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Systematic Review
Clinical Pathology

Gorham–Stout disease with involvement of the jaws: a systematic review

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Abstract. The purpose of this study was to systematically review all published cases of Gorham–Stout disease (GSD) involving the jaws and to identify the clinico-radiological and histopathological features associated with persistence of the lesions, as well as the best treatment options available. An electronic search was undertaken in November 2018. Eligibility criteria included publications with sufficient information to confirm the diagnosis. Eighty-six publications reporting 89 cases were included. Features observed included symptomatic disease (51.1%), swelling (34.1%), pathological fracture (31.8%), history of previous trauma (32.1%), high alkaline phosphatase levels (24.3%), and predominance of vascular tissue (72.4%). Nearly a quarter of the patients were only followed up, with no treatment implemented. Most treatments consisted of some type of surgery with/without additional therapies (42.0%), drugs (20.5%), and radiotherapy (14.8%). Half of the cases were found to persist after some treatment modality, and five patients died. Among the variables investigated, only a lesion crossing the midline showed an association with persistence of the disease. There remains much to understand about GSD, a rare condition with no clear consensus on the aetiopathology, an unpredictable clinical course, and no standard treatment. The high rate of persistence after treatment was found to be associated only with the lesion crossing the midline.

Key words: Gorham–Stout disease; massive osteolysis; jaw; clinical features; treatment; persistence following treatment.

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Gorham–Stout disease (GSD), also called Gorham disease or vanishing bone disease, among many other names, is an extremely rare bone disease of unknown aetiology. The clinical progression and prognosis is unpredictable, and treatment is uncertain. Resorption, initially localized to one bone, often extends to involve those adjacent[1]. The lesions of this condition are histopathologically characterized by extensive loss of bony matrix replaced by a proliferation of thin-walled capillary-sized vascular channels, and at a later stage by fibrous connective tissue[2]. The first case reported in the literature was in 1838[3], involving an arm. GSD with involvement of the jaws is considered to be a rare condition, with the first case being reported in the literature in 1924[4].

The aim of this study was to integrate the available data published in the literature on GSD involving the jaws into an updated comprehensive comparative analysis of its features, as well as to identify

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the clinico-radiological and histopathological features associated with persistence of the disease. An analysis of the literature regarding the best treatment options available for this condition was also performed.

Materials and methods

This study followed the PRISMA Statement guidelines[5].

Search strategies

An electronic search without time restrictions was undertaken in November 2018 in the following databases: PubMed/MEDLINE, Web of Science, Science Direct, J-Stage, and LILACS. The following terms were used in the search strategies: (''Gorham disease'' OR ''Gorham's disease'' OR ''Gorham-Stout disease'' OR ''Gorham Stout disease'' OR ''Gorham syndrome'' OR ''Gorham's syndrome'' OR ''Gorham-Stout syndrome'' OR ''Gorham Stout syndrome'' OR ''massive osteolysis'' OR ''idiopathic massive osteolysis'' OR ''disappearing bone disease'' OR ''vanishing bone disease'' OR ''vanishing bone disorder'' OR ''phantom bone disease'') AND (mandible OR maxilla OR jaw OR maxillofacial OR face).

Google Scholar was also checked. A manual search of all related oral pathology, maxillofacial, and specialist dental and oral journals was performed. The reference lists of the identified studies and relevant reviews on the subject were also checked for possible additional studies. Publications with lesions identified by other authors as being GSD, even not having the term 'Gorham disease' in the title of the article, were also re-evaluated by one of the present study authors (R.S.G.).

Inclusion and exclusion criteria

Publications reporting cases of patients with GSD with involvement of at least one of the jaws and with enough information to confirm the diagnosis were included. The criteria listed by Heffez et al.[6], with minor modifications, were used to diagnose a patient with GSD: (1) biopsy showing angiomatous tissue or fibrous connective tissue; (2) absence of cellular atypia; (3) minimal or no osteoclastic response and absence of dystrophic calcifications; (4) evidence of progressive local bone resorption; (5) the lesion is not ulcerative and does not provoke cortical expansion; (6) absence of visceral involvement; (7) osteolytic radiographic pattern; (8) negative hereditary, metabolic, neoplastic, immunological, and infectious aetiology; (9) monocentric occurrence.

