Interdisciplinary Neurosurgery 17 (2019) 79–83

Contents lists available at ScienceDirect

Interdisciplinary Neurosurgery

journal homepage: www.elsevier.com/locate/inat

Review Article

A rare case of spine disappearing bone disease: Lesson learned and review of the literature☆

G. Barbagli (M.D.)*, I. Barni (M.D.), S. Romoli (M.D.)

Spine Surgery Unit, Azienda Ospedaliero Universitaria Careggi, Firenze, Italy

ABSTRACT

Disappearing bone disease, also known as Gorham's disease, is a rare idiopathic musculoskeletal disorder characterized by clinical and radiological disappearance of bone caused by a proliferation of non-neoplastic vascular tissue. The disease was first reported by Jackson in 1838 in a boneless arm. Primary involvement of the spine is rare and has been described in about 20 cases only. Gorham's disease is progressive in most patients and high morbidity and mortality is seen in patients with spinal involvement. We present on a case of a thirty-two-year-old man admitted to our department for acute onset of paraplegia and sensitive anesthesia below T1 level; a CT scan showed a C6–C7 fracture of the body, involving the posterior elements and characterized by high instability with 20° of kyphosis. The patient underwent a C2-T7 posterior fixation. At the 3-month follow-up, the patient recovered partial motility on the lower limbs and the implant appeared stable. In general, no single treatment modality has proven effective in arresting the disease. Only eight cases have been treated by surgical fixation. In fact, the literature review we performed showed paucity concerning the correct treatment, in particular, the timing of surgery. In light of this and given the very poor prognosis once neurological deficits appear, we support the surgical treatment soon after the spinal deformity and/or impending fracture is diagnosed.

1. Introduction

Gorham-Stout's disease, also known as disappearing bone disease or phantom bone disease is an exceedingly rare musculoskeletal disorder characterized by bone resorption, not associated with bone formation and vascular or lymphatic vessel proliferation, and soft-tissue swelling. Virtually only the bone in the body could be involved, with a propensity for the shoulder and pelvic girdle but rarely the spine. The disease was first reported in 1883 by Jackson, who described a case of a “boneless arm” 12-year old boy with advanced osteolysis of the humerus. Generally, the disease progression is slow, nevertheless, prognosis remains unpredictable. Overall mortality is quite low (13%) but becomes significantly worse with the involvement of the spine (33%) or thorax (52%). Due to the rarity of this disease, treatment is based on the specific presentation, as long-term outcome data is not available in this population.

2. Materials and methods

We carried out complete literature review using key-words including “Gorham-Stout disease”, “disappearing bone disease”, “cervicothoracic fixation”, “vanishing bone disease” and “idiopathic osteolysis” on Pubmed and MEDLINE database. All reports in English were included in the present study. Data on age, gender, spine segment and level, medical comorbidities/complications and type of treatment were recorded. Regarding the case report, signed written consent was obtained from the patient for the publication of his case. Information on the presenting history, radiological appearance, surgical management, and pathological report of his CG, were collected from the medical records and directly obtained from the patient. We reviewed clinical notes and imaging reports, with the evaluation of short-term clinical follow-up of a single case of Gorham-Stout Disease treated at our institution.

3. Results

3.1. Patient's history, clinical status, and neuroimaging

A 32-year old male was admitted to our emergency department for acute onset of paraplegia and anesthesia on the lower limbs associated with paresthesia on the 4th and 5th fingers of the right hand.

The patient also reported priapism and hypoesthesia below T1 level. A CT scan previously performed at an outside hospital (3 months before) showed a C7 wedge-type fracture (Fig. 1). Probably due to the lack of symptoms and the gravity of the underlying vanishing bone disease, that fracture had been previously treated conservatively in other medical centers. In fact, the diagnosis of Gorham- Stout Syndrome was established three years ago on a histopathologic examination of a CT-

☆ The authors have nothing to declare.

