Combined neodymium-doped yttrium aluminum garnet laser and sclerotherapy in Gorham-Stout syndrome

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Bone involvement is relatively rare in vascular malformations. Gorham-Stout disease, also referred to as *vanishing bone disease*, is characterized by osteoclast activation and osteolysis caused by proliferating lymphatic endothelial cells. We present the case of a 12-year-old boy who had Gorham-Stout disease at the age of 8 years. The clinical course was complicated by pathological fractures and localized intravascular consumption coagulopathy. Sclerotherapy and embolization therapy led to normalization of the coagulation parameters and significant improvement of the clinical findings. We speculate that this effect may be attributable to the elimination of lymphatic endothelial cells. (J Am Acad Dermatol 2018;4:458-61.)

Key words: endovascular laser photocoagulation; Gorham-Stout syndrome; localized consumption coagulopathy; sclerotherapy; vanishing bone disease.

INTRODUCTION

Vascular malformations (VMF) preferentially include skin and subcutaneous tissue. They can also involve deeper tissue sections and internal organs, but bone involvement is comparatively rare. Gorham-Stout disease (GSD), also referred to as *vanishing bone disease*, is characterized by osteolysis caused by expanding lymphatic tissue. It was first described in 1955 by US pathologists L. Whittington Gorham (1885-1968) and Arthur Purdy Stout (1885-1967).[1] About 200 cases have been described so far.

The pathogenesis of GSD is not fully understood. Endoglin overexpression (CD105)[2] in the vascular endothelium or activation of osteoclasts by lymphatic endothelial cells (LEC)[3] and/or interleukin-6[4] are currently under investigation.

GSD is characterized by a slowly progressing course leading to the partial or complete dissolution of bone tissue. Therapeutic options are limited. Here we report a case successfully treated by a combination of sclerotherapy plus neodymium-doped yttrium aluminum garnet (Nd:YAG) laser coagulation.

Abbreviations used:

GSD:	Gorham-Stout disease
LEC:	lymphatic endothelial cells
MRI:	magnetic resonance imaging
Nd:YAG:	neodymium-doped yttrium aluminum garnet
VMF:	vascular malformations

CASE REPORT

The patient presented at birth with dilated cutaneous venules in a circumscribed area of the right shoulder/neck region (Fig 1, *A*). Pregnancy was uneventful, and the family history was negative for vascular or other malformations. The lesion was noted to vary in size depending on intrathoracic pressure; it increased up to 2-fold with crying.

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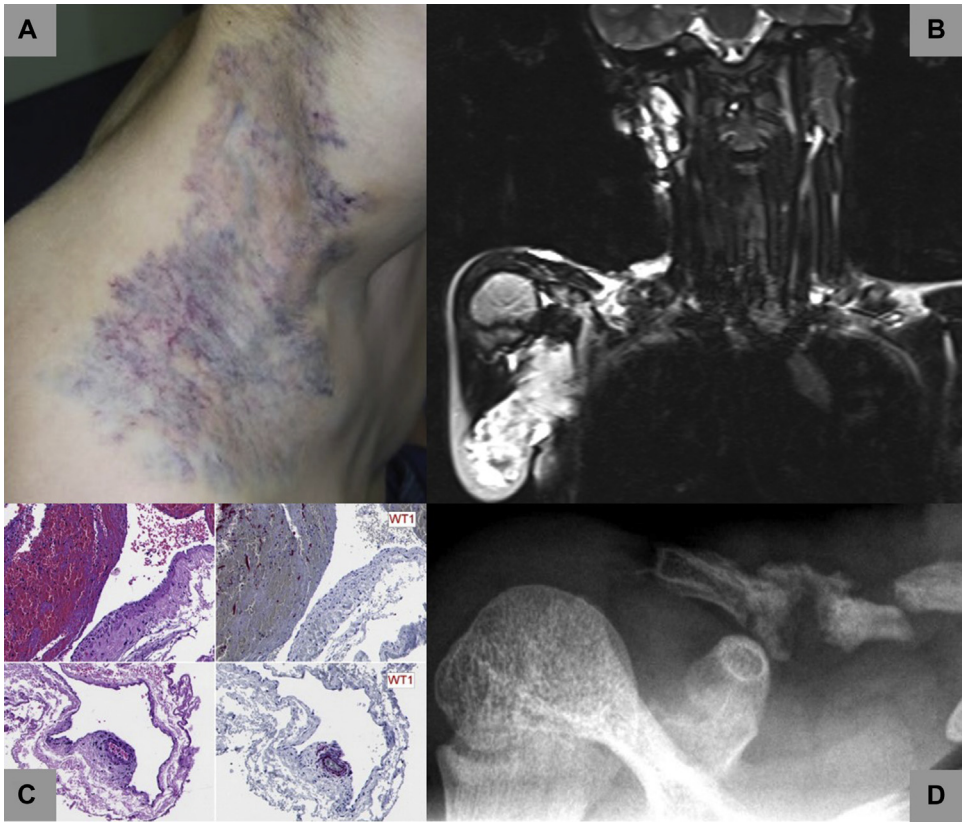