Study selection

The titles and abstracts of all reports identified through the electronic searches were read independently by the authors. For studies appearing to meet the inclusion criteria, or for which there were insufficient

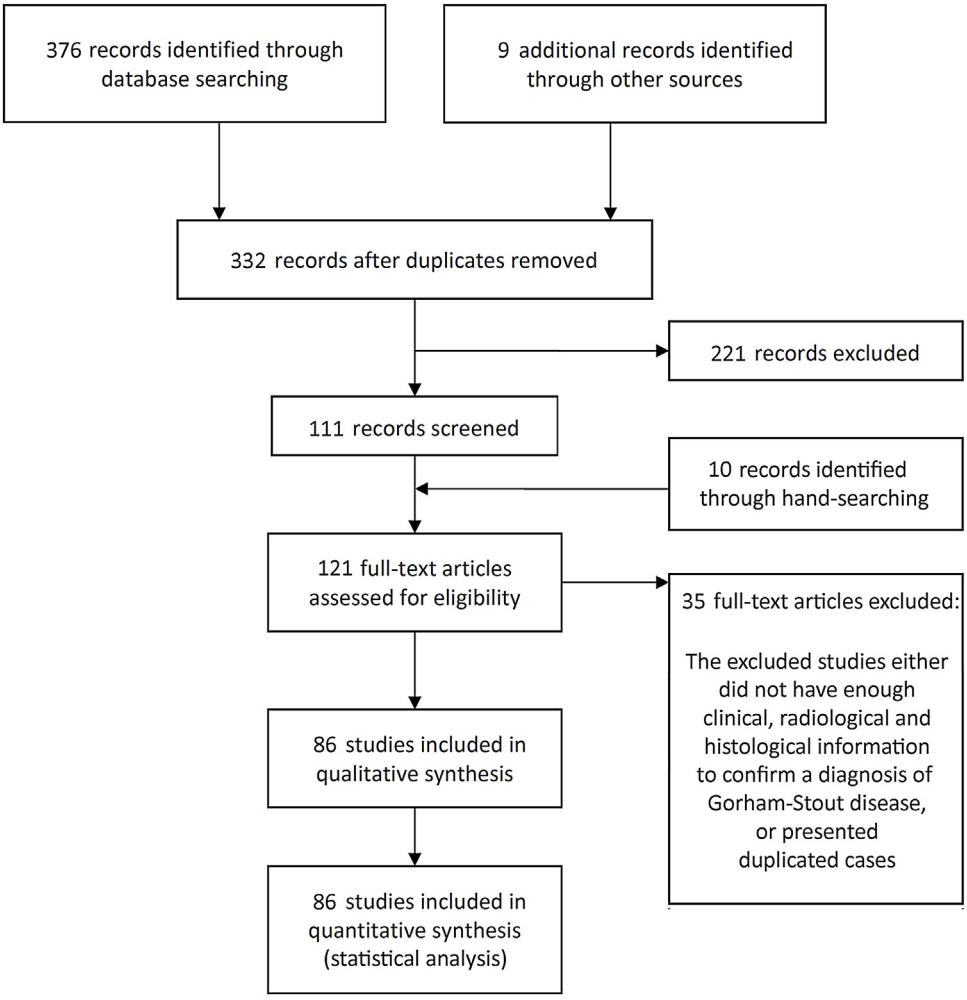

Fig. 1. Study screening process.

data in the title and abstract to make a clear decision, the full report was obtained. Disagreements were resolved by discussion between the authors. The clinical and radiological aspects, as well as the histological description of the lesions reported in the publications were thoroughly assessed by one of the authors (R.S.G.), an expert in oral pathology, in order to confirm the diagnosis of GSD.

