after surgery. Further management was continued by the referring outside hospital, where the patient received two sets of a 4-week intensified chemotherapy regimen followed by 3 months of maintenance therapy according to the LCH-REG-DE-2013 protocol. Full-body MRI 13 months after neurosurgical resection showed no signs of intracranial recurrence and no other manifestations that could typically be expected in cases of LCH. Our patient has maintained a very good clinical condition during outpatient care within the follow-up period of

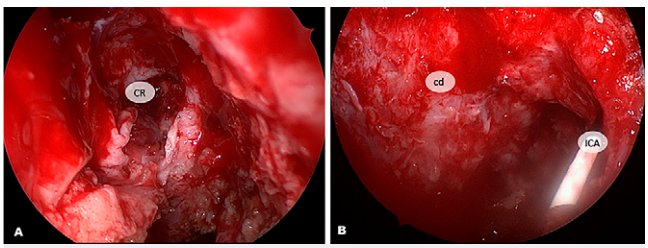


**FIG. 2.** Endoscopic views via a transsphenoidal approach of the surgical field. **A:** Exposure of the clival recess (CR) after creating a nasoseptal and reverse flap. **B:** After tumor resection, the clival dura (cd) was exposed and the petrous internal carotid artery (ICA) was detected via Doppler.

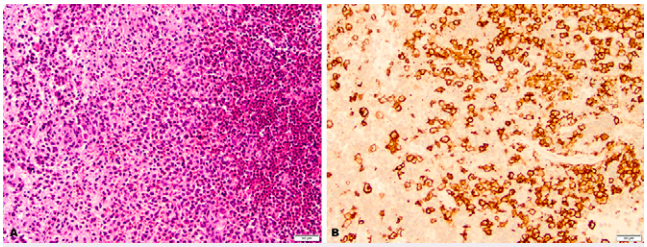


**FIG. 3. A:** Hematoxylin and eosin stain showing the high presence of small lymphocytes almost masking the presence of Langerhans cells. **B:** Immunohistochemical CD1a staining. Note the typical high CD1a positivity of Langerhans cells, unlike usual macrophages and histiocytes.

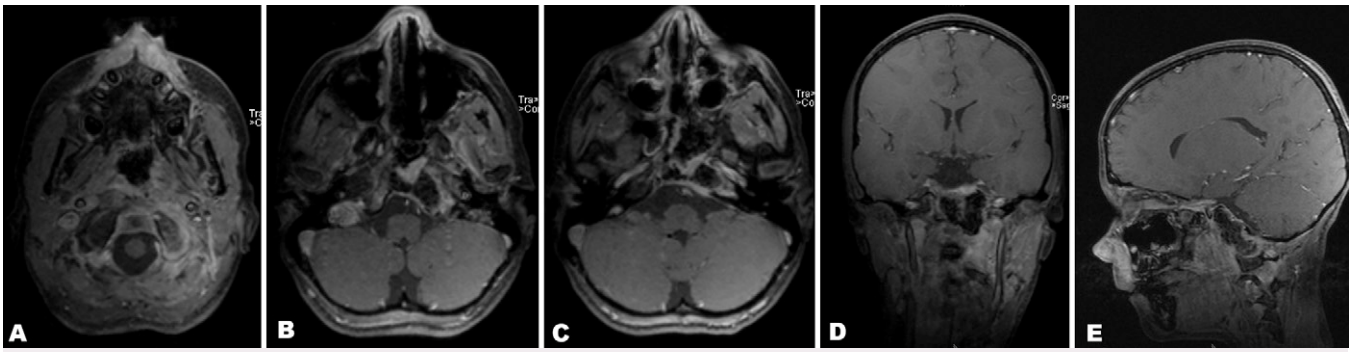


**FIG. 4.** Axial (**A–C**), coronal (**D**), and sagittal (**E**) contrast-enhanced T1-weighted MRI with fat saturation performed 1 day after surgery, showing near total tumor resection of the bony tumor part.

32 months. Follow-up MRI revealed no tumor recurrence and no further bony lesions (Fig. 5). The unusual initial symptoms resolved completely after surgery, and she returned to school, receiving grades above average.

