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A rare cause of childhood chylothorax: Gorham-Stout disease

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The authors stated that the written consent was obtained from the parents of the patient presented with images in the study.

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Abstract

Gorham syndrome is an extremely rare bone disease, with only a limited number of cases reported worldwide. It is characterized by progressive bone resorption associated with abnormal proliferation of lymphatic vessels, making it a rare case in medical literature. This disorder can lead to serious complications including chylothorax, especially in children. Early diagnosis and treatment are crucial in the prevention of life-threatening outcomes. This report presents a case of a young child with recurrent pleural effusion and bone lesions, eventually diagnosed with Gorham's disease. A three-year-old patient was admitted with recurrent pleural effusion, chylothorax, and pneumothorax. Imaging revealed multiple lytic bone lesions, suggestive of bone destruction. A lung biopsy confirmed lymphatic dilation, supporting a diagnosis of Gorham's disease. The patient's condition was evaluated through a multidisciplinary approach involving pulmonology, pathology, and radiology teams. Treatment included a combination of pharmacotherapy and dietary modifications, which successfully stabilized the patient's condition. The child has since been closely monitored, with no significant recurrence of symptoms. The progression of the disease can be life-threatening, particularly when the thoracic duct is involved, leading to recurrent pleural effusions. In this particular case, early diagnosis through a collaborative medical approach allowed for prompt treatment. Ongoing monitoring is essential in preventing relapses and ensuring long-term health outcomes for the patient.

Keywords: Gorham-Stout disease, chylothorax, pleural effusion, sirolimus

Introduction

Gorham-Stout disease (GSD) is an extremely rare bone disease, with only a limited number of cases reported worldwide. The incidence in children in the UK was 0.0014% (1.4 per 100,000) [1]. The majority of cases are observed in children and young adults without a familial inheritance pattern. The disease is characterized by progressive bone resorption associated with abnormal proliferation of lymphatic vessels. Clinical manifestations vary depending on the location of the affected area and the extent of bone destruction. Involvement of bones forming the chest cage, such as thoracic vertebrae and ribs, lead to prominence of respiratory symptoms [2,3]. We aimed to present a case of a three-year-old patient presenting with chylothorax in the context of the literature.

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Case presentation

A three-year-old Caucasian boy presented with a two-week history of fever and cough. He was born at term, weighing 2790 g, via cesarean section. No history of neonatal intensive care unit admission was reported. Vaccinations were up to date for his age. There was no consanguinity between the parents. There was no family history of chronic lung disease, asthma, or tuberculosis.

Past medical history: One year ago, the child presented to a hospital with sudden onset fever, tachypnea, and dyspnea. Bilateral pneumothorax was detected and managed with chest tube insertion, but lung expansion could not be achieved due to massive air leak and 70% saturation. Upon worsening of his clinical condition, a bullous area was excised from the right apex of the lung. Four months ago, he had a fracture of the right femur without a history of trauma. Two weeks ago, a chest tube was inserted due to bilateral pleural effusion detected on a chest X-ray. He was observed with a chest tube for five days, and then referred to our center due to recurrent pleural effusion after tube removal.

Physical examination: Dyspnea, tachypnea, and retractions were observed. His vital signs were saturation: 99%; respiratory rate: 98/min; blood pressure: 96/67 mmHg. Height: 92 cm (-1.52 SDS); body weight: 12 kg (-2.15 SDS). On auscultation, breath sounds decreased on the right side, and crepitant rales were present on the left side. There was no wheezing or rhonchi, nor was there any clubbing or chest deformity. There was a BCG scar. Hepatosplenomegaly was absent. Other system examinations were unremarkable. Laboratory examination revealed: Hb:10.9 g/dl, WBC:5300/mm^3, plt:411000/mm^3, lymphocytes:1900/mm^3. CRP was negative. The chest X-ray showed a cavitary area in the right apex, basal pleural effusion in the right lower lobe, and increased nonhomogeneous infiltration in the bilateral lower lobes (Figure 1). Pleural fluid appeared dirty yellow-white. Triglyceride level was 232 mg/dL; and cholesterol was 67.2 mg/dL, suggestive of chylothorax. Direct radiography showed intramedullary hypodense millimetric lytic lesions at the 4-5th anterior ribs. MRI showed osteolytic signal increase areas in T8-T11-12 vertebral bodies without contrast enhancement (Figure 2) lytic lesions in the left occipital bone (Figure 3). Bone mineral density was -1.87 SDS. Thoracic CT angiography was normal. Whole-body bone scintigraphy revealed abnormally increased metabolism in cervical 6 and thoracic 11-12 vertebral bodies and adjacent ribs. Cystic lesions were seen in the spleen on an ultrasound (Figure 4). Lower extremity radiography revealed callus tissue from the previous fracture in the midshaft of the right femur. Lung tissue excised during bullectomy was reevaluated histopathologically and subpleural lymphatic dilation and cystic lymphatic vessels were observed (Figures 5,6,7).