* Corresponding author at: Azienda Ospedaliero-Universitaria Careggi, Largo Palagi 1, Firenze, Italy.
E-mail address: barbagli.giovanni@gmail.com (G. Barbagli).

https://doi.org/10.1016/j.inat.2019.03.001
Received 13 April 2018; Received in revised form 7 February 2019; Accepted 14 March 2019

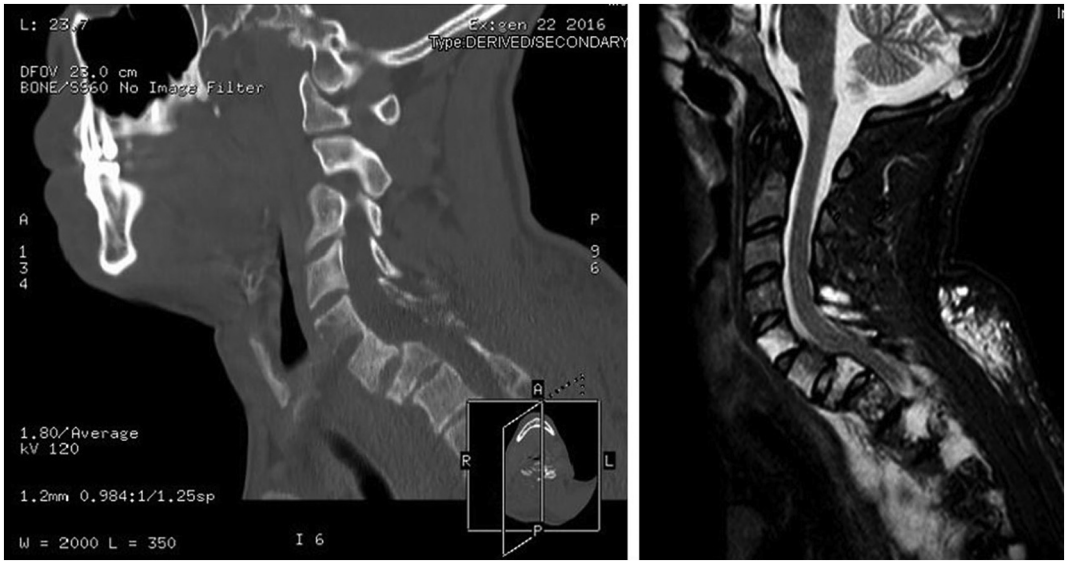

Fig. 1. The CT scan and the MRI scan, performed 4 months before the acute onset, show a C7 wedge fracture without clear signs of instability and myelopathy.

guided biopsy on the right shoulder.

The patient started, at the time, the medical therapy based on Sirolimus for > 6 months with no signs of regression.

At the admission to our department, the patient underwent a new CT scan, which depicted a dramatic worsening of the radiological picture with the appearance of sudden cervical instability and rising of kyphosis > 15° at the same level of the aforementioned fracture. An MRI was performed in order to assess the myelopathy and confirmed the severity of the cord compression (Fig. 2). At the examination, the patient showed reduced muscle tone, identified as Medical Research Council (MRC) power grade 3 on the upper extremities, slightly worse on the left side and paraplegia. Discriminative and non-discriminative touch anesthesia below T1 was observed. The patient's past medical history was remarkable for various episodes of chylothorax drained many times, elephantiasis on the lower limbs, multiple severe sepses and numerous events of cellulitis wavered in lumber abscess treated by surgery.

3.2. Surgery

The patient was administered general anesthesia and a posterior screw fixation from C2 to T7, with multiple osteotomies, and open reduction of the fracture, was performed (Fig. 3). This very long construct was necessary in order to get the proper stabilization and the correction of the cervical kyphosis. The proximal and distal extents of the construct are explained by the intention of bypassing the involved vertebral segments and the necessity to find solid anchor points for pedicle screws. During surgery, it was noted the C7 bone quality was soft and spongy. The vertebral body had a very thin cortex, especially on the cervical tract as well as the vascularity of the bone itself. Moreover, we observed an important diffuse alteration of the posterior vertebral elements that forced us to skip some screws during the operation. The muscolo-tendineus posterior tissue appeared widely swelled and a serum-like fluid mixed to thin blood spilled out from angiomatous-like lesions spreading throughout the subcutaneous tissue. All placed screws were verified to be firmly attached to the bone. The X-ray, performed

