Case Report

J Korean Soc Radiol 2024;85(2):451-455
https://doi.org/10.3348/jksr.2023.0044
eISSN 2951-0805

JOURNAL of THE KOREAN SOCIETY of RADIOLOGY

Role of Lymphatic Embolization in Chylothorax Associated with Gorham–Stout Disease: A Case Report

고함-스타우트병과 연관된 유미흉 치료에서 림프관 색전술의 역할: 증례 보고

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Received April 24, 2023
Revised July 20, 2023
Accepted August 18, 2023

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A 45-year-old male patient with spontaneous chylothorax and osteolysis in the right 1st and 2nd ribs was diagnosed with Gorham–Stout disease based on clinical manifestations and bone biopsy. The chylothorax temporarily decreased after a successful selective lymphatic embolization. The patient presented with recurrent chylothorax, mild chest discomfort, and progressive osteolysis (despite administering sirolimus) during the follow-up period of 15 months.

Index terms Gorham–Stout Disease; Chylothorax; Lymphatic Embolization

INTRODUCTION

Gorham–Stout disease, also known as "vanishing bone disease," is rare and characterized by progressive osteolysis and loss of cortical bone due to intraosseous lymphatic malformations (1). It can involve any bone in the body (2) but is commonly localized to the clavicle, cranium, ribs, and cervical spine (1), inducing osseous matrix destruction and lymphovascular proliferation (3). It usually affects patients younger than 40 years, with an average age at diagnosis of 25 years (4). Early diagnosis is difficult because of the lack of disease-specific symptoms. Treatment guidelines have not been estab-

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lished; medical treatment, including bisphosphonates and sirolimus, can be considered for mild symptoms, and surgery, radiation therapy, and interventional treatment are needed when symptoms progress or functional problems occur (5). Herein, we present a case of temporary relief of chylothorax with lymphatic embolization in a patient who was first diagnosed with Gorham–Stout disease in his 40s.

CASE REPORT

A 45-year-old male with a chest tube visited the outpatient clinic with refractory right pleural effusion. He had no previous medical or surgical history, except for chest pain caused by lifting heavy objects 2 months earlier. Chest CT showed an osteolytic lesion in the right 1st rib and a fracture in the right 2nd rib, which were interpreted as trauma-related findings rather than primary or secondary bone lesions (Fig. 1A, B).

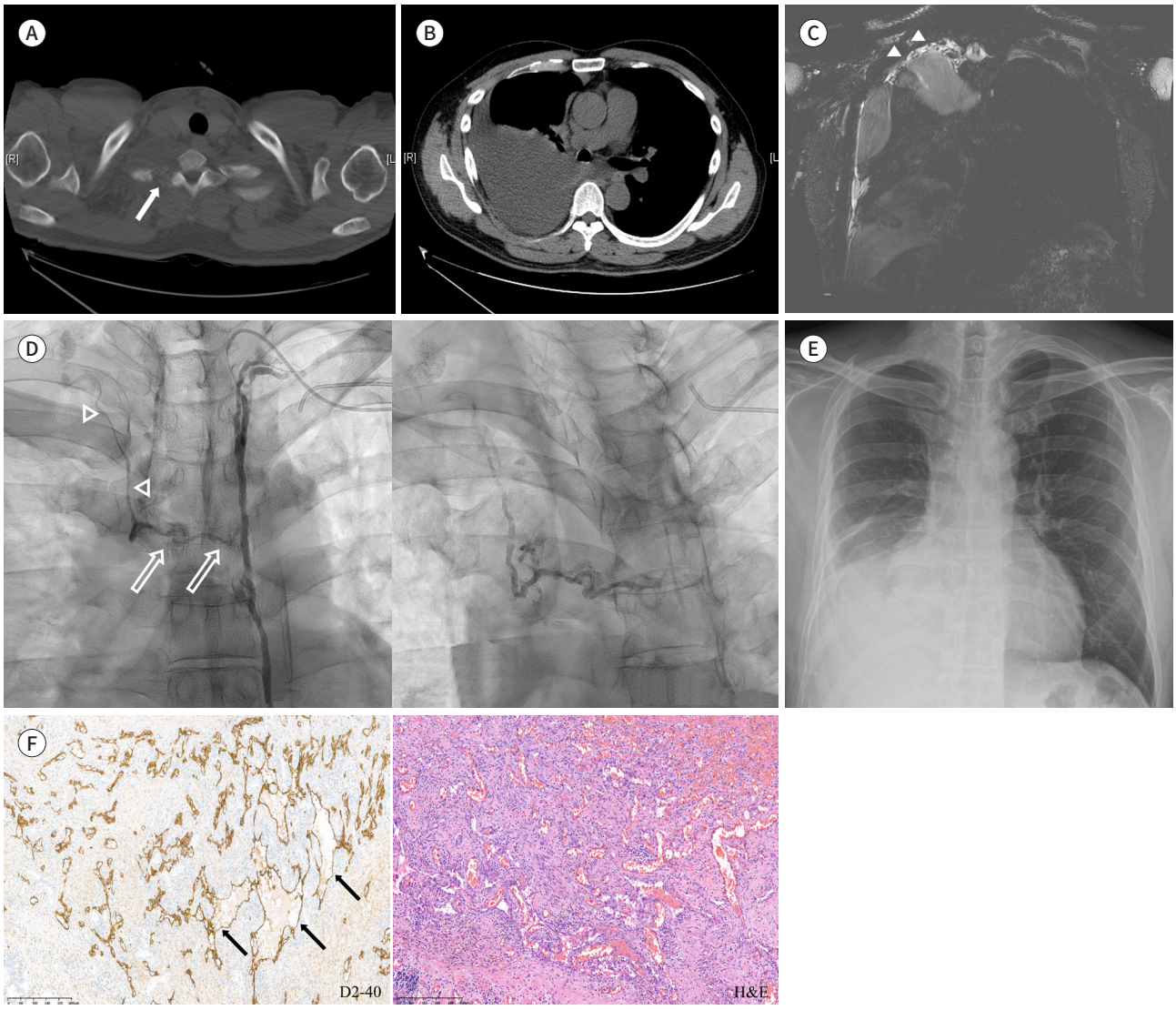
Upon admission, the triglyceride level in the pleural effusion was 335 mg/dL, suggesting chylothorax. Noncontrast MR lymphangiograms showed suspicious leakage and web-like lymphatic channels around the right lower neck and subclavian vein (Fig. 1C). With the impression of traumatic chylothorax, lymphatic embolization was considered in a multidisciplinary discussion. An intranodal lymphangiogram showed no abnormalities, except for prominent lymphatic channels in the right upper hemithorax. A subsequent thoracic ductogram showed no definite contrast leakage (Fig. 1D), and embolization was not performed during this session.