## Discussion

We present a very rare localization of an EG affecting the clivus with atypical symptoms. To our knowledge, there have been nine cases reported prior to this case with involvement of the clivus since 1992, emphasizing this as a rare localization of an EG.[4–11] Therapeutic strategies differed as follows. Five patients had undergone biopsy followed by adjuvant therapy.[4,6–8,11] Adjuvant chemotherapy was administered in two patients,[8,11] a combination of adjuvant chemotherapy and radiotherapy was provided in two other patients,[4,7] and one patient was handled strictly conservatively without adjuvant treatment after biopsy.[6] No specific treatment information was given in two cases.[9] In only two previous reports, surgical excision of the mass was part of the therapy,[5,10] with one case receiving adjuvant radiotherapy due to subtotal resection.[10] All cases reported on the clinical improvement of their patients and resolution of the masses on follow-up imaging.

### Observations

In previous reports, most patients presented with cranial nerve function affected, almost exclusively the abducens nerve.[4–7,9,10] One of the patients had multiple cranial nerve palsies.[8]

Our case, however, did not present with any cranial nerve palsy but instead with unspecific weight loss and fatigue, leading to medical investigations. Interestingly, our patient presented with head turning, grimacing, and arm lifting that were initially suspicious for a focal hyperexcitability that was eventually ruled out by electroencephalography. We did not find any organic cause responsible for these ballism-like movements, and they were not reported again after surgery and in the course of adjuvant therapy.

Previous reports often described biopsy and nonsurgical therapy in patients. Some patients, including ours, underwent an extended surgical procedure with subtotal resection. Additionally, adjuvant chemotherapy was administered. Furthermore, in view of the literature, we present the longest follow-up (32 months) so far. Follow-up studies showed no recurrent growth.

### Lessons

An EG located in the clivus is rare, with only nine previously published reports within the last 30 years. Biopsy, or if the lesion is easily accessible, subtotal resection followed by a chemotherapeutic regimen (in our case, according to the LCH-REG-DE-2013 protocol) is the standard of care.

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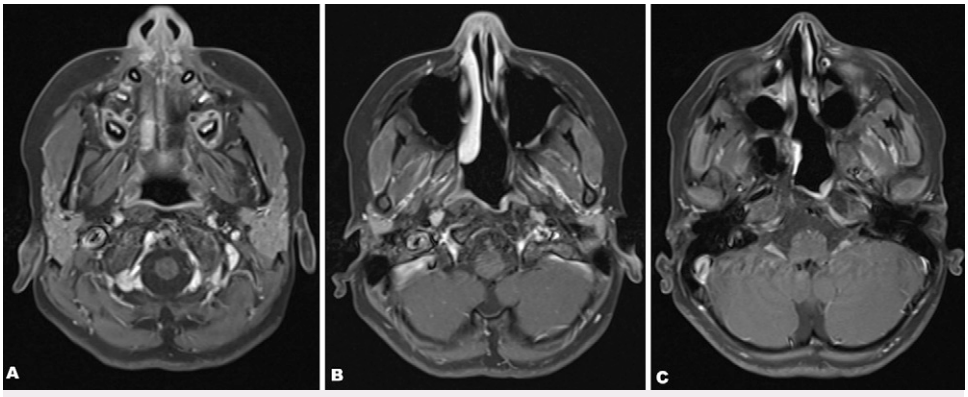


**FIG. 5. A–C:** Axial contrast-enhanced T1-weighted MRI performed 32 months after surgery and chemotherapy, showing complete remission of the lesion.

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### Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

### Author Contributions

Conception and design: Weidemeier, Fleck, Hosemann, Lode, Schroeder. Acquisition of data: Weidemeier, Fleck, Hosemann, Vogelgesang, Ehlert, Schroeder. Analysis and interpretation of data: Weidemeier, Fleck, Ehlert, Lode. Drafting the article: Weidemeier. Critically revising the article: Weidemeier, Fleck, Vogelgesang, Schroeder. Reviewed submitted version of manuscript: Fleck, Ehlert, Lode, Schroeder. Approved the final version of the manuscript on behalf of all authors: Weidemeier. Administrative/technical/material support: Weidemeier, Hosemann. Study supervision: Schroeder.

### Correspondence


Martin E. Weidemeier: University Medicine Greifswald, Germany. martin.weidemeier@med.uni-greifswald.de.