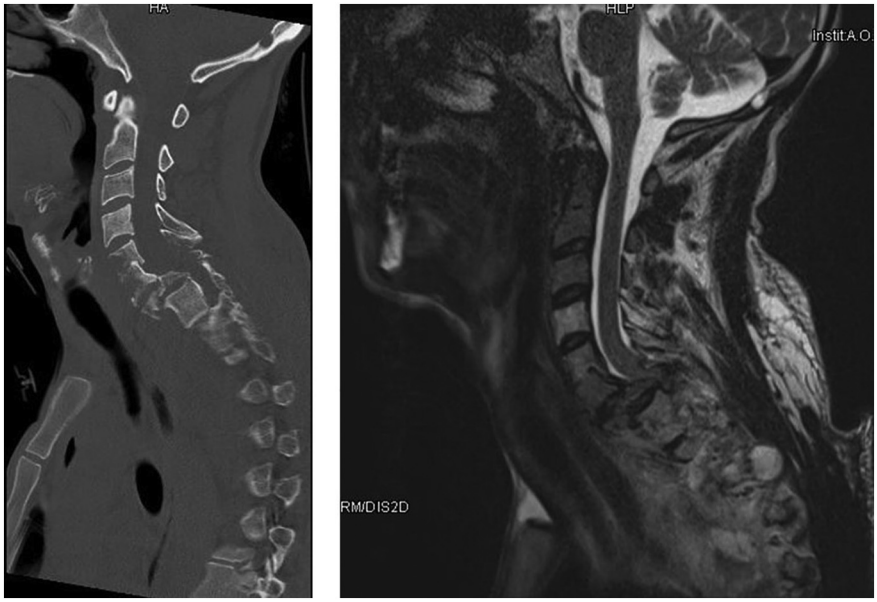

Fig. 2. The CT scan and the MRI, performed at the access to ER, show a severe worsening of the picture either on the entity of the fracture and on the presence of kyphosis (> 15°).

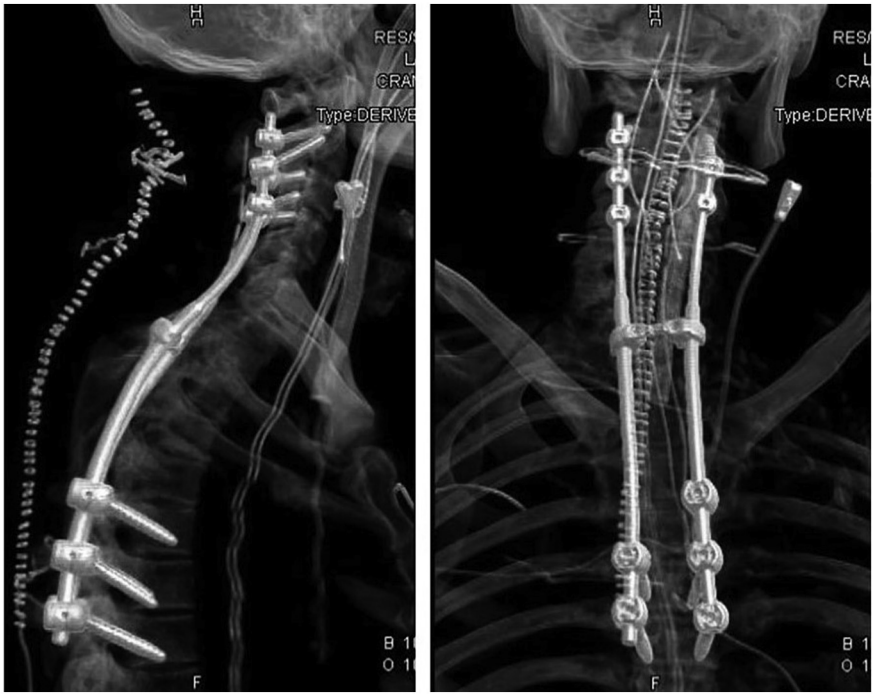

Fig. 3. The 3-D reconstruction shows the C2-T7 posterior fixation with multiple osteotomies.

immediately after the procedure, verified correct screws positioning.