Based on the multidisciplinary evaluation of the current clinical, radiological, and pathological findings, a diagnosis of GSD was made. For the treatment, oral feeding was maintained, but the diet was modified to include medium-chain triglyceride (MCT)-based foods. The patient received pulse steroid therapy for three days followed by oral prednisolone for 45 days. Due to a lack of response to corticosteroid therapy, alpha interferon 2-beta was initiated, starting at 1.5 million U/m^2 three times a week for two weeks, then increased to 3 million U/m^2. Propranolol was administered at a dose of 4 mg/day for four months. As pleural effusion persisted, both interferon 2-beta and propranolol were stopped and sirolimus treatment was introduced at a dose of 0.8mg/m^2/day twice daily in liquid form for six months. The patient was monitored with sirolimus blood level and no side effects were observed. After six months of sirolimus therapy, the patient's symptoms fully resolved. During the five-year follow-up period, no new bone fractures or pleural effusion occurred, and the patient has continued on the MCT diet.

Figure 1: X-ray: Intramedullary hypodense millimetric lytic lesions in the anterior vertebral bodies of 4-5 (white arrows), fusion defect in the vertebral bodies of 5-6, linear band-like pleuroparenchymal in the lower lobe of the right lung, basal pleural effusion with a diameter of 7 mm

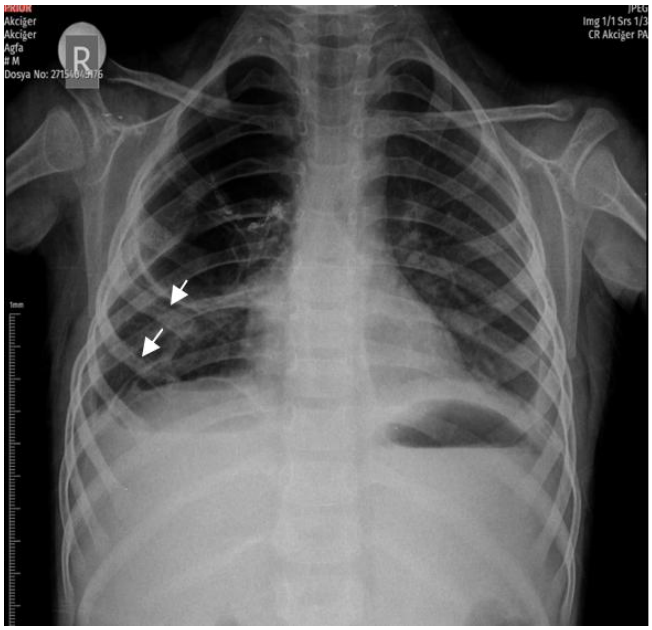


Figure 2: MR: Signal increases without contrast uptake are present in the vertebral bodies of T8-T11-12 (white stars).