Data extraction

The following data were extracted: patient's sex and age, duration of the lesion prior to treatment, history of previous (local) facial trauma, lesion location (maxilla/mandible), involvement of other/adjacent bones (mono- or polyostotic involvement), pathological fracture of the jaw bones, cortical bone destruction, presence of swelling, clinical symptoms, involvement of skin, levels of alkaline phosphatase in serum, histopathological appearance of the tissue obtained from the last surgery (predominance of either vascular or fibrous tissue), treatment performed, persistence of bone resorption, and follow-up period. Authors were contacted for possible missing data.

Analyses

A descriptive analysis was performed based on mean, standard deviation (SD), and percentage values. The Kolmogorov–Smirnov test was used to test the normality of the distribution of variables and Levene's test was used to evaluate homoscedasticity. The Student *t*-test or Mann–Whitney test was performed to compare two independent groups, depending on the normality of the data. The Pearson χ^2 test or Fisher's exact test was used for categorical variables, depending on the expected count of events in a 2×2 contingency table. Whenever possible, the probability of persistence of bone resorption after treatment was calculated using the odds ratio (OR) and 95% confidence interval (95% CI). The level of statistical significance was set at $P < 0.05$. All data were analyzed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA).

Results

Literature search

The study selection process is summarized in Fig. 1. The search strategy in the databases resulted in 376 papers; nine additional eligible papers were found through

Table 1. Demographic and clinical features of cases of Gorham–Stout disease involving the jaws described in the literature.

Variables	
Number	89
Age (years), mean ± SD (range)	31.7 ± 18.4 (0–76; *n* = 88)
Male	32.4 ± 18.1 (5–76; *n* = 54)
Female	31.2 ± 18.8 (6–72; *n* = 32)
P-value[a]	0.792
Sex, *n* (%)	
Male	55 (63.2)
Female	32 (36.8)
Unknown	2
Involvement, *n* (%)	
Monostotic	56 (62.9)
Polyostotic	33 (37.1)
Unknown	0
Jaw, *n* (%)	
Maxilla	6 (6.7)
Monostotic	2 (2.2)
Polyostotic (but not affecting the mandible)	4 (4.5)
Mandible	64 (71.9)
Monostotic	54 (60.7)
Polyostotic (but not affecting the maxilla)	10 (11.2)
Maxilla + mandible	19 (21.4)
Unknown	0
Other bones involved, *n* (%)[b]	
Zygomatic	15 (16.9)
Pterygoid	5 (5.6)
Sphenoid	8 (9.0)
Frontal	4 (4.5)
Orbit	9 (10.1)
Temporal	15 (16.9)
Occipital	6 (6.7)
Parietal	4 (4.5)
Hyoid	2 (2.2)
Cervical vertebrae	7 (7.9)
Skull base	14 (15.7)
Lesion crossed the midline, *n* (%)	
Yes	45 (50.6)
No	44 (49.4)
Unknown	0
Cortical bone perforation, *n* (%)	
Yes	85 (97.7)
No	2 (2.3)
Unknown	2
Swelling, *n* (%)	
Yes	30 (34.1)
No	58 (65.9)
Unknown	1
Symptomatic, *n* (%)	
Yes	45 (51.1)
No	43 (48.9)
Unknown	1
Alkaline phosphatase levels, *n* (%)	
High	9 (24.3)
Normal	28 (75.7)
Unknown	52
Pathological fracture (jaws), *n* (%)	
Yes	28 (31.8)
No	60 (68.2)
Unknown	1
Histology of last surgery, *n* (%)	
Fibrous	19 (25.0)
Vascular	55 (72.4)
Fibrous/vascular	2 (2.6)
Unknown	13
History of previous trauma, *n* (%)	
Yes	9 (32.1)
No	19 (67.9)
Unknown	61

Table 1 (*Continued*)