3.3. Post-operative course

Following the procedure, the patient was transferred to the Neuro-intensive Care Unit. The awakening from the anesthesia was gradual but good. The patient's post-operative neurologic improved slightly, in particular on the upper limb's strength. The MRC strength grade improved to 4 in the right upper arm and to 3 in the left. The patient remained, instead, paraplegic. Full blood count, inflammatory markers and autoantibodies screen were all normal. One week postoperative, a progressive increase of the lymphatic collection in both lungs, especially on the left side was noticed and the patient underwent pleurectomy and decortication of the left lung. The post-operative course was satisfactory and at 3-month follow-up, the chylothorax appeared stable as well as the implanted screws. At 4-month post-operative, the patient began physical therapy and rehabilitation until the appearance of septic shock, a few weeks later. The patient and his family were informed that the data from this case would be submitted for publication, and the patient provided his consent. The patient died 10 months after surgery in the Intensive Care Unit, following cardio-respiratory distress.

4. Discussion

In the current literature, we were able to identify > 60 cases of spinal involvement in Gorham- Stout Disease, 17 with cervical involvement were found [1]. Of these, 9 cases were treated by surgery but only 8 reported the patient undergoing fusion (Table 1). To our knowledge, we present the 9th known case. The pathological process is, still, poorly understood [1–23], and as Gorham and Stout first described in the early 1950s the vanishing bone disease “is usually associated with angiomatosis of blood vessels and sometimes of lymphatic vessels, which seemingly are responsible for it” [6]. In point of fact, one of the main features is the presence of unusually wide capillary-like vessels, as we documented intraoperatively, where the blood flow is reasonably slow; that feature may lead to local hypoxia and the lowering of the pH with subsequent activation of hydrolytic enzymes [3].

As many authors reported, the pathological process could be based on that mechanism resulting in a progressive replacement of normal bone by an aggressively expanding but non-neoplastic vascular tissue [3,4,6–9]. This process can affect one or multiple bones in axial or appendicular skeleton; the most common site of involvement is the shoulder, followed by the pelvis, the ribs, and the skull [1,12]. Spine involvement is much more uncommon and tends to make the prognosis more severe [1]. The disease has not well-defined age or gender relation as well as race or geographic one. Clinical manifestations vary and depend on the affected site. The symptoms' spectrum includes pain, functional impairment and swelling on the affected region [6]. The probably most important issue of the Gorham-Stout disease is the complications of the syndrome.

The pleural effusion and chylothorax (which complicated the syndrome in > 15% of cases [15]) can dramatically influence the respiratory function and represent a life-threating situation [15]; tetra or paraplegia, as consequence of spinal cord involvement, may occur in patients who have involvement of the cervico-thoracic vertebrae with resultant osteolysis [6,8,16]. The involvement of the thoracic spine and the subsequent extension of lymphangiectasia into the pleural cavity or by the invasion of the thoracic duct could explain the pathological fundamental of the chylothorax [9,16]. The natural history of Gorham's disease is unpredictable and, in some cases, spontaneous regression has been reported [5,16,17]. As mentioned before and documented by many authors, the spinal involvement is usually associated to a poor prognosis [1,6]. Especially, the spinal and chest involvement are the most frequent causes of death in patients with Gorham's disease [15,16]. The affection of the spine leads to neurological decline, which is the main cause for the patient immobilization and the subsequent comorbidities. According to the literature, there is no evidence on which could be the best treatment, either single or a combination of multiple therapies. In fact, therapeutic modalities encompass operative and non-operative options, like radiation therapy, anti-osteoclastic medications as bisphosphonates, alpha-2 interferon, anti-VEGF-A antibody or the mammalian target of rapamycin (mTOR) inhibitor, Sirolimus [2,3,5,6,10,16,22,23].

Our review demonstrated that these modalities occasionally don't lead to satisfactory results, especially if used in single-modality fashion

Table 1
Literature review of the nine cases treated by surgery.

