Case report

Thoracic osteotomy for Gorham-Stout disease of the spine: a case report and literature review

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Conflict of interest

The authors declare that they have no conflict interests.

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Summary

Introduction:

Gorham-Stout syndrome is an aggressive, non-heritable skeletal disease characterized by osteolysis following minor trauma. The primary involvement of the spine is less common (10%) and has been described in only about 20 cases; there is no consensus about the best way to treat this condition.

Purpose of the study:

To report a case of Gorham-Stout syndrome involving the thoracic spine and to review the literature in order to suggest a post-operative treatment to prevent osteolysis.

Case report:

A thirty-year-old female patient was admitted to the unit in March 2013 for a pathologic T4 fracture. X-rays and CT scan revealed the onset of T4 osteolysis and an increase in thoracic kyphosis (the local kyphosis was up to 100°). We performed surgery by posterior approach, combining posterior fixation with screws and rods from T3 to T9, decompression and vertebral osteotomy of 65°. The immediate outcome of surgery was good and the patient returned home after 24 days. At 6 and 12 months of follow-up, the patient was walking normally with no neurological sequelae.

Conclusion:

We report a case of Gorham-Stout syndrome involving the thoracic spine that was successfully treated by interpedicular osteotomy associated with a 6 month follow-up. We suggest that this strategy can provide good results, because after fusion, the disease process remains stable. Because of the lack of cases reported, surgeons must be careful when using multiple treatments, because these treatments have many side effects.

Level of evidence: level IV case report

Keywords: Gorham-Stout syndrome, spine, surgical treatment, interferon

Introduction

Gorham-Stout syndrome is an aggressive, non-heritable skeletal disease described by L.W. Gorham in 1954 [1]. Its specific features are: onset of osteolysis occurring a long time after a minor trauma. It is a form of angiomatosis, with an overgrowth of small blood vessels observed in bone biopsies. It is not a non-malignant disease and X-rays show defects in the affected bone. The disease progresses slowly and may stop spontaneously.

The etiology and pathogenesis of the disease remain unknown despite about 200 cases reported in the literature. It differs from the other forms of idiopathic osteolysis [2] and corresponds to type IV of the classification proposed by Hardegger et al. The age at onset is from 1 month to 75 years, though it occurs most commonly in the second and third decades. In most cases, only a single bone is involved but in some patients several bones are affected, together with joints and intervertebral discs. Associated infiltrative soft tissue abnormality is often found.

The diagnosis is based on clinical, radiologic [3] and histologic evidence [4]. Clinically, patients are asymptomatic until a pathological fracture occurs. Four stages of the disease have been recognized on X-rays. Over time, a proliferation of thin-walled sinusoidal channels of lymphatic origin leads to the formation of fibrous connective tissue, resulting in progressive bone loss. The disease can be divided into an early stage with intramedullary and cortical vessels proliferation, and a later stage characterized by destruction and resorption of bone. Several lymphangiogenic pathways that may play a relevant role in Gorham's disease have been suggested such as PDGF, LYVE-1, IL6 or VEGF [5–7]. However, there is no biological marker of the disease and routine laboratory parameters are usually within normal range. The apparent contradiction concerning the presence or not of increased osteoclasts number may be explained by the different phases of the syndrome

Because of the lack of studies into the syndrome, there is no consensus about the best way to treat this condition [8]. Most cases of Gorham–Stout disease resolve spontaneously, but the prognosis remains unpredictable. Some cases progress to complete bone absorption, whereas others are self-limiting. With spinal or thoracic involvement, life-threatening complications can occur [9], and up to 16% of cases can be fatal.

Purpose of the study:

To report a case of Gorham-Stout syndrome of the thoracic spine and to review the literature in order to evaluate medical treatment.

Case report:

A thirty-year-old female patient was admitted to the unit in an emergency on March 2013 for pathologic T4 fracture.

The fracture occurred in 2003 after a minor trauma: she fell from a chair. In the following months, back pain occurred. X-rays and CT scan were performed showing the onset of T4 osteolysis. A vertebral biopsy, performed in a highly specialized hospital, showed a proliferation of small blood vessels, dilated vascular spaces and positive staining for CD31, CD34, factor 8 and actin. The examiner diagnosed Gorham-Stout disease. The fractured vertebra had started to disappear. For this reason the patient had been treated with bisphosphonates (zoledronic acid, IV) for three years (2010 to 2013). But this treatment was not effective and the vertebra continued to disappear, resulting in a dislocation of the thoracic spine.