Variables	
First treatment, *n* (%)	
None	20 (22.7)
Debulking	1 (1.1)
Curettage	3 (3.5)
Enucleation	1 (1.1)
Marginal resection	5 (5.7)
Segmental resection[c]	5 (5.7)
Segmental resection[c] + radiotherapy	1 (1.1)
Segmental resection[c] + drugs	1 (1.1)
Segmental resection[c] + reconstruction plate	3 (3.5)
Segmental resection[c] + autogenous graft + reconstruction plate	6 (6.8)
Radiotherapy	13 (14.8)
Autogenous graft	7 (8.0)
Alloplastic graft + reconstruction plate	1 (1.1)
Reconstruction plate + drugs	1 (1.1)
Reconstruction plate	1 (1.1)
Drugs	18 (20.5)
'Surgery'	1 (1.1)
Unknown	1
Persistence of resorption after first treatment, *n* (%)	
Yes	37 (51.4)
No	35 (48.6)
Unknown	17
Death, *n* (%)	
Yes	5 (5.6)
No	84 (94.4)
Unknown	0
Duration of symptoms until first consultation (months), mean ± SD (range)	41.9 ± 47.3 (1–204; *n* = 57)
Time between biopsy and first treatment (months), mean ± SD (range)	10.0 ± 22.5 (0–144; *n* = 47)
Follow-up time after first treatment (months), mean ± SD (range)	39.4 ± 48.8 (0–300; *n* = 73)
Total follow-up time (months), mean ± SD (range)	47.1 ± 49.7 (1–300; *n* = 73)

SD, standard deviation.
[a] Comparison of the mean age between male and female patients (Mann–Whitney test).
[b] Percentage in relation to the total number of cases (*n* = 89).
[c] Resection with continuity defect.

Table 2. Persistence of resorption—for the lesions with available information about treatment and persistence of resorption.

Treatment	Persistence of resorption/total (% persistence)
None	7/11 (63.6)
Debulking	0/1 (0)
Curettage	3/3 (100)
Enucleation	0/1 (0)
Marginal resection	2/4 (50)
Segmental resection[a]	2/5 (40)
Segmental resection[a] + reconstruction plate	2/3 (66.7)
Segmental resection[a] + autogenous graft + reconstruction plate	1/6 (16.7)
Autogenous graft	5/6 (83.3)
Alloplastic graft + reconstruction plate	1/1 (100)
Reconstruction plate	0/1 (0)
'Surgery'	1/1 (100)
Surgical	17/32 (53.1)
Reconstruction plate + drugs	0/1 (0)
Segmental resection[a] + drugs	1/1 (100)
Surgical + drugs	1/2 (50)
Drugs	10/15 (66.7)
Radiotherapy	2/12 (16.7)
Total	37/72 (51.4)

[a] Resection with continuity defect.

Google Scholar and 10 papers through hand-searching. Finally, a total of 86 publications reporting 89 cases were included for analysis (**Supplementary Material**, File S1).

Description of the studies and analyses

Table 1 presents the demographic and clinical features of all 89 cases of GSD with involvement of at least one of the jaws. The mean (± SD) age of the patients was 31.7 ± 18.4 years, and nearly two-thirds of them were male. Thirty-three patients presented polyostotic GSD, in which adjacent bones were involved. Concerning the jaws, the maxilla was the only jaw bone involved in six patients, the mandible was the only jaw bone involved in 64 patients, and both jaw bones were involved in 19 patients. In 50% of the cases, the lesion crossed the midline of the body. Cortical bone perforation was observed in almost all cases. Half of the patients were symptomatic, about one-third presented swelling at the lesion site, about one-third presented pathological fracture of the involved jaw during the course of the disease, about one-third of the patients had a history of previous trauma, and approximately a quarter of the patients had high levels of alkaline phosphatase. On histopathological analysis of the samples obtained from the patient's last surgery, almost three-quarters of the cases showed a predominance of vascular tissue.