Case	Author	Age/sex	Spine segment/level	Complications	Medical treatment	Surgical treatment	Outcome
1	Schell et al. [1]	31 y.o./W	C1, C2, C3, C4	N/A	No	Occiput-T2 posterior + C2-T2 anterior	NDP
2	Ganal-Antonio et al. [3]	14 y.o/W	C7-T1	Yes	No	1° C5-T3 posterior fusion + C6-T2 anterior fusion 2° C2–C5 anterior fusion + C1–C5 posterior fusion 3° Occiput-C1 posterior + T3–T9 posterior fusion 4° T9–T11 posterior fusion	Death
3	Gabriel David et al.	23 y.o./M	T1–T2	Yes	No	C4-T5 posterior fusion	Neurological deficits but NDP
4	Ozawa et al. [10]	15 y.o./M	C1–C5	No	RT + CHT	C2–C5 anterior fusion	NDP
5	Kohno et al. [16]	27 y.o/M	C2	YES	RT + ASH + IVZ	1° C1–C2 laminectomy + suboccipital decompression + halo brace 2° Occiput-C5 posterior fusion 3° transoral odontoidectomy + C2–C3 vertebrectomy	NDP
6	Chong Ng et al. [17]	49 y.o/M	C2-C3	YES	N/A	1° occiput-C6 posterior decompression and fusion 2° C3–C5 anterior fusion with iliac crest 3° C2–C5 revision surgery from posterior 4* anterior revision surgery with cage 5° posterior revision surgery	NDP
7	Sferopoulos et al. [19]	2 y.o/M	C1–C2	YES	N/A	1° C1–C2 laminectomy 2° multiple surgeries	Death
8	Girn et al. [20]	2 y.o./W	Occiput-C1	N/A	Pamidronate + RT	Laminectomy	N/A
9	Lekovic et al. [21]	10 y.o./M	Clivus + petrous + C1–C2	YES	Halo vest + RT	Occiput-C4 posterior fusion + transoral odontoidectomy	Neurological deficits

Complications: either peri-operative and post-operative, N/A: not available, NDP: no disease progression, RT: radiotherapy, CHT: chemotherapy, IVZ: intravenous zolendronic acid, ASH: alendronate sodium hydrate.

and radiotherapy should be proposed only for poor surgical candidates [18] as well as the medical therapy has only to be initiated preferentially in patients with no spinal deformity [2,3,16]. Even if, as mentioned by many authors [18], these conservative procedures, in some cases, halt the progression of the disease [22,23], the correct dose and the posology either for the medical treatment and for radiotherapy are far to be well defined [12,22]; hence the utility of these conservative therapies as the unique approach to the disease is questionable. Not surprisingly, the medical therapy started by our patient did not gain a satisfactory regression of the osteolytic process and the choice of conservative treatment led to the progression of the disease and to an acute onset of the severe neurological complications.

Furthermore, in the review of the literature we performed, we have observed a trend in holding up the surgical treatment, even if a spinal deformity is diagnosed, primarily because the patient is still neurological silent. Thus, we could assert that the vast majority of surgeries were performed as “last hope” when the spinal deformity was already determined, the other therapeutic modalities failed and the patient showed neurological signs of severe myelopathy. In our opinion, this trend is at least arguable.

Unlike the other manuscripts about this severe disease, we discuss here for the first time to our knowledge, the timing of spinal surgery rather than the choice between medical or non-medical therapy. Some authors propose a conservative treatment, once the spinal deformity has appeared but the patient is still clinical silent, in order to arrest the progression of the bony reabsorption. As reported, we have to clarify that this disease could also affect the posterior elements as the muscolotendineus-ligamentous part of the spine which are widely recognized as key factors in maintaining the spine stability [10]. Actually many articles maintain the stability of spinal construct. Moreover, as pointed out in literature, we have to consider that as soon as a spinal deformity appears the patient will likely show neurological symptoms and will easily develop comorbidities [10,16]. Notably, there are authors reporting the fact that, when spinal fixation is performed, the patient will undergo a better clinical outcome [1].

Considering all these findings, it is evident that spine fusion surgery is at least reasonable when performed in the case of spine deformity occurred even if the patient is clinically silent. In this state, some attention has to be taken: first, it is mandatory explaining to the patient the reasons why he or she should have a surgery without clinical issues and focusing on the potential benefit in avoiding the severe neurological complications in case of spinal instability; secondly the choice of the right modality of surgical treatment is crucial.