On admission, the patient had a pyramidal syndrome (bilateral Babinski sign and enhanced reflexes). Her visual analogic scale rated 7. CT scan and MRI showed major osteolysis of the fractured vertebra, resulting in an increased thoracic kyphosis (local kyphosis was up to 100°). EOS, a low dose radiation system (Eos imaging®, Paris, France) showed major sagittal imbalance with a C7 plumb line falling in front of the femoral heads (Figure1). The indication for surgery was based on the recent neurological symptoms, that cause important gait disturbance.

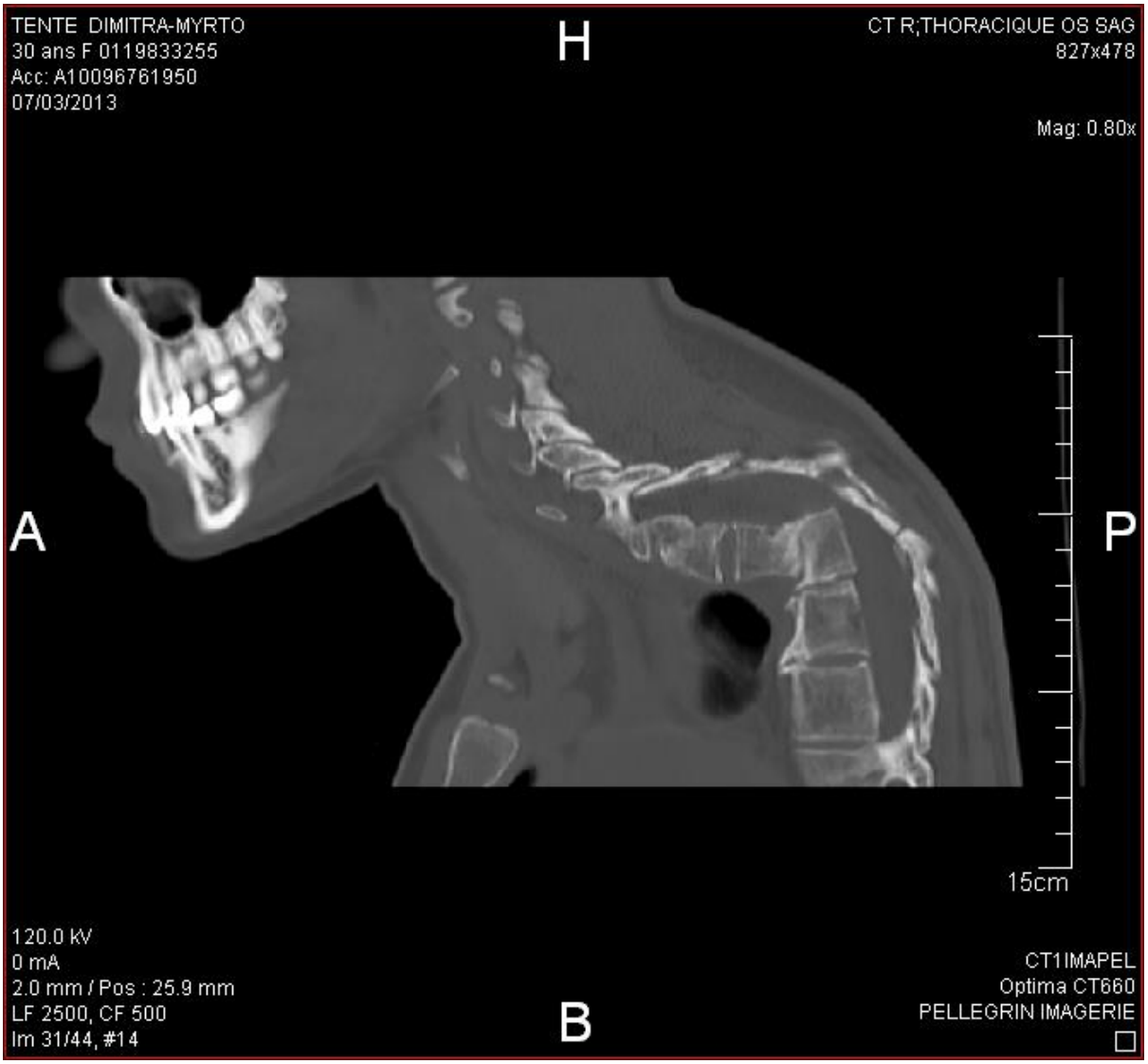
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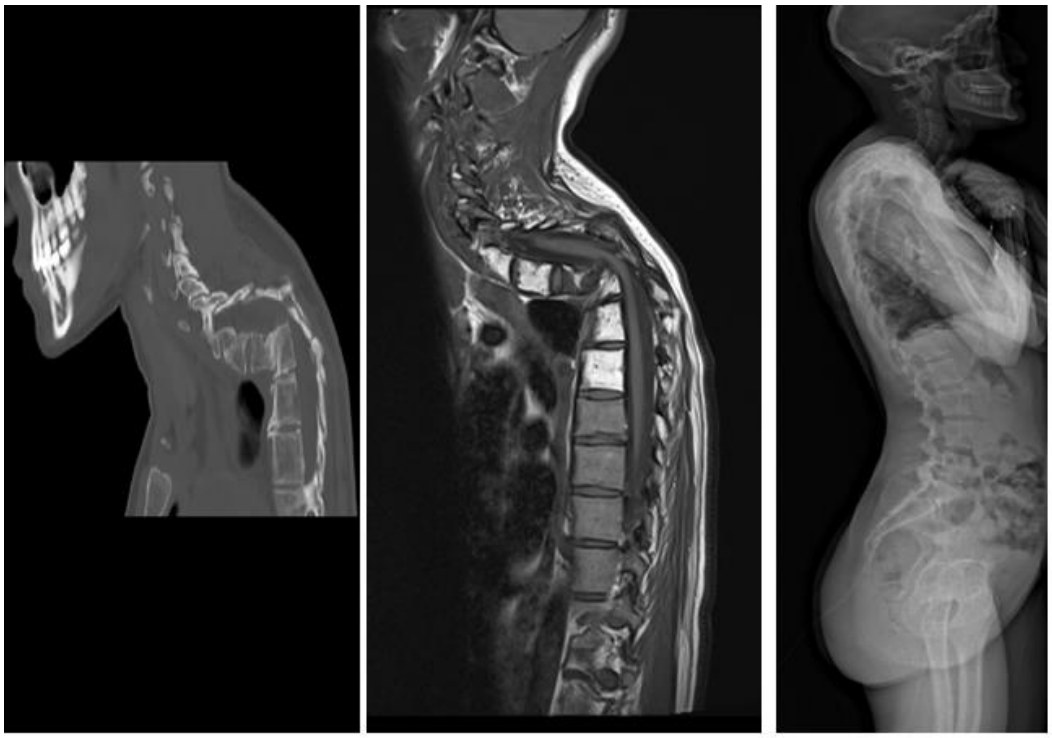
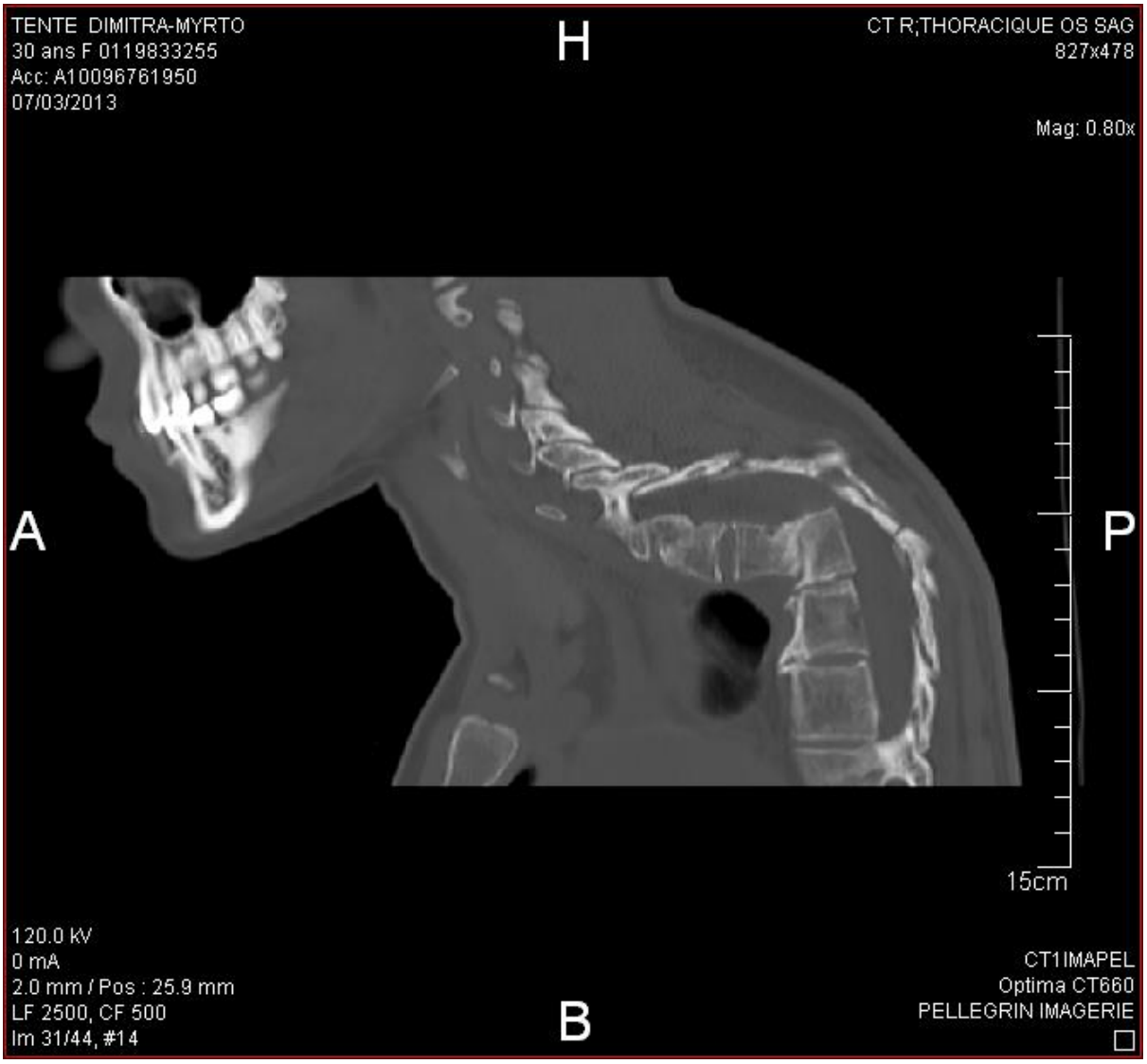
Figure 1: Pre-operative imaging: major local kyphosis and sagittal imbalance