Nearly a quarter of the patients were only followed up, with no treatment implemented. Among the other patients, a great variety of treatments were performed, but most consisted of some type of surgery with/without additional therapies (42.0%), drugs (20.5%), and radiotherapy (14.8%). Drugs commonly used were bisphosphonates, corticosteroids, calcitonin, chemical compounds containing calcium, alpha interferon, vitamin D, or a combination of these. One case treated with cisplatin + 5-flurouracil was reported (with no persistence of resorption, followed up for 120 months) and another case treated with denosumab (with no follow-up information). The patients had usually experienced a relatively long previous history of the disease (mean of 3.5 years) before they sought professional medical help, and that period reached 17 years in one patient. Patients were followed up for a mean time of 4 years. The rate of persistence of resorption after first treatment was slightly higher than 50%. Table 2 shows the persistence of resorp-

tion according to the treatment implemented.

Five cases of death were reported, of which three could be related to the condition. In one case, the patient died after spontaneous pathological fracture of the affected cervical vertebrae with subsequent transection of the spinal cord[7]. In another case, the patient died due to haemodynamic instability, cardiac arrest, and brain death – the lesion extended into the intracerebral space through the foramen magnum[8]. In the third case, with the involvement of several facial, skull, and vertebral bones, the patient became bedridden due to increasing pain and neck instability[9]. This patient eventually became deaf and dumb and lost her sight in the left eye. The patient was suspected to have committed suicide after the tracheal cannula was found to be out of place. In the other two cases, it was not possible to clearly associate the patient's death with the disease. One of these patients developed acute schizophrenia and suddenly collapsed and died[10]. The other patient died of severe pleural effusion after receiving radiation therapy[11].

Table 3 shows the rate of persistence of resorption for GSD according to different factors. The presence of a lesion that crossed the midline was the only factor suggested to have an influence on the persistence of resorption after the first treatment.

Discussion

The aim of this study was to integrate the available data published in the literature on GSD with involvement of the jaws into an updated comprehensive analysis of its features, as well as the options for treatment and the frequency of recurrence. A review of pathological lesions and conditions is important because it provides information that can improve diagnostic accuracy, allowing pathologists and surgeons to make informed decisions and refine treatment plans to optimize clinical outcomes[12–16].

Many supposed cases of GSD were excluded during the selection process for this review. The reason for this was that the team providing treatment to these patients did not perform any biopsy when no surgical treatment was implemented, or did not perform histopathological examinations when one or many surgeries were performed. Some of the diseases included in the differential diagnosis can only be ruled out by microscopic examination. Thus a certain degree of uncertainty was brought to the diagnosis, even though the clinical and radiological features of the cases might have matched those of patients with GSD.

The differential diagnosis of GSD in the jaws (**Supplementary Material**, Table S1) includes infection (osteomyelitis), neoplastic diseases (Langerhans cell histiocytosis, Ewing sarcoma, angiosarcoma), endocrine disorders (e.g., osteolytic hyperparathyroidism)[17,18], and other conditions/syndromes that present with osteolysis, such as Hajdu–Cheney syndrome, generalized lymphatic anomaly, and Paget disease[19]. Nevertheless, progressive and unusually substantial bone destruction without evidence of repair is almost pathognomonic for Gorham disease[20].

Table 3. Persistence of resorption for the cases of Gorham–Stout disease involving the jaws according to different factors—for the lesions with available information about both the persistence of resorption and the factors included here.

Factor	Persistence of resorption/total (% persistence)	*P*-value	OR (95% CI)	*P*-value
Involvement				
Monostotic	24/45 (53.3)	0.786[a]	1	
Polyostotic	13/26 (50.0)		0.875 (0.333–2.300)	0.787
Jaw				
Maxilla (a)	2/4 (50.0)	0.595[b] (a–b)	1.304 (0.171–9.970)	0.798
Mandible (b)	30/53 (56.6)	0.515[b] (a–c)	0.556 (0.059–5.241)	0.608
Maxilla + mandible (c)	5/14 (35.7)	0.138[a] (b–c)	0.426 (0.126–1.444)	0.171
Lesion crossed the midline				
No	14/36 (38.9)	0.024[a]	1	
Yes	23/35 (65.7)		3.012 (1.145–7.926)	0.026
Cortical bone perforation				
No	0/2 (0)	0.211[b]	[c]	
Yes	37/67 (55.2)			
Swelling				
No	23/46 (50.0)	0.507[a]	1	
Yes	14/24 (58.3)		1.400 (0.517–3.791)	0.508
Symptomatic				
No	20/36 (55.6)	0.642[a]	1	
Yes	17/34 (50.0)		0.800 (0.312–2.049)	0.642
Alkaline phosphatase levels				
Normal	8/19 (42.1)	0.516[b]	1	
High	4/8 (50.0)		1.375 (0.262–7.220)	0.707
Histology of last surgery				
Fibrous	6/14 (42.9)	0.306[a]	1	
Vascular	28/48 (58.3)		1.867 (0.560–6.223)	0.310
Pathological fracture (jaws)				
No	23/49 (46.9)	0.130[a]	1	
Yes	14/21 (66.7)		2.261 (0.778–6.570)	0.134

OR, odds ratio; CI, confidence interval.

[a] Pearson χ^2 test.

[b] Fisher's exact test.

[c] In at least one case, the value of the weight variable was zero. Such cases are invisible to statistical procedures and graphs, which need positively weighted cases.

So far, there is no clear consensus on the aetiopathogenesis of GSD. Many hypotheses have been raised (**Supplementary Material**, Table S2) since Gorham and Stout proposed that haemangiomatosis would lead to hyperaemia causing excessive bone destruction[21]. Hypotheses include local hypoxia/acidosis and endothelial dysplasia[22,23], enhanced osteoclastic activity or increased sensitivity of osteoclast precursors to humoral factors[24–27], lack of thyroid C cells and calcitonin[28], and proliferation of lymphatic vessels[29,30], among others. A molecular analysis of a patient with PTEN hamartoma tumour syndrome and GSD suggested that *PTEN* mutation could be the first of two or more steps in the development of GSD[31]. More recently, the whole genome signature was investigated in the lesions and healthy tissues of a patient with GSD[32]. After filtering for the mutated genes related to osteogenesis or osteolysis, the investigators suggested that *TNFRSF11A* and *TREM2* were the driver genes for the disease, but further studies are necessary to confirm this finding.

Despite the fact that the criteria of Heffez et al. establish an angiomatous lesion[6], it has long been observed that some lesions develop into more fibrous lesions[2]. Thus, fibrous-looking lesions were not excluded, since these are found in some cases. After the autopsy of a patient suspected to have committed suicide because of the consequences of the advancement of the disease, with analysis of tissue from several sites, Kawasaki et al. pointed out that progressive resorption of bone in GSD is not always accompanied by pathologically significant vascular proliferation[9].

The natural history of the process is unpredictable. Some cases are self-limiting with stability of the affected part[33]. The reports in the literature show a great variety of treatments performed, with radiotherapy appearing to provide better results in comparison to the other types of treatment. However, due to the limited number of cases, it is best concluded that none of the treatments has clearly been shown to be effective or associated with a better prognosis in comparison to the others. In some cases, the patient's first consultation took place after the osseous resorption had already become inactive, i.e. the disease process had already spontaneously arrested[34], or when the affected bone had already completely disappeared[35]. In many other cases there was no long-term follow-up after the last therapeutic procedure performed. It is, therefore, not possible to state conclusively that the prognosis for patients with GSD is good.

No reasonable explanation could be identified for the possible influence of lesions that crossed the midline on the persistence of resorption after the first treatment. This could be related to the fact that the continuous process of resorption would lead these lesions to become large enough to reach the contralateral side of the head and neck region, and larger lesions in a more advanced phase of resorption would be more difficult to deal with. However, this is a mere assumption.

Due to the low incidence of GSD, the current literature is confined to case reports and case series. There is no standard treatment so far and the therapy depends on the patient's condition. Therapy might include surgery, radiotherapy, and drugs, with varying degrees of success[32].

In conclusion, half of the cases of GSD were found to persist after some treatment modality and five patients died. Among the different clinico-radiological and histopathological variables investigated, only the fact of crossing the midline showed an association with persistence of the lesion. There remains much to understand about GSD, a rare condition with no clear consensus on the aetiopathogenesis, an unpredictable clinical course, and no standard treatment.

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Competing interests

There are no conflicts of interest to declare. RSG is a research fellow at CNPq, Brazil.

Ethical approval

Not applicable.

Patient consent

Not required.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ijom.2019.03.002.

References

1. Halliday DR, Dahlin DC, Pugh DG, Young HH. Massive osteolysis and angiomatosis. *Radiology* 1964;**82**:637–44.
2. Johnson PM, McClure JG. Observations on massive osteolysis: a review of the literature and report of a case. *Radiology* 1958;**71**:28–42.
3. Jackson JBS. A boneless arm. *Boston Med Surg J* 1838;**18**:368–9.
4. Römer O. *Die Pathologie der Zδhne Handbuch der Speziellen Pathologischen Anatomie und Histologie*, vol. 4. Berlin: Springer Verlag; 1924. p. 135–499.
5. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med* 2009;**151**:264–9. W64.
6. Heffez L, Doku HC, Carter BL, Feeney JE. Perspectives on massive osteolysis: Report of a case and review of the literature. *Oral Surg Oral Med Oral Pathol* 1983;**55**:331–43.
7. Ellis DJ, Adams TO. Massive osteolysis: report of case. *J Oral Surg* 1971;**29**:659–63.
8. Lee S, Finn L, Sze RW, Perkins JA, Sie KC. Gorham Stout syndrome (disappearing bone disease): two additional case reports and a review of the literature. *Arch Otolaryngol Head Neck Surg* 2003;**129**:1340–3.
9. Kawasaki K, Ito T, Tsuchiya T, Takahashi H. Is angiomatosis an intrinsic pathohistological feature of massive osteolysis? Report of an autopsy case and a review of the literature. *Virchows Arch* 2003;**442**:400–6.
10. Hampton J, Arthur JF. Massive osteolysis affecting the mandible. *Br Dent J* 1966;**120**:538–41.
11. Kim MK, Hong JR, Kim SG, Lee SK. Fatal progression of Gorham disease: a case report and review of the literature. *J Oral Maxillofac Surg* 2015;**73**:2352–60.
12. Chrcanovic BR, Gomez RS. Squamous odontogenic tumor and squamous odontogenic tumor-like proliferations in odontogenic cysts: an updated analysis of 170 cases reported in the literature. *J Craniomaxillofac Surg* 2018;**46**:504–10.
13. Chrcanovic BR, Gomez RS. Ameloblastic fibrodentinoma and ameloblastic fibro-odontoma: an updated systematic review of cases reported in the literature. *J Oral Maxillofac Surg* 2017;**75**:1425–37.
14. Chrcanovic BR, Gomez RS. Calcifying epithelial odontogenic tumor: an updated analysis of 339 cases reported in the literature. *J Craniomaxillofac Surg* 2017;**45**:1117–23.

15. Chrcanovic BR, Gomez RS. Cementoblastoma: an updated analysis of 258 cases reported in the literature. *J Craniomaxillofac Surg* 2017;**45**:1759–66.
16. Chrcanovic BR, Gomez RS. Melanotic neuroectodermal tumour of infancy of the jaws: an analysis of diagnostic features and treatment. *Int J Oral Maxillofac Surg* 2019;**48**:1–8.
17. Patel DV. Gorham's disease or massive osteolysis. *Clin Med Res* 2005;**3**:65–74.
18. Saify FY, Gosavi SR. Gorham's disease: a diagnostic challenge. *J Oral Maxillofac Pathol* 2014;**18**:411–4.
19. Evrenos MK, Ozkaya M, Yaman M, Proff LY. Case report: Gorham–Stoute syndrome with involvement of majority of mandible, and partial maxillary, temporal and zygomatic bones. *J Maxillofac Oral Surg* 2016;**15**:335–8.
20. Kotecha R, Mascarenhas L, Jackson HA, Venkatramani R. Radiological features of Gorham's disease. *Clin Radiol* 2012;**67**:782–8.
21. Gorham LW, Stout AP. Massive osteolysis (acute spