

A case of generalized lymphatic anomaly causing skull-base leakage and bacterial meningitis

Abstract

Generalized lymphatic anomaly (GLA) is a multifocal lymphatic malformation that affects the skin, thoracic viscera, and bones. A 7-year-old boy presented with fever and disturbance of consciousness, and bacterial meningitis was diagnosed. Computed tomography and magnetic resonance imaging revealed middle skull-base leakage due to lymphatic malformation. Past history included facial palsy due to cystic tumors in the right petrous bone 4 years before onset of meningitis. At that time, pericardial effusion had been found and GLA had been diagnosed by pericardial biopsy. He achieved complete recovery under intensive care with antibiotics and mechanical ventilation. At the 3-year follow-up, the patient was healthy with no recurrence of meningitis. We should consider GLA among the differential diagnoses for osteolytic diseases in the pediatric population.

Key Words: generalized lymphatic anomaly, skull-base leakage, bacterial meningitis, magnetic resonance imaging, osteolytic disease, femur

Introduction

Imaging studies are useful for pediatric patients with bacterial meningitis, not only to obtain detailed information on inflammation of the meninges, but also to identify complications such as brain abscess, subdural abscess, subdural effusion, and brain infarction. Furthermore, we should not miss lesions that cause bacterial meningitis, such as otitis media, sinusitis and skull-base leakage resulting from tumor or trauma.

Generalized lymphatic anomaly (GLA) is defined by the International Society for the Study of Vascular Anomalies (ISSVA) as a multifocal lymphatic malformation that may affect the skin, superficial soft tissue, and abdominal and thoracic viscera, and often involves bones [1]. Lymphatic malformations comprise dilated lymphatic channels or cysts lined by endothelial cells with a lymphatic phenotype. Although the bone lesions affected by GLA are generally non-progressive, we describe herein the radiological features of GLA with skull-base leakage leading to life-threatening bacterial meningitis. Although GLA is a rare disease, we suggest this pathology as an important radiological differential diagnosis of osteolytic diseases in childhood.

Case report

A 7-year-old Japanese boy was admitted to our hospital with a 3-day history of fever and rapidly progressing disturbance of consciousness. Clear nasal discharge had been found 3 days before admission. His past history included right facial palsy that had been noticed at 3 years old. Computed tomography (CT) had revealed cystic lesions in the right petrous bone. Furthermore, pericardial effusion had been found incidentally during the examinations. Pericardial fenestration and ligation of the

thoracic duct had been performed. Lymphatic malformation had been diagnosed from pericardial biopsy. The petrous bone tumors had been followed without surgical treatment at another hospital, because surgery was considered to involve a risk of damage to the auditory nerve. When he was 6 years old, his family had moved to our prefecture, but had not consulted any hospitals.

Physical examination revealed: body temperature, 39.3°C; heart rate, 134 beats/min; blood pressure, 80/63 mmHg; SpO₂, 90% (room air); and Glasgow Coma Scale, 8 (E4, V1, M3). Opisthotonus and nuchal rigidity were evident. Dysphagia and inspiratory stridor were also found. Laboratory findings were as follows: white blood cell count, 4900/μl; hemoglobin, 11.1 g/dl; platelets, 3.9 ×10⁴/μl; C-reactive protein, 15.8 mg/dl. Cerebrospinal fluid (CSF) showed the following: cells, 320/μl (neutrophils, 193/μl; lymphocytes, 63/μl; histiocytes, 64/μl); protein, 327 mg/dl; and glucose, 0 mg/dl. CT was performed using a 256-channel multidetector-row scanner (Brilliance i-CT; Philips Medical Systems, Best, the Netherlands), revealing destruction of the middle skull base by cystic tumors (Fig. 1). Both panipenem and ceftriaxone were started, along with dexamethasone and intravenous immunoglobulin. Because respiratory condition rapidly deteriorated due to nasal and oral bleeding and dysphagia, mechanical ventilation was initiated after endotracheal intubation. *Streptococcus pneumoniae* was grown from a CSF culture. Antimicrobial susceptibility testing showed that the strain was susceptible to both panipenem and ceftriaxon. On hospital day 8, magnetic resonance imaging (MRI) using a 1.5-T system (Ingenia 1.5 T; Philips Medical Systems) showed cystic tumor in the right petrous bone and mastoid cells with ruptured dura mater, and similar tumors in the neck (Fig. 2). The cystic tumors were considered to represent lymphatic malformations. The tumors appeared