Fig 1. **A**, Dilated cutaneous venules in the right shoulder/neck area at the age of 11 years. **B**, The MRI found a fresh hemorrhage into the lymphangiomatous portion and venous ectasias. **C**. Characteristic thin-walled malformative lymphatic vessels with WT1-negative endothelia (lower row). Some malformative vessels show thrombi with incipient intravascular papillary endothelial hyperplasia (upper row). **D**, Pathologic fracture of the right clavicle.

At the age of 18 months, an abrupt increase of the lesion was noted. Magnetic resonance imaging (MRI) showed extension of the vascular lesion from the right parotid to the supraclavicular region and the right upper arm with a fresh hemorrhage within a lymphangiomatous tissue (Fig 1, *B*). Central parts of the vascular malformation were subsequently resected. The inaccessible areas and peripheral areas were treated by interstitial Nd:YAG laser (3 sessions).

Histopathology found a combination of a superficial mainly lymphatic malformation and osteoclastic destruction of bone (Fig 1, *C*) in accordance with GSD. Of note, the number of SATB2-positive osteoblasts was markedly reduced.

At the age of 8.9 years, the patient complained of acute pain in his right shoulder, pronounced when lifting the right arm. A radiograph showed a pathologic fracture of the right clavicula with a central osteolytic core (Fig 1, *D*).

Between the ages of 8 and 11 years, the patient underwent 11 courses of percutaneous sclerotherapy (Lipiodol [ethiodol 3% sodium tetradecyl sulfate]), followed by subcutaneous injections of low-molecular-weight heparin and bed rest for 2 days. Sclerotherapy was performed at intervals of 2 to 4 months (sites: right trapezius, deltoid, sternocleidomastoid, jugular, and axillary region, respectively). In addition to sclerotherapy, Nd:YAG laser (9J/cm^2) was applied in the cervicothoracic and supraclavicular region (3 sessions).

This treatment led to a marked reduction of the size of the lesion. It was accompanied by a normalization of the (slightly) decreased platelet counts and a significant decrease of the elevated D-dimer levels (Fig 2).

Follow-up radiography of the clavicular region 5 years after initiation of therapy found complete resolution of the pseudarthrosis.

DISCUSSION

Since GSD is a rare and clinically variable entity, there is no consensus on the most effective treatment approach yet. As depicted in Table I, available treatment options gave highly variable results.[5]

Our patient responded well to a combination of surgery plus sclerotherapy and Nd:YAG laser