Osteolytic bone lesions were further evaluated using PET/CT and bone biopsy, as multiple stages of bone destruction were observed. FDG uptake in the right 1st and 2nd ribs increased (maxial standardized uptake value = 4.0), and the pathological diagnosis was Gorham–Stout disease (Fig. 1F). Lymphatic embolization was the first treatment option in a multidisciplinary discussion. Using the left basilic vein approach, the thoracic duct opening was selected using a 5-F catheter (Kumpe; Cook Medical Inc., Bloomington, IN, USA). The thoracic duct was cannulated using a 1.7-F microcatheter (Veloute; Asahi Intecc, Nagoya, Japan) and a 0.016” microguidewire (Meister; Asahi Intecc). Prominent aberrant lymphatic channels were selectively embolized with diluted glue (1:1) (Fig. 1D).

The daily chest tube drainage gradually decreased, and the patient was discharged. However, at the 4-month follow-up, he revisited the outpatient clinic with mild symptoms (chest discomfort), and a chest radiograph showed right pleural effusion (Fig. 1E). Percutaneous catheter drainage was performed to relieve the symptoms. Additional lymphatic interventions were considered effective only for symptom relief because the previous interventional approach could not prevent the recurrence of chylothorax or the progression of osteolysis. Therefore, treatment with sirolimus was initiated. Despite medication, the patient presented with a newly developed pain in the right shoulder. Chest CT performed at the 15-month follow-up (after administering sirolimus for 1 month) showed a newly developed osteolytic lesion in the right scapula, suggesting a pathological fracture.

Prior to enrollment, the patient provided written informed consent in accordance with the principles outlined in the Helsinki Declaration, affirming his voluntary participation in this case report.

Fig. 1. A 45-year-old male patient with spontaneous right chylothorax.
A, B. Chest CT images with bone window setting show osteolytic lesions (arrow) at the right 1st rib. Right pleural effusion is also noted.
C. A coronal MR lymphangiography image shows web-like lymphatic channels (arrowheads) around right lower neck and the subclavian vein.
D. Pre-embolization thoracic ductogram (left) shows an aberrant lymphatic channel (arrows) going toward right upper hemithorax off the thoracic duct (arrowheads). There was no definite contrast leakage. In second session, the aberrant channel was selectively embolized with diluted glue (1:1) (right).
E. A 4-month follow-up chest radiograph shows recurrence of right chylothorax.
F. On H&E staining (× 130) and D2-40 immunostaining (× 130), the specimen (1st and 2nd ribs, pleura) shows proliferation of thin-walled lymphatic channels (arrows) without evidence of malignancy. The pathologic findings are compatible with Gorham–Stout disease.
H&E = hematoxylin and eosin