hypointense on T1-weighted imaging (T1WI) and hyperintense with contrast enhancement of the walls on T2-weighted images (T2WI). Clinical symptoms were relieved by treatment. The patient was extubated on hospital day 9, and enteral feeding gradually recovered. We also identified asymptomatic pleural effusion on X-ray during hospitalization. With administration of panipenem for a total of 15 days and continuous rehabilitation, the patient achieved complete recovery and was discharged on hospital day 42. His parents did not agree to resection of the petrous bone tumor and reconstruction of the middle skull base. At 1 year after discharge, the patient complained of hip pain and MRI revealed multiple cystic lesions of bilateral femora (Fig. 3). As of the 3-year follow-up, no relapse of bacterial meningitis or CSF rhinorrhea has been identified and the osteolysis in the femora has shown almost no change.

Discussion

GLA is synonymous with “systemic lymphangiomatosis” or “generalized cystic lymphangiomatosis”. In accordance with the ISSVA classification, we avoid using the term lymphangiomatosis, which implies increased endothelial cell turnover [1]. GLA is regarded as a result of abnormal development of the lymphatic system. Histologically, this benign malformation of lymphatic vessels manifests as endothelium-lined cystic spaces containing homogeneously eosinophilic material or chyle. Optimal treatment for GLA has yet to be established and has been limited to surgical resection, drainage, and radiation. Recently, systemic treatment with imatinib, or sirolimus has been tried, but remains limited to a few case series [2-3].

In the present case, lymphatic malformation in the right petrous bone caused ipsilateral facial palsy and CSF leakage leading to pneumococcal meningitis. Surgical resection of the tumor and repair of the skull base were not performed because a sufficient view of the lesion was difficult to secure and the parents did not agree to aggressive treatment. Fortunately, we did not find any relapse of CSF leakage and meningitis, probably because connective tissue might have covered the site of CSF leakage. To the best of our knowledge, only two cases of CSF leakage due to lymphatic anomaly have been reported [4-5]. Both previous cases also showed osteolysis of the middle skull base due to lymphatic anomaly, and underwent surgery due to repeated recurrences of meningitis. The results of surgery were uneventful for one patient [4], but the other showed recurrent meningitis and needed prophylactic antibiotics [5].

Langerhans' cell histiocytosis (LCH), fibrous dysplasia, Gaucher's disease, congenital fibromatosis, neurofibromatosis, Gotham-Stout disease (GSD) and metastasis should be considered among the radiological differential diagnoses for osteolytic lesions (Table 1) [6]. LCH is the main differential diagnosis for GLA, due to the possibility of organ involvement (lung, spleen, liver). On CT and MRI, bone lesions of LCH show peripheral sclerosis with perilesional edema, periosteal reaction and enhancement [6]. Fibrous dysplasia can be differentiated by a slightly heterogeneous signal on T2 short tau inversion recovery (STIR) sequences. Furthermore, visceral involvement is absent in fibrous dysplasia. In the early stage, the bone lesion of GSD starts with evidence of endosteal scalloping and cortical thinning [7]. The osteolysis in GSD is so progressive that almost complete resorption results, which is why GSD is also known as 'vanishing bone disease'. Furthermore, an

infiltrative soft-tissue abnormality adjacent to the area of osseous involvement is considered characteristic of GSD. On the other hand, the key radiological feature of GLA is variably sized lymphatic channels present in the medulla. Although the bone lesions of GLA can slowly increase in number and size to the point of appearing as 'multiple cystic lesions', cortical destruction is not involved.