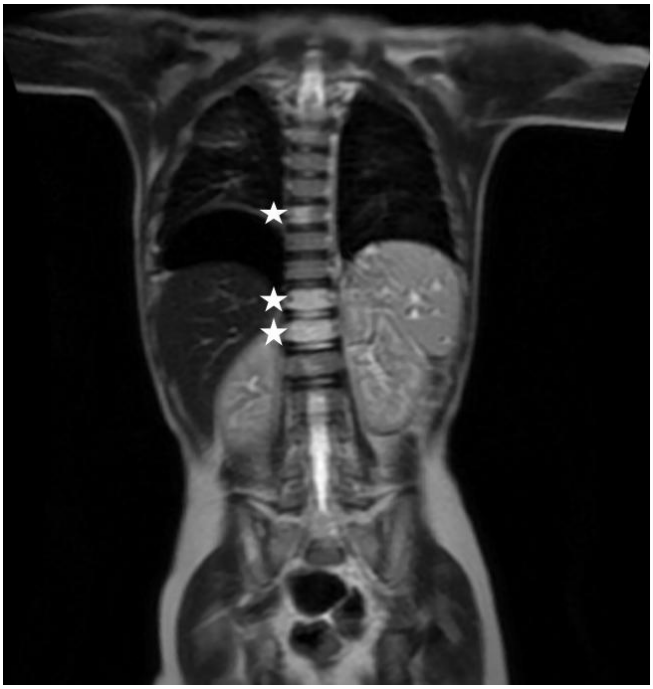


Figure 3: Lytic lesions at the occipital bone (black stars). Figure 1d: US: Cystic lesions in the spleen (thick black arrows).

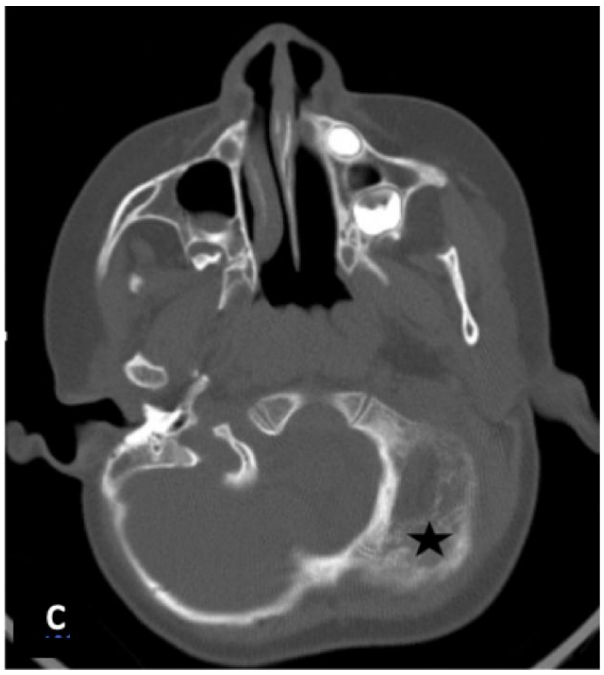


Figure 4: US: Cystic lesions in the spleen (thick black arrows).

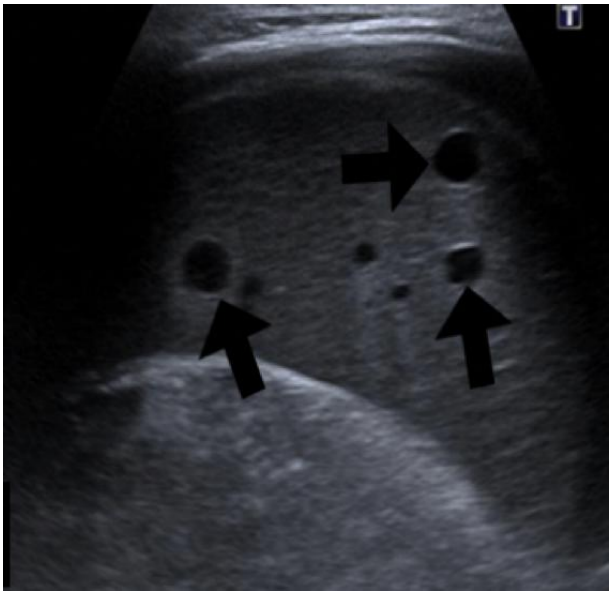


Figure 5: Subpleural lymphatic dilatations (thick blue arrow). Stained with hematoxylin and eosin, and magnified 40 times.

