Case Report

Pediatric giant cell reparative granuloma of the lower clivus: A case report and review of the literature

ABSTRACT

Giant cell reparative granuloma (GCRG) is a benign nonneoplastic granulomatous lesion and is rare in the cranial bone. We present a pediatric case of this lesion arising from the condyle and lower clivus. A 9-year-old girl presented with slowly progressive hoarseness and dysphagia. She showed left glossopharyngeal, vagus, and hypoglossal nerve palsy. An osteolytic lesion around the lower clivus and condyle joint was accompanied by deformation of the craniovertebral junction. An endoscopic endonasal approach was used to decompress the cranial nerve and confirm the pathological finding. The lesion around the condyle was not resected to preserve occipito-cervical stability. The residual lesion has been observed carefully for 6 months, and regrowth has not occurred. GCRG is a rare granulomatous lesion in the cranial bone. This case is the first report of a pediatric clival GCRG. Treating pediatric GCRG may be helpful.

Keywords: Giant cell reparative granuloma, lower clivus, pediatric case

INTRODUCTION

Giant cell reparative granuloma (GCRG) is a benign nonneoplastic granulomatous lesion that arises most commonly in the maxilla and mandible in children and young adults.[1,2] The term "giant cell reparative granuloma" was introduced by Jaffe in 1953 to describe a lesion that occurred following a trauma that caused an intraosseous hemorrhage.[3] Distinguishing GCRGs from other osteolytic bone lesion tumors, such as brown tumors, aneurysmal bone cysts, and true giant cell tumors (GCTs), is difficult. However, GCRGs are distinct from these lesions, which are true neoplasms.[3] Few cases of pediatric GCRGs that occurred in the cranial bone have been reported.[4-13]

We describe a rare pediatric case of GCRG treated with surgical resection via an endoscopic endonasal approach for a lower clival lesion. We discuss the etiology, clinical course, radiological findings, and management. We also review cases of pediatric GCRG that have been reported in the literature. To our knowledge, infiltration of the craniovertebral junction by a clival bone GCRG has not been previously described in the literature.

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CASE REPORT

A previously healthy 9-year-old girl presented with a 1-year history of slowly progressive hoarseness and dysphagia. She had no significant history of trauma. The patient denied any neck pain or headache upon presentation to our hospital. Neurological examination revealed left glossopharyngeal, vagus, and hypopharyngeal nerve palsy. Her laboratory data were normal, showing no abnormalities of calcium metabolism or hormones.

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Imaging findings revealed a large mass that occupied the clivus. Computed tomography (CT) revealed a calcification of mass lesion with osteolytic changes in the clivus [Figure 1a-c]. The lesion extended from the condyle to the sella turcica. Bilateral condyles were invaded by the lesion and had slightly collapsed. The margin of the lateral side was the medial side of the bilateral internal carotid arteries. The mass also involved the left jugular foramen and hypoglossal canal. Magnetic resonance imaging showed that the lesion had relatively low intensity in both T1- and T2-weighted images and was heterogeneously enhanced by gadolinium [Figure 2a-c]. A heavy T2-weighted image revealed that the left glossopharyngeal nerve, vagus nerve, and hypoglossal nerve were encased by the mass. A whole-body CT scan and positron emission tomography revealed no other lesions.

An endoscopic endonasal transclival approach was performed to confirm the pathological finding and to decompress the left lower cranial nerves. Intraoperatively, the lesion was hemorrhagic and white-yellow in color, and consisted of relatively soft tissue [Figure 3a]. Some hard calcifications were present in the lesion as well. The lateral side of the lesion was resected until the C5 portion of the medial side of the internal carotid artery was exposed [Figure 3b]. The upper side of the lesion was resected until normal dura and bone were exposed [Figure 3c]. On the left inferior lateral side, the left hypoglossal canal was opened [Figure 3d]. The lesion around the condyle was not resected to preserve occipito-cervical stability. Transient bilateral abducens nerve palsy newly appeared and disappeared within 3 months. No other complications such as cerebrospinal fluid leak or meningitis occurred. Postoperative imaging findings showed that the lesion was resected between the dorsum sellae and lower clivus without the condyle joint [Figure 4]. Over the last 6 months without other treatment, the residual lesion has not regrown. The deformation of the craniovertebral junction has not changed compared to preoperative findings.

The pathological findings demonstrated an area of calcification with abundant spindle-shaped fibroblasts and multinucleated giant cells. Some focal hemorrhage was present that was surrounded by osteoclast giant cells and inflammatory cell infiltration including neutrophils. No atypical mitotic figures and no mononucleated tumor cells were observed. In addition, immunohistochemical staining revealed that both H3.3G34W and K36M were negative. The final diagnosis was a GCRG [Figure 5].

DISCUSSION

GCRG is a benign nonneoplastic granulomatous lesion of the bone that often occurs in the maxilla and mandible.[1,2] Other

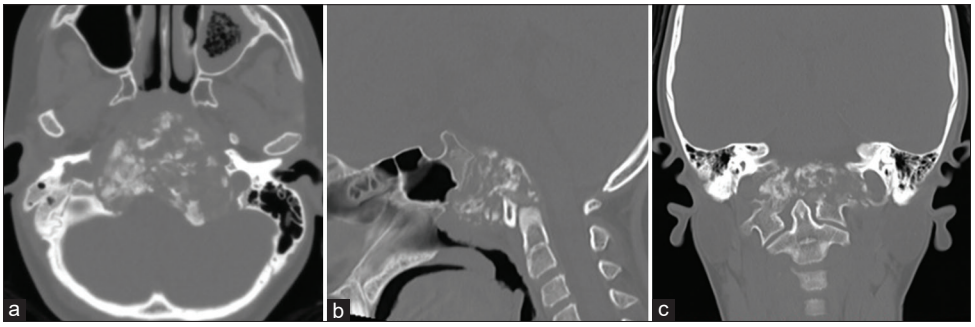

Figure 1: Computed tomography images of the illustrative case. (a-c) Preoperative nonenhanced bony computed tomography revealing calcification including an osteolytic lesion. Coronal view revealing a lytic lesion that occupied the condyle and C1 lateral mass. Sagittal view showing the lytic lesion which extends to the upper clivus

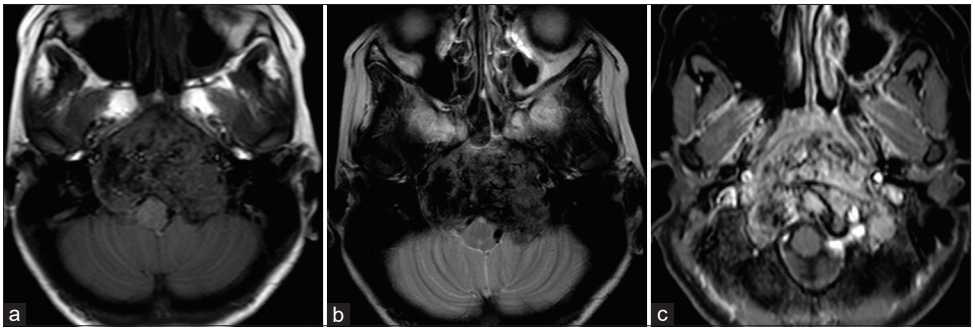

Figure 2: Preoperative magnetic resonance images revealing that the lesion had low intensity on T1- and T2-weighted images. The lesion is enhanced heterogeneously by gadolinium administration. (a) T1-weighted image, (b) T2-weighted image, (c) gadolinium-enhanced image

sites described in the literature include the hands and feet, axial skeleton, long bones, facial bones, sphenoid, ethmoid bones, orbit, nose, and cranial vault.[1,2,7,9,14] The first case in the clivus was reported in 2012.[14] This entity occurs most commonly in children or young adults with no clear gender predilection.[6,15,16] It is a locally aggressive lesion. However, no report of metastasis or malignant transformation has been published, unlike GCTs which are true neoplasms.[7,17] In our case, the osteolytic lesion was located around the lower clivus and condyle joint and was accompanied by deformation of the craniovertebral junction. It rarely affects patients under the age of 10 years.[5,8,10,11] To our knowledge, this is the first case of a pediatric GCRG that originated from the lower clivus. Table 1 shows a summary of reported pediatric GCRG cases in the cranium.[4-13]

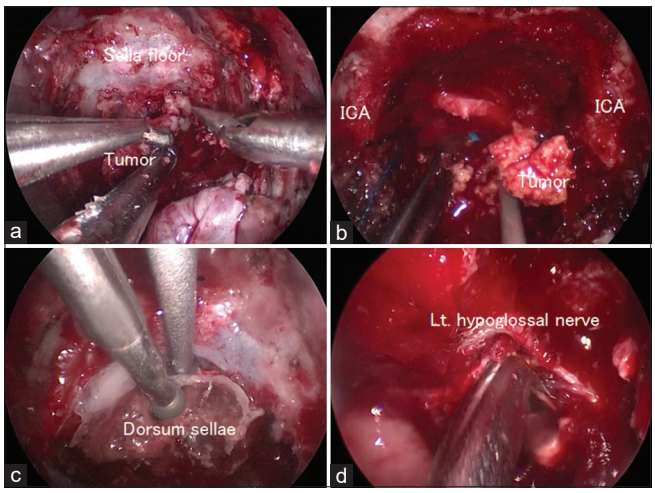

Figure 3: Intraoperative photographs of the illustrative case. An endoscopic endonasal transclival approach is performed to confirm the pathological finding and to decompress the left lower cranial nerves. (a) The lesion below the sellae turcica is exposed. The lesion is hemorrhagic and white-yellow in color, and consists of relatively soft tissue. (b) The lateral side of the lesion is resected until the bilateral internal carotid arteries are exposed. (c) The upper side of the lesion near the dorsum sellae is drilled out. (d) Near the left lateral side of the lesion, the left hypoglossal canal is opened

Imaging findings and pathological findings of the GCRG reflect reactive lytic changes. However, these findings are nonspecific, and distinguishing GCRG from other osteolytic bone lesion tumors, such as brown tumors, aneurysmal bone cysts, and true GCTs, is difficult.[8,14] CT often reveals lytic areas, and magnetic resonance imaging reveals an area with low to iso-intensity on T1- and T2-weighted images. Contrast-enhanced imaging shows that the lesion can be variable and sometimes has a highly vascular state. Histologically, GCRGs are characterized by abundant spindle-shaped fibroblastic cells and multinucleated giant cells surrounding focal areas of the hemorrhage.[6,8,18] Hemosiderin deposits and osteoid formation have also been

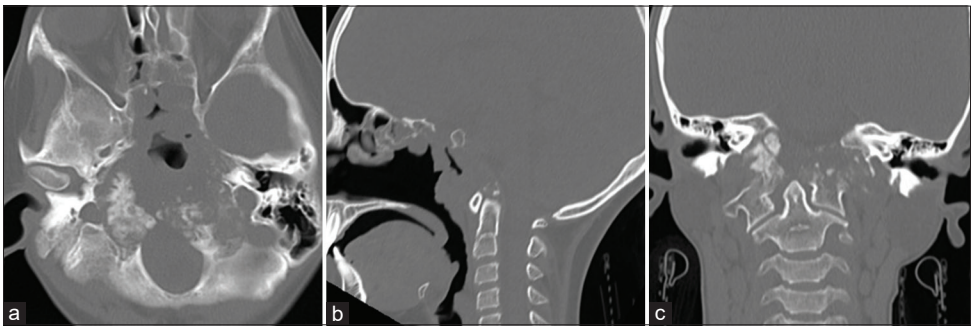

Figure 4: Postoperative nonenhanced bony computed tomography images of the illustrative case: (a-c) The lesion is resected between the dorsum sellae and lower clivus without the condyle joint

Table 1: Summary of reported pediatric giant cell reparative granuloma cases in the cranium

Author(s)	Age/sex	Trauma	Location	Therapy	Follow-up
Coloclasure *et al*., 1981[4]	10/male	N/A	Temporal bone	Total resection	Well at 6 years
Maruno *et al*., 1997[5]	3/female	No	Temporal bone	Total resection	Recurrence at 1 year
Gupta and Agrawal, 1999[13]	15/female	No	Maxilla	Partial resection	Recurrence at 6 months
Sharma *et al*., 2002[6]	12/male	Yes	Temporal bone	Total resection	Well at 10 months
Boodeker *et al*., 2003[7]	17/female	No	Temporal bone	Total resection	Well at 2 years
Magu *et al*., 2003[12]	12/female	No	Parapharyngeal	Biopsy + radiation	N/A
Morris *et al*., 2004[11]	7/female	No	Nasal cavity	Total resection	Well at 6 months
Ruiz *et al*., 2007[10]	6/male	Yes	Mandible	Total resection	Well at 2 years
Moser *et al*., 2008[9]	15/female	No	Temporal bone	Total resection	N/A
Conley *et al*., 2014[8]	3/female	No	Temporal bone	Total resection	Well at 1 year
Present case	9/female	No	Lower clivus	Subtotal resection	Well at 6 months

N/A - Not available

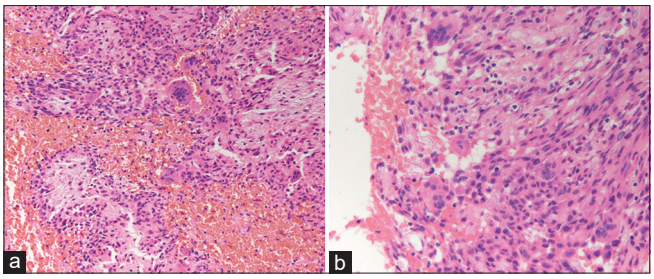

Figure 5: Pathological findings (H and E): (a) Multinucleated giant cells surrounding the focal hemorrhage are seen. (×100) (b) Abundant spindle-shaped fibroblast cells and multinucleated giant cells are present (×200)

described. Distinguishing GCRGs from GCTs is important. GCRGs are locally aggressive lesions. The differences between GCRGs and GCTs are the origin and mitotic activity. The origin of GCRGs is periosteal connective tissue. On the other hand, GCTs arise from the connective tissue of the bone marrow.[1] GCTs have higher mitotic activity and lack hemorrhages and hemosiderin deposits. Immunohistochemical staining is also effective to distinguish a GCRG from a GCT.[14] Histone H3.3G34W is highly specific for GCTs.[19] Chondroblastoma could be also considered due to its features of hemosiderin pigment, scattered giant cells, and calcification. Chondroblastoma is also ruled out by immunohistochemical staining for histone H3K36M, which is highly specific for chondroblastoma.[19]

The etiology of GCRGs is unclear, although the most commonly accepted theory is a reactive response to an intraosseous hemorrhage, a periosteal reaction, and subsequent osteolysis secondary to either trauma or chronic inflammation.[4,20]

The first treatment of choice is complete surgical resection. Recurrence rates after total resection are 10%–20%.[7,16,21] On the other hand, the recurrence rate following incomplete resection by simple curettage is 50%.[7,22] In the cases in which complete resection is not possible, postoperative radiation is recommended.[7,17,21,23] One report indicated that the radiation dose should vary according to the patient's age and the structure of the lesion.[7]

Regarding the present case, we suspect that chronic minor instability of the condyle joint caused the granulomatous lesion. A CT scan revealed that the condyle was occupied by the lesion and had slightly collapsed. The instability of the condyle may have caused the granulomatous lesion. Alternatively, the instability of the condyle may not have caused the invasion. According to this hypothesis, occipito-cervical fixation can be effective for preventing the progression of granulomatous changes. However, at this time, fixing the undeveloped cervical bone would have been difficult because the patient was only 9 years old. We consider occipito-cervical fixation to be safe in the cases in which the patient is aged above 15 years. Postoperative radiation therapy has not been performed and may carry the potential risk of sarcomatous transformation in the decades to come.[7,17] We were concerned that complications from radiation therapy would occur in this young patient. If the residual lesion regrows, we may consider performing further radical resection including occipito-condyle fixation and additional radiation therapy.

CONCLUSION

We describe a rare pediatric case of a GCRG that developed in the lower clivus involving the condyle. In this case, chronic minor instability of the condyle may have caused the granulomatous reaction. The clinical course of this case will be helpful to establish the treatment for GCRGs that arise at the lower clivus.

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Conflicts of interest
There are no conflicts of interest.

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