In conclusion, although GLA is uncommon, lymphatic malformation should be considered as a radiological differential diagnosis of skull-base leakage in the pediatric population.

References

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Figure captions

Fig. 1 Plain computed tomography on admission. **a)** Axial view; **b)** coronal view. The right petrous bone is destroyed and shows leakage. A tumor-like lesion is seen at the site (circle).

Fig. 2 Magnetic resonance imaging on hospital day 8. **a)** Coronal T2WI shows cystic lesions in the petrous bone (arrow). **b)** Coronal contrast-enhanced T1WI shows enhancement of the walls of cystic lesions and continuous meninges (arrow).

Fig. 3 Magnetic resonance imaging of the lower extremities.

- a)** Coronal T2WI shows multiple high-intensity lesions in bilateral metaphyses (arrows). No changes in surrounding tissue or thinning of the bone cortex are apparent.
- b)** Coronal T1WI shows low-intensity cystic lesions (arrows).

Table caption

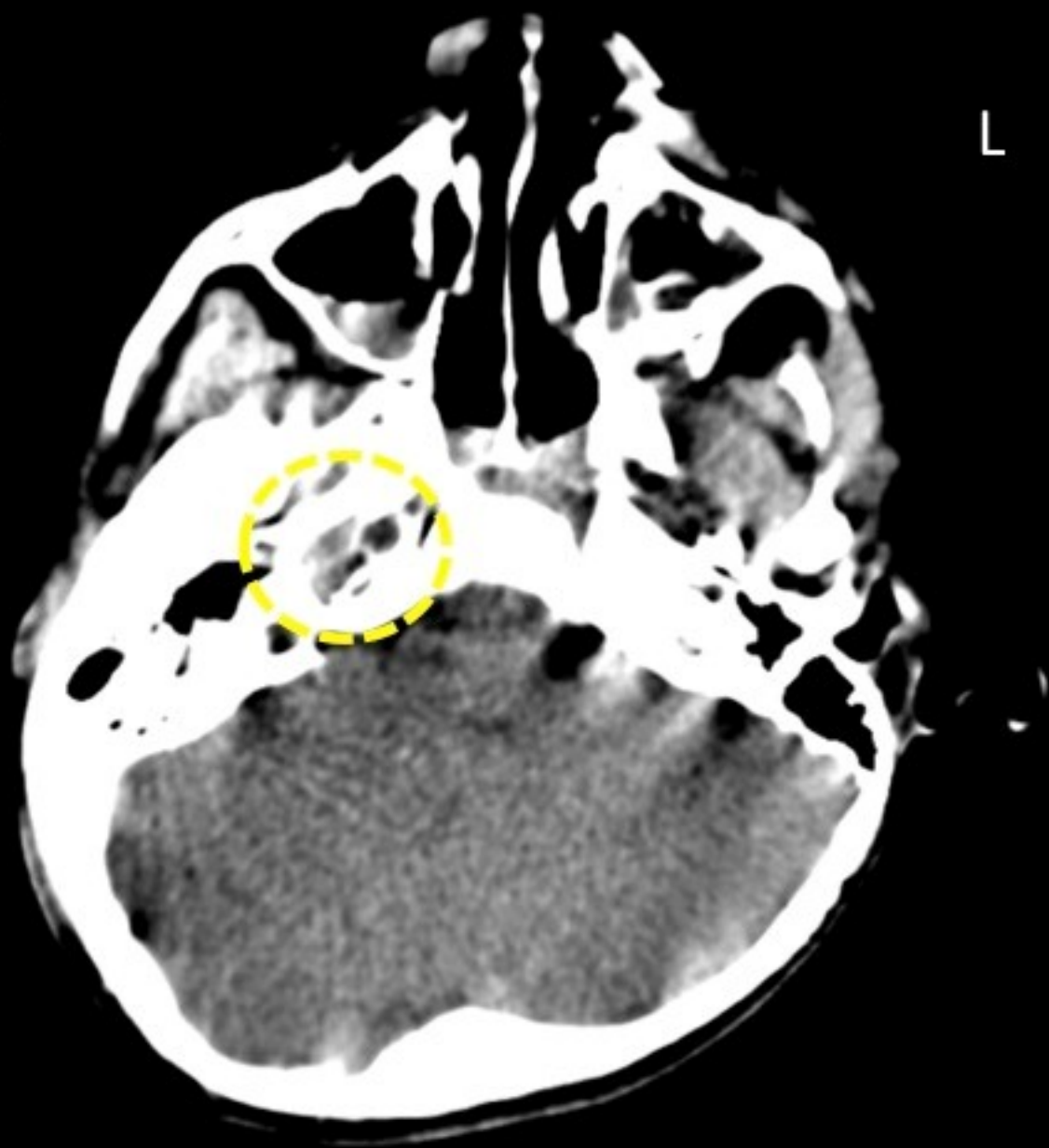
Radiological characteristics of differential diagnoses for multiple osteolytic lesions [6]