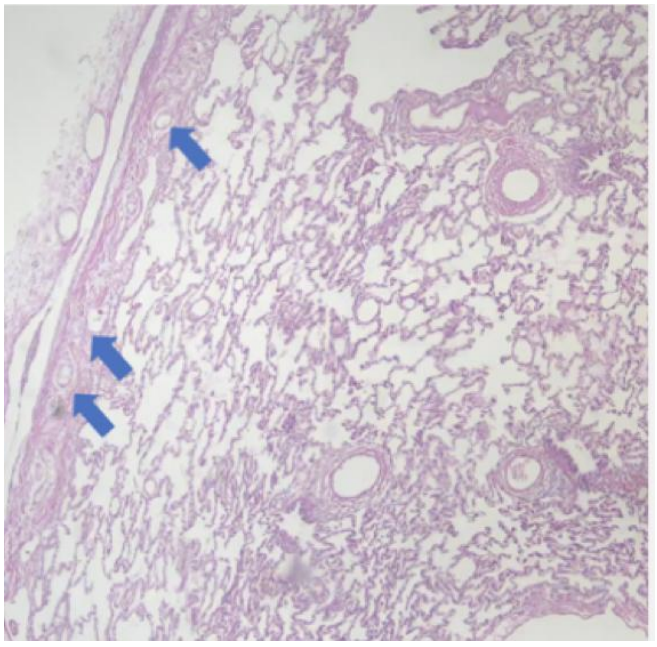


Figure 6: Subpleural cystic lymphatic dilatations (blue arrow), bull formation (blue star), emphysematous areas (green star). Stained with hematoxylin and eosin, and magnified 40 times.

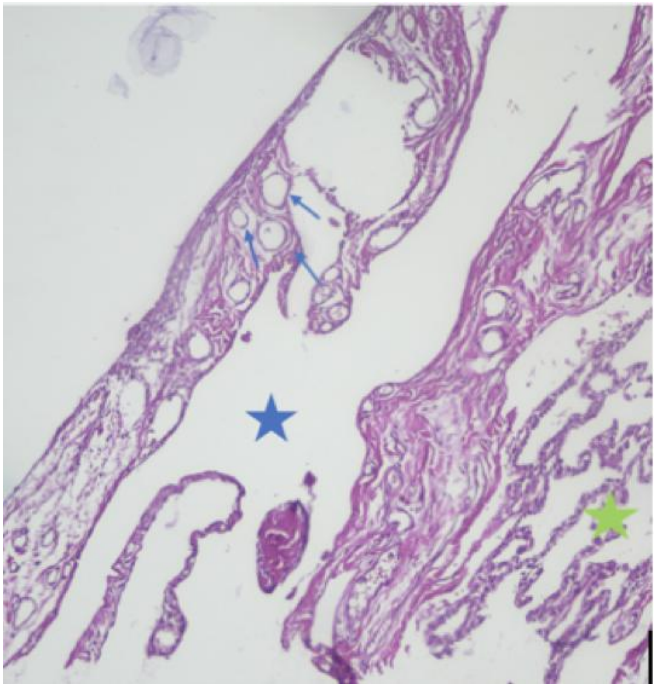
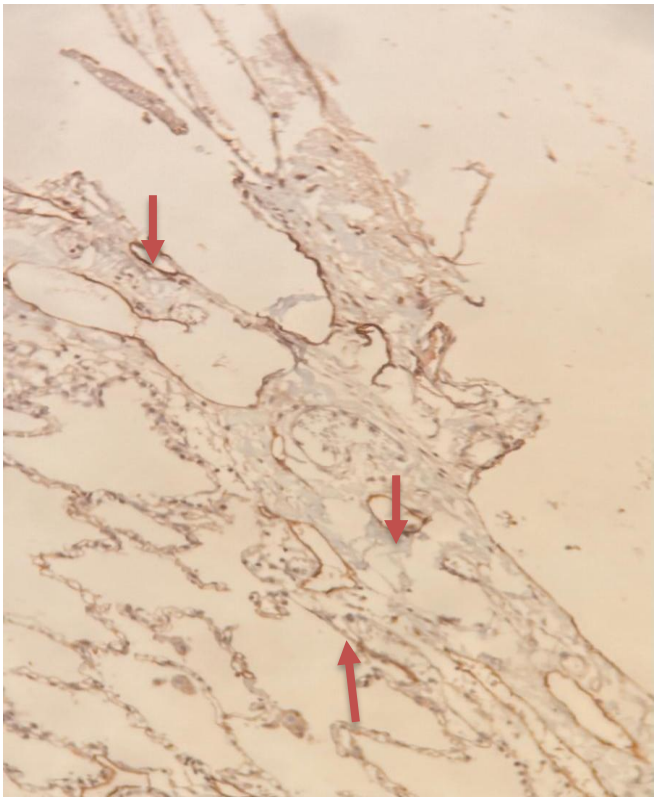