We performed surgery using posterior approach combining pedicular fixation with screws and rods from T1 to T9, decompression and vertebral subtraction osteotomy of 65° using O-ARM® (Medtronic®, Minneapolis, USA) spinal cord monitoring (MEP, SSEP). To enhance the fusion in the face of the poor bone quality, a postero-lateral graft was made with local bone chips and BMP2. After surgery, the neurological status of the patient was improved. She had no further signs of spinal cord compression. Post-operative local kyphosis was measured at 55°. The patient was advised to wear a brace including a cervical collar for three months.

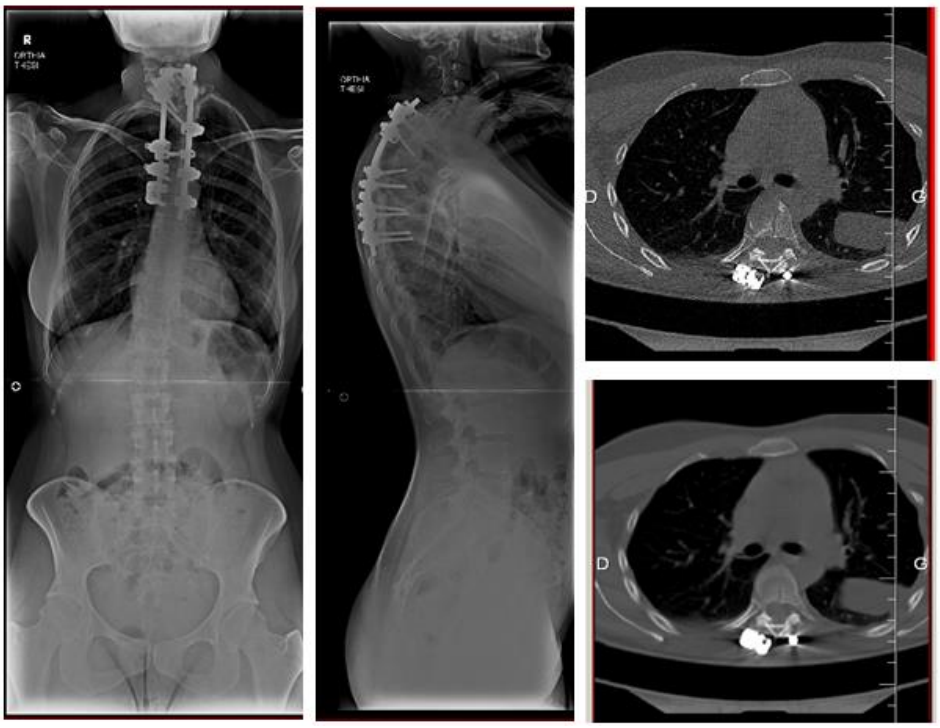
No post-operative complications were encountered. Immediate surgical outcome was good and the patient returned home after 24 days.