GLA; generalized lymphatic anomaly, LCH; Langerhans' cell histiocytosis GSD;

Gorham Stout disease

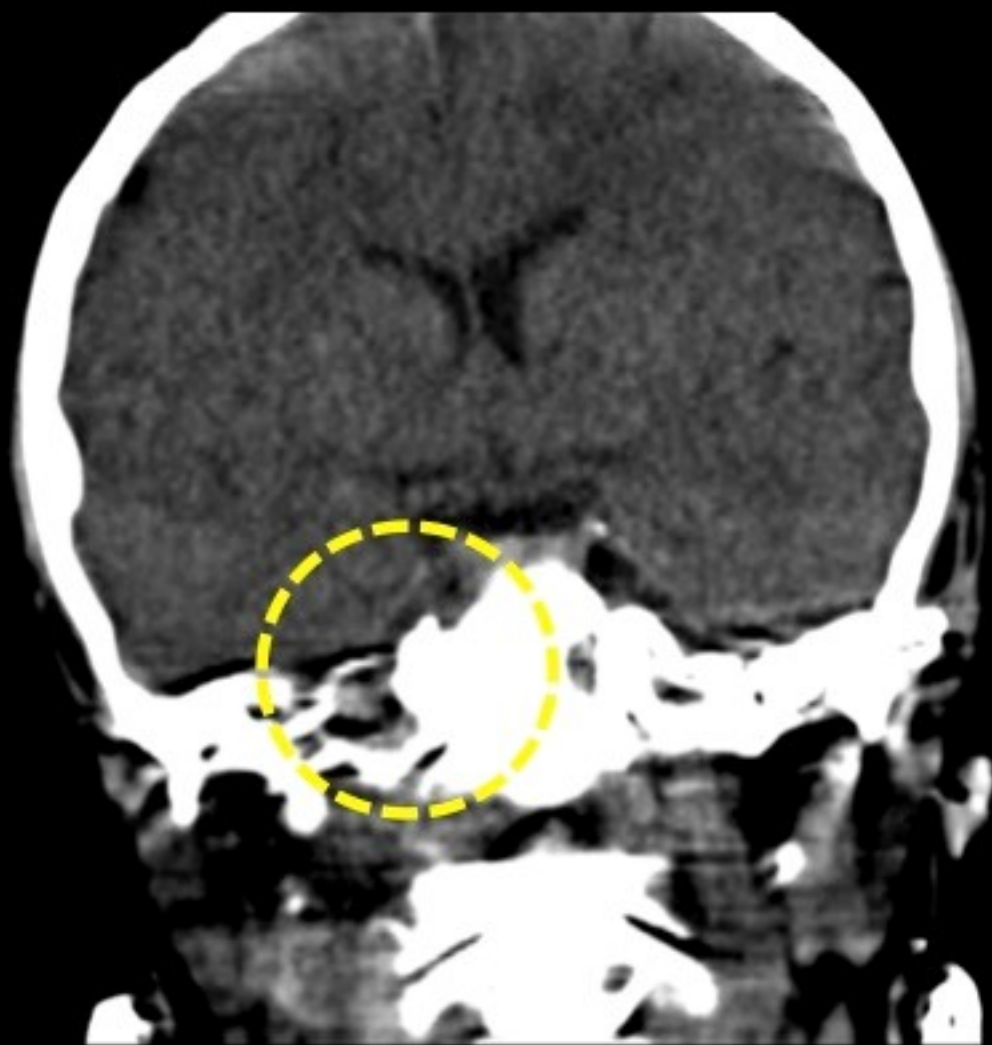