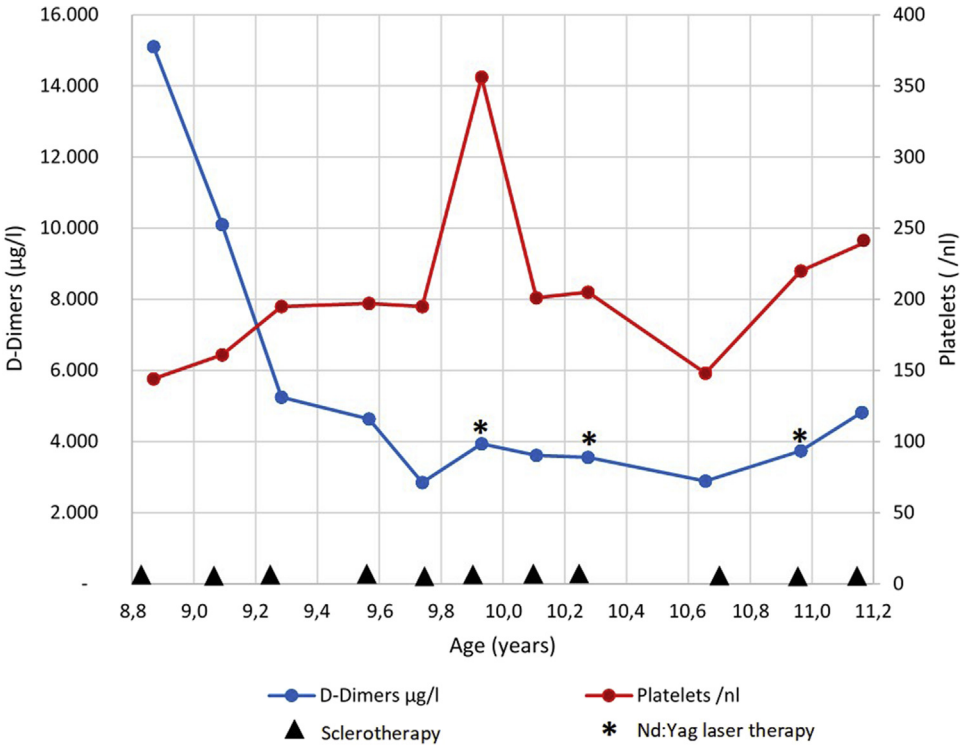

Fig 2. Time course of fibrinolysis parameters during sclerotherapy and Nd:YAG laser therapy.

Table I. Treatment modalities in previously published cases of GSD

Treatment modality	No. of cases	Controlled: No bone resorption seen	Not controlled: Progressive bone resorption
Radiation alone (40-45 Gcy in 2 Gcy fractions)	8	6	2
Surgery combined with radiation	2	2	0
Surgery alone (resection alone/resection with endoprosthetic reconstruction/biological reconstruction)	29	13	6
Medical treatment (vitamin D, calcium, interferon, cyclophosphamide, bisphosphonate)	25	19	4
Total	64	40 (62.5%)	12 (18.8%)

Note. Twelve patients of 64 were lost to follow-up and are not listed.
Modified Ellati et al.[5]

therapy. This multimodal therapy was well tolerated and effective, but multiple treatment sessions were required over the course of 4 years.

In a review of 21 patients with vascular anomalies who were treated with sclerotherapy (average number of sessions, 3.7; range, 2 to 8), good or excellent results were obtained in 16 of 21 (76%), and sclerotherapy was well tolerated.[6]

A combination of endovenous laser and sclerotherapy proved successful in 27 of 29 patients with chronic ulcers.[7] The recently reported combination of sunitinib plus taxol may be an alternative medical treatment option.[8]

About one-third of pediatric VMF patients are affected by localized intravascular coagulation and have D-dimer levels greater than 500 ng/mL.[9] Lesion size, presence of phleboliths, truncal location, and spongiform morphology on MRI were correlated with localized intravascular coagulation.[10] As shown in Fig 2, laser plus sclerotherapy was accompanied in our patient by normalization of localized intravascular coagulation. We speculated that determination of D-dimer levels might be helpful as a surrogate parameter of disease activity in GSD, but further studies are required to corroborate this assumption.

Finally, recent findings that LECs stimulate osteoclasts[3] imply that LECs, not osteoblasts, are the primary culprits in GSD. In fact, histology of our patient showed activated osteoclasts but decreased numbers of *SATB2*-positive osteoblasts. The authors

found that osteoclast activation could be blocked by a neutralizing antibody.[3] We hypothesize that our approach of combined endovascular laser and sclerotherapy has a similar effect: by eliminating LECs, osteoclast activation is terminated, and osteolysis stopped.

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