As it has recently been reported, a general rule to be accepted should be that of performing spinal fusion with the construct as long and as strong as possible [15]. Indubitably, this concept comes along with the right choice of the anchor points to the spine. The Gorham's disease leads to the disruption of all the bony elements of the spine; even though many of these elements are not directly involved in the spine instability of that patient, inserting pedicle screws in those elements could in part explain the relatively high rate of hardware failure found in the literature. We admit this manuscript presents some bias. First, it is a case report and our experience with Gorham-Stout Disease is limited; secondly, even though the patient had started physical rehabilitation very soon without any concern, died 10 months after surgery and the follow-up is not long enough to test the long-term stability of the construct. Nevertheless, we are persuaded that the spinal fusion, performed by an expert surgeon, with a long construct on the well-chosen anchor points, could represent a reasonable choice in trying to prevent much more severe complications in this disease, far to be fully understood.

5. Conclusion

Given our experience, the literature review and the lack of strong evidence supporting the medical treatment as the best choice of treatment, we suggest an “early surgery” in cases with spinal deformity and/or impending fracture. Once a severe neurological deficit occurs, these patients often develop a severe pulmonary complication such as pleural effusion or chylothorax which make the prognosis much more severe. When the correct surgery is performed in the right anchor points to the non-involved vertebrae, despite the severe osteolysis of the Gorham's

disease, the relatively long-term stability of the spinal fixation system may represent the key to protecting the patient from severe neurological sequelae of spinal involvement.

References

[1] A. Schell, J.M. Rhee, A. Allen, L. Andras, F. Zhou, Surgical management of Gorham disease involving the upper cervical spine with occipito-cervical-thoracic fusion: a case report, Spine J. 16 (7) (2016 Jul) e467–e472, https://doi.org/10.1016/j.spinee.2016.02.020 (Epub 2016 Mar 11).

[2] T. Aizawa, T. Sato, S. Kokubun, Gorham disease of the spine: a case report and treatment strategies for this enigmatic bone disease, Tohoku J. Exp. Med. (2) (2005) 187–196 Feb.

[3] Anne Kathleen Ganal-Antonio, MD, Dino Samartzis, DSc, Cora Bow, MCMSc, BHS, Kenneth M.C. Cheung, MBBS, MD, FRCS, FHKCOS, et al. Disappearing bone disease of the humerus and the cervico-thoracic spine: a case report with 42-year follow-up. Spine J. 16 (2016) e67–e75 (Case Report).

[4] B. Bode-Lesniewska, A. von Hochstetter, G.U. Exner, J. Hodler, Gorham-Stout disease of the shoulder girdle and cervico-thoracic spine: fatal course in a 65-year-old woman, Skelet. Radiol. 31 (2002) 724–729, https://doi.org/10.1007/s00256-002-0568-y.

[5] C. Maillot, T. Cloche, J.-C. Le Huec, Thoracic osteotomy for Gorham-Stout disease of the spine: a case report and literature review, Eur. Spine J. (2014), https://doi.org/10.1007/s00586-014-3613-3.

[6] Dipak V. Patel, MD, MSc Orth, MS Orth, FCPS. Gorham's disease or massive osteolysis. Orth. Clinical Medicine & Research Volume 3, Number 2: 65–74.

[7] Samson Lee, MD; Laura Finn, MD; Raymond W. Sze, MD; Jonathan A. Perkins, MD; Kathleen C. Sie, MD. Gorham stout syndrome (disappearing bone disease). Two additional case reports and a review of the literature. Arch Otolaryngol Head Neck Surg. 2003;129(12):1340–1343. doi:https://doi.org/10.1001/archotol.129.12.1340.

[8] Vasileios S. Nikolaou, Dimitrios Chytas, Demitrios Korres, Nicolas Efstathopoulos, Vanishing bone disease (Gorham-Stout syndrome): a review of a rare entity, World J Orthop 2218-5836, 5 (5) (2014 November 18) 694–698 (online).

[9] Vijay Sekharappa, Justin Arockiaraj, Rohit Amritanand, Venkatesh Krishnan, Kenny Samuel David, Sundararaj Gabriel David. Gorham's disease of spine. Asian Spine J 2013;7(3):242–247.

[10] Satoshi Tateda, Toshimi Aizawa, Ko Hashimoto, Haruo Kanno, Susumu Ohtsu, Eiji Itoi, Hiroshi Ozawa, Successful Management of Gorham-Stout Disease in the CervicalSpine by combined conservative and surgical treatments: ACase report, Tohoku J. Exp. Med. 241 (4) (2017) 249–254, https://doi.org/10.1620/tjem.241.249 Apr.