We chose not to treat the patient with medications such interferon alpha, because of the many adverse effects and also because this treatment has no proven efficacy.

At 6 and 12 months of follow-up, the patient was walking normally with no neurological sequelae, the visual analogic scale rated 2. The fracture site was pain-free and a brace was not used after the 3rd month (Figure 3). At 6 months, chylothorax was diagnosed after sudden onset of dyspnea. It was a medium-volume pleural effusion (less than a third of the left chest

cavity on CT-scan). The dyspnea was well controlled with a short oxygen therapy. The chylothorax resolved on its own without any surgical or medical treatment in two months.

Figure 3: Follow-up imaging at 6 months: consolidation and stabilization of the disease.



Discussion:

Gorham and Stout described a distinct histologic pattern that consisted of an abnormal increase in intraosseous capillaries, the absence of osteoclasts in the area of bone loss, and fibrosis. This was highlighted by Heffez et al. in 1983, who suggested the following diagnostic criteria:
1) The presence of angiomatous tissue in biopsy
2) Absence of cellular atypia
3) Minimal or no osteoblast response and no dystrophic calcification
4) Evidence of local progressive bone resorption
5) Non-expansile, non-ulcerative lesion
6) Absence of visceral involvement
7) Osteolytic radiographic pattern
8) Negative hereditary, metabolic, neoplastic, immunogenic, or infectious etiology

The primary involvement of the spine is less common (10%) and has been described in only about 20 cases. The progressive osteolysis causes kyphosis, kyphoscoliosis, subluxation or even dislocation of the spine. There is also infiltration of adjacent soft tissue which is destructive, but without evidence of malignancy. There are no general symptoms. Paraplegia may occur in patients with spinal cord compression due to vertebral involvement, and can increase mortality to over 30%.
Treatment of Gorham-Stout disease is difficult due to the variable natural history of the disease. Spontaneous arrest can be expected after an indeterminate period, and the disease then seems to remain stable indefinitely.

Many therapies have been proposed in addition to surgery (Table 1).

Table 1: Proposed therapies for Gorham-Stout syndrome

Reference	Sex; age	Localisation	Therapy	Follow-up	Result
Hagberg H, 1997	M; 19	cervical and thoracic spine	Interferon+bisphosphonate + radiotherapy	1.5 years	good
Mawk JR, 1997	M; 7	upper cervical spine	radiotherapy	unkown	good
Flörchinger A, 1998	F; 25	upper cervical spine	surgery	1 month	good
	F; 6	thoracic spine	surgery	1 year	good
Bode-Lesniewska B, 2002	F; 65	cervical and thoracic spine	radiotherapy +surgery	15 months	death
Leslie C, 2003	M; 49	cervical spine	surgery	1.5 years	good
Toshimi A, 2005	M; 10	thoracic spine	surgery + bisphosphonate	3 years	good
Bethany M, 2005	F; 31	thoracic and lumbar spine	radiotherapy	3 years	good
Takahashi A, 2005	F; 2	thoracic and lumbar spine	Interferon	10 months	good
Pfleger A, 2006	M; 18	chylothorax	Interferon + bisphosphonate	12 months	good
Lehmann G, 2008	F; 61	lumbar spine	bisphosphonate + radiotherapy	17 years	good
Kose M, 2009	F; 10	thoracic and lumbar spine	Interferon	6 months	good
Grunewald, 2010	M; 2,5	left clavicule	bevacizumab	27 months	good
Deveci M, 2011	M; 6	thoracic spine	Interferon+ bisphosphonate	4 months	ineffective
Brodszki N, 2011	F; 4	thoracic and lumbar spine	Interferon + radiotherapy	0.5 year	good
Silva S, 2011	F; 42	thoracic spine	bisphosphonate	6 months	good
Reinhard H, 2011	M; 38	upper cervical spine	radiotherapy	24 months	progression
	F; 61	lumbar spine	radiotherapy	204 months	progression
	F; 24	cervical spine	radiotherapy	46 months	progression
	M; 30	lumbar spine	radiotherapy	38 months	no progression
	M; 44	cervical spine	radiotherapy	54 months	no progression
	M; 46	lumbar spine	radiotherapy	12 months	no progression
Shimizu, 2012	F; 64	left hand	Interferon + bisphophonate	5 years	good