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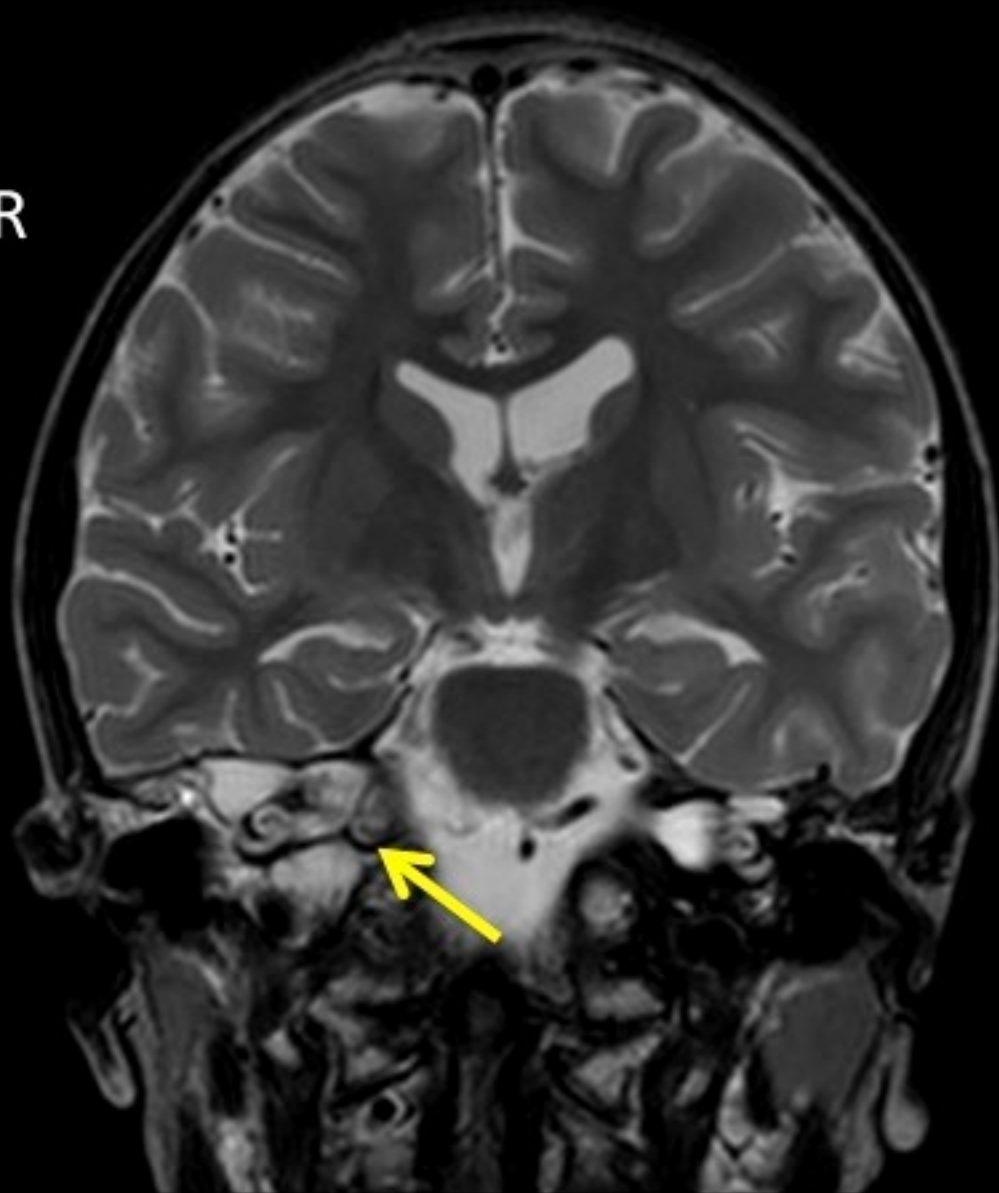
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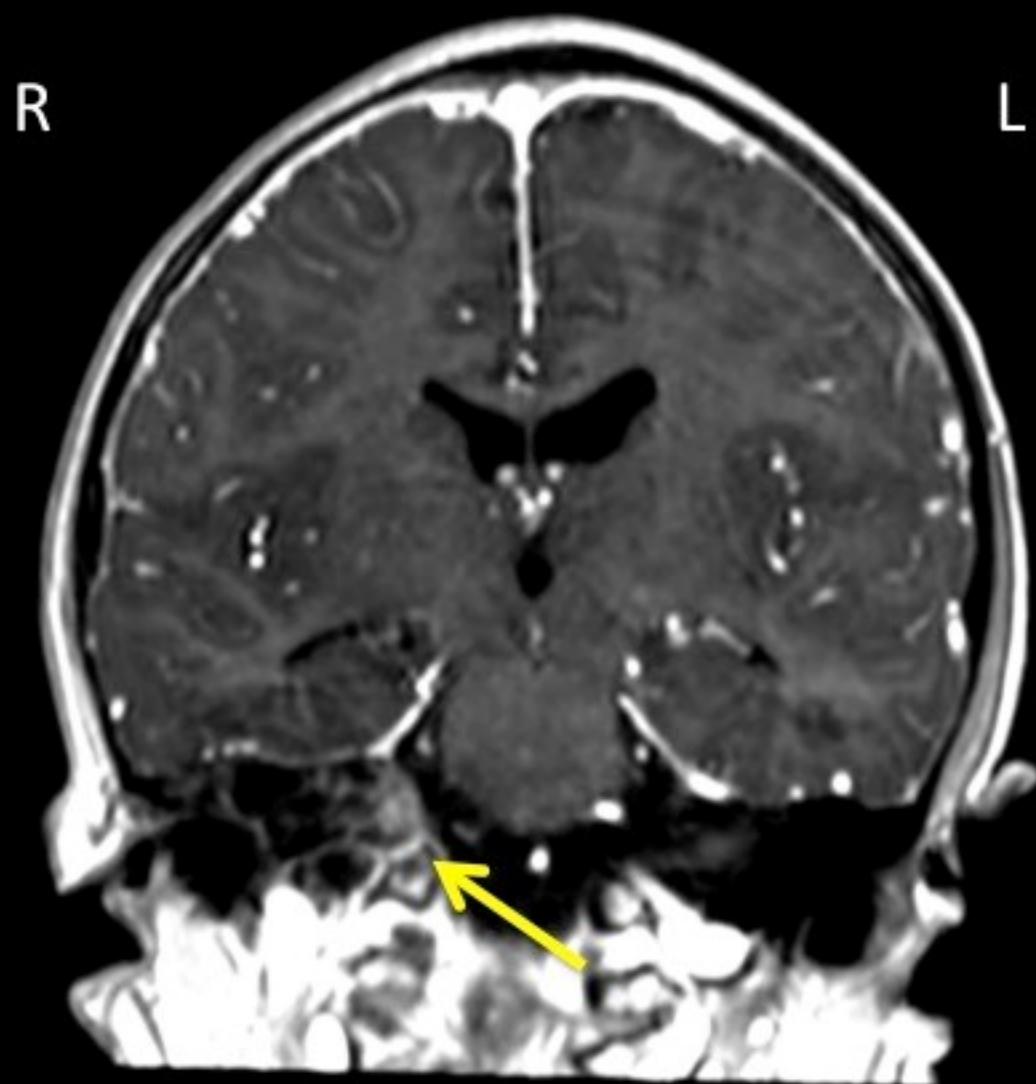
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