DISCUSSION

Gorham–Stout disease is usually diagnosed in patients younger than 40 years, with an average age of 25 years (4). Its incidence is unknown, as only approximately 350 cases have been reported in the past 70 years. In the early stages, patients are asymptomatic and the affected bones can show patchy osteoporosis. As the disease progresses, symptoms such as pain and

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swelling develop, and complete bone resorption and pathological fractures occur, leading to complications like scoliosis, chylothorax, infection, and even cerebrospinal fluid leakage (1, 3). Initially, the diagnosis was difficult because of the rare incidence of the disease and clinical settings, including age, past medical history, and symptoms. This information appeared irrelevant during the patient's first visit. Crucial clues included bone changes at different stages of osteolysis and fracture. On laboratory testing, elevated serum bone-specific alkaline phosphatase (BAP), C-terminal telopeptide of type 1 collagent (CTX-1), interleukin-6 (IL-6), ligand for receptor activator of nuclear factor kB (RANKL) can be detected (1).

The definite pathognomonic mechanism of Gorham–Stout disease is unknown, but it is known that the activation of osteoclasts and lymphogenesis in the affected bone are essential for disease development (1). In this context, the pathological hallmarks include the proliferation of intraosseous thin-walled lymphatic vessels and the activation of osteoclasts, inducing progressive osteolysis (4). There should be no findings suggesting malignancy. Upon immunochemical staining, osteoclast and monocyte marker (CD-68), lymphatic endothelial markers (D2-40), vascular endothelial markers (CD-31 and CD-34), vascular endothelial growth factor (VEGF), and VEGF receptor 3 can be used to investigate the origin of vessels in bone lesions (1, 6).

Treatment for this condition is as difficult as the diagnosis. Although curative treatments have not been established yet, several palliative modalities have been proposed. Medical treatment focuses on antiosteolysis (bisphosphonates) and antiangio/lymphangiogenesis (sirolimus [mTOR inhibitor] and bevacizumab [anti-VEGF-A antibody]). The use of albumin, immunoglobulin, blood transfusion, propranolol, calcitonin, vitamin D, calcium, corticosteroids, and IFN α-2b has been attempted (1, 3, 4, 7). Surgical resection of the affected bone and ligation of the lymphatic channels have also been performed to control the symptoms. If surgery is not feasible, radiation therapy can be performed to slow the osteolysis and angiogenesis. A previous study showed that radiation therapy may prevent disease progression in 77%–80% of patients (8).

Several cases of Gorham–Stout disease-related chylothorax have been reported. Patients have undergone various treatments, such as medication, pleurodesis, thoracic duct ligation, and radiation therapy, to control the chylothorax (9, 10). In the present case, the chylothorax temporarily improved after selective embolization of the leaking branch of the thoracic duct. It is assumed that as the disease progresses, new foci of lymphatic leakage develop, causing symptom recurrence. Accordingly, embolization of the entire thoracic duct may be more effective, although this has not yet been validated.

In conclusion, this case has several implications for clinicians and interventional radiologists. Interventional lymphatic embolization can be helpful in symptomatic Gorham–Stout disease-related chylothorax. Since the disease can progress asymptomatically, either regular follow-up or concurrent systemic treatment should be considered.

Author Contributions

Conceptualization, Y.M., H.D., S.S.; data curation, Y.M., H.D., H.S.; formal analysis, Y.M., H.D.; investigation, Y.M., H.D., H.S.; methodology, Y.M., H.D.; project administration, Y.M., H.D.; resources, Y.M., H.D.; software, Y.M., H.D.; supervision, Y.M., H.D.; validation, all authors; visualization, Y.M., H.D., H.S.; writing—original draft, Y.M., H.D.; and writing—review & editing, Y.M., H.D.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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Funding

None

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고함-스타우트병과 연관된 유미흉 치료에서 림프관 색전술의 역할: 증례 보고

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특이 외상력 없이 우측 1, 2번 갈비뼈 골용해와 자발성 유미흉을 주소로 내원한 45세 남환이 임상 양상과 골생검을 통해 고함–스타우트병으로 확진된 증례를 보고하고자 한다. 자발성 유미흉의 치료를 위해 림프관 색전술을 시행하였고 성공적인 시술 직후 유미흉은 호전되었다. 하지만 15개월간의 관찰 동안 시롤리무스(sirolimus) 투여에도 불구하고 유미흉이 재발되었고 흉부 불편감과 골용해는 진행되었다.

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