Surgical treatment alone [10–12]

Surgical strategies with resection of the lesions and bone reconstruction using grafts or protheses have been reported. Surgery, when possible, provides the best chance for cure. It is definitely indicated in cases of pathologic fracture. Immobilization of the affected bone does not impact prognosis. In most cases, after fusion, the disease remains stable after surgery, neuropathy is decreased and new bone is formed.

Bisphosphonates [13–16]

Some histologic studies have suggested that osteolysis is due to the increased number of stimulated osteoclasts and that early potent anti-osteoclastic therapy such as calcitonin or bisphosphonates may prevent local progressive osteolysis. Treatment with bisphosphonates may normalize serum levels of IL6, thus decreasing osteoclastic activity. Bisphosphonates are currently shown to be anti-angiogenic and able to induce apoptosis of tumor cells. Local or systemic administration of bisphosphonates has been proposed. Local administration produces fewer side effects, such as gastro-intestinal irritation, osteonecrosis of the jaw and ocular inflammation, but it is difficult to perform since a calcium phosphate ceramic is required as a drug delivery vehicle. Bisphosphonates are used primarily because of their sustained analgesic effect.

Radiation therapy [17,18]

Radiotherapy with moderate doses (40-45 Gy in 2 Gy fractions) seems effective in decreasing osteolytic activity, but response remains unpredictable. It may arrest endothelial cell proliferation and limit the progress of the disease. When many vertebrae are involved, radiation therapy should not be used because of later adverse effects, including induced secondary malignancy. The best time for starting radiotherapy is controversial.

Bevacizumab [19]

Other anti-angiogenic drugs such as bevacizumab, 10 mg/kg once/month IV, have been prescribed to decrease levels of circulating VEGF. To our knowledge, only one case has been published documenting this treatment with good results. However, it concerned a young child and there is no evidence to recommend this drug in adults.

Interferon alpha [6,20,21]

Cell cultures from a soft tissue lesion produced inflammatory cytokines, mainly IL6, TNFα, and VEGF. Interferon possesses marked anti-angiogenic properties and may be useful in vessel proliferation disorders by down-regulating VEGF expression, or by inhibiting proliferation and migration of lymphatic endothelial cells. It has a suppressive effect on the growth of both osseous and soft tissue lesions. Interferon must be taken for more than one year because the symptoms tend to improve 10 to 16 months after the start of treatment. This treatment also has a wide range of side effects, mostly hematological toxicity, hepatic toxicity, nausea, and psychiatric effects.

Combination therapies [22–24]

All these treatments may have an additive effect. Even if there is no proof of effect, radiotherapy is usually recommended for progressive and symptomatic localized lesions, whereas interferon may be the best choice for patients with extensive lesions. Bisphosphonates have an additive effect on the suppression and remodeling of osseous lesions. None of them has demonstrated its superiority over others (Table 2).

Table 2: Summary of the effect of each treatment

Intervention	Good results
Radiotherapy	2 of 2
Surgery	3 of 4
Interferon + bisphosphonate	1 of 2
Interferon	3 of 3
Bisphosphonate	1 of 2

Conclusion

We report a case of Gorham-Stout syndrome involving the thoracic spine that was successfully treated by transpedicular osteotomy with 12 months of follow-up. We suggest that this strategy can provide good results, because after fusion, the disease stabilized. Because of the lack of reported cases, surgeons must be careful when using multiple treatments, due to the adverse side effects of adjuvant therapies.

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