[11] Gedam PN, A.C. Dhamangaonkar, A.N. Parekh, A rare case of progressive Gorham's disease of right shoulder girdle and cervical spine in a child: 10 year follow-up and a review of literature, Journal of Orthopaedic Case Reports 5.4 (2015) 30–33 (PMC. Web. 8 Oct. 2017).

[12] P. Hu, X. Yuan, X. Hu, F. Shen, J. Wang, Gorham-Stout syndrome in mainland China: a case series of 67 patients and review of the literature, J Zhejiang Univ Sci B 14 (8) (2013) 729–735, https://doi.org/10.1631/jzus.B1200308.

[13] S.F. Dunbar, A. Rosenberg, H. Mankin, D. Rosenthal, H.D. Suit, Gorham's massive osteolysis: the role of radiation therapy and a review of the literature, Int. J. Radiat. Oncol. Biol. Phys. 26 (3) (1993) 491–497 Jun 15.

[14] E. Carbó, Ó. Riquelme, A. García, J.L. González, Vertebroplasty in a 10-year-old boy with Gorham-Stout syndrome, Eur. Spine J. 24 (Suppl. 4) (2015 May) S590–S593, https://doi.org/10.1007/s00586-015-3764-x (Epub 2015 Jan 14).

[15] Sell P. Expert's comment concerning grand rounds case entitled “Thoracic osteotomy for Gorham-Stout disease of the spine: a case report and literature review” by C. Maillot et al.,Eur Spine J: doi https://doi.org/10.1007/s00586-014-3613-3. Eur. Spine J. DOI https://doi.org/10.1007/s00586-017-5122-7.

[16] Motonori Kohno, Yoichi Aota, Takuya Kawai, Hidetoshi Murata, Tomoyuki Saito, Surgical treatment of Gorham's disease with massive osteolysis of the skull and cervical spine: a case report and review of literature, NMC Case Report Journal 2 (2015) 80–84.

[17] Leslie Chong Ng, MRCS, and Phillip Sell, FRCS Gorham Disease of the Cervical Spine—A Case Report and Review of the Literature SPINE Volume 28, Number 18, pp E355–E358 ©2003, Lippincott Williams & Wilkins, Inc.

[18] S.K. Srivastava, R.A. Aggarwal, P.S. Nemade, S.K. Bhoale, Vanishing bone disease of chest wall and spine with kyphoscoliosis and neurological deficit: a case report and review of literature, Indian Journal of Orthopaedics 51 (1) (2017) 107–114, https://doi.org/10.4103/0019-5413.197559.

[19] N. K. Sferopoulos, D. Anagnostopoulos, J. K. Webb Cystic Angiomatosis of Bone with Massive Osteolysis of the Cervical Spine. Eur. Spine J. (1998) 7: 257–259 © Springer-Verlag 1998.

[20] H.R.S. Girn, G. Towns, P. Chumas, P. Holland, A. Chakrabarty, Gorham's disease of skull base and cervical spine – confusing picture in a two-year-old, Acta Neurochir. 148 (2006) 909–913, https://doi.org/10.1007/s00701-005-0806-x Case Report.

[21] Lekovic GP, Mariwalla NR, Horn EM, Chang S, Rekate HL, Theodore N. Skeletal dysplasia involving the subaxial cervical spine report of two cases and review of the literature. Neurosurg. Focus. 20 (2): E8, 2006.

[22] Vanessa García, Gloria Alonso-Claudio, M-Teresa Gómez-Hernández, Antonio-J Chamorro, Sirolimus on Gorham-Stout disease. Case report, Colomb Med (Cali) 47 (4) (2016 Oct-Dec) 213–216.

[23] Stuart L. Cramer, DO, Shi Wei, MD, Ph.D., Arnold C. Merrow, MD, and Joseph G. Pressey, MD. Gorham-stout disease successfully treated with sirolimus and zoledronic acid therapy. J. Pediatr. Hematol. Oncol. 2016 Apr;38(3):e129–32. doi: 10.1097/MPH.0000000000000514.