Figure 7: Enlarged lymphatic vessels (pink arrow) (Immunohistochemical d240 analysis X40)



Discussion

Gorham-Stout disease can progress aggressively or proceed with spontaneous remission, characterized by vascular and lymphatic channel proliferation and bone osteolysis. The disease may not be detected until it presents with clinical symptoms, such as pathological bone fracture, pericardial effusion, or chylothorax [2,3].

The etiology of chylothorax includes various factors, such as lymphatic malformations, injury to the thoracic duct, and lymphadenopathy, as well as mass effect, surgery, and trauma. In the presence of benign chylous effusion and lytic bone lesions with an unidentified etiology, GSD, a subgroup of complicated

lymphatic anomalies, should be considered in the differential diagnosis [4]. The incidence of chylothorax in patients with GSD has been reported to be 22-44% in previous years. However, in a 2022 study evaluating the etiology of chylothorax in childhood, GSD accounted for 30% of the causes of chylothorax. In the same study, bone involvement was detected, especially vertebrae, in all seven cases with GSD [5]. Extraosseous involvement in GSD is also known as splenic involvement [6]. Our specific case demonstrated cystic lesions indicative of splenic involvement of the disease.

The symptoms of our patient began at the age of two, which is quite an early onset, since GSD is often seen in older children and adolescents [3,5]. The absence of any symptoms during the prenatal and postnatal periods rules out reasons such as hydrops fetalis or injury to the thoracic duct at birth. There was no history of surgery or injury in the period leading up to the development of pleural effusion in our patient. Although chylothorax can occur secondary to high central venous pressure, various tumoral causes, and infections and sarcoidosis causing pressure, these were excluded in our case.

The diagnosis of Gorham-Stout disease in this patient took six months due to its rarity and the absence of standard treatment guidelines. The multidisciplinary approach, involving pulmonology, pathology, oncology, and radiology teams, was crucial in reaching the correct diagnosis and selecting an appropriate treatment strategy amidst the challenges posed by this complex condition.

The prognosis of GSD varies depending on the extent of involvement. While spontaneous remission is possible, the disease can also progress aggressively and lead to life-threatening complications. Treatments like sirolimus offer hope, but careful monitoring is necessary due to potential side effects and the risk of recurrence. With early diagnosis and treatment, long-term survival is achievable, though complications such as pleural effusion may recur even years later. Although there is no standard care protocol for chylothorax treatment, the most recommended approach is to start with dietary changes (TPN, MCT), followed by octreotide and finally surgical intervention [3,5,7]. Surgery is recommended when there is a significant deterioration in nutritional status despite conservative treatment or when daily chylous fluid drainage exceeds 10 ml/kg.

However, because conservative treatments may take time to be effective, alternative treatments have been proposed. Such alternatives include propranolol, a β2 adrenergic receptor blocker that reduces proangiogenic factor expression, and alpha-interferon, which inhibits lymphatic vessel proliferation [3]. Sirolimus, an mTOR inhibitor, has shown efficacy in treating lymphatic malformations, including Gorham-Stout disease. However, its use is associated with several potential side effects. Common adverse effects observed in children include stomatitis, gastrointestinal issues, hyperlipidemia, and infections due to its immunosuppressive properties. In rare cases, sirolimus can cause thrombocytopenia and impair wound healing. Despite these risks, the benefits of sirolimus in managing lymphatic malformations often outweigh the side effects when monitored closely in a controlled setting [8].

Conclusion

Gorham-Stout disease should be considered in chylothorax with accompanying bone lesions in patients of all ages. Treatment strategies for GSD are generally experimental due to the lack of randomized controlled trials and standardized guidelines. Treatment is aimed at alleviating symptoms, preventing disease progression, and preserving skeletal integrity. Surgical interventions and angiogenesis inhibitors such as sirolimus may be tried in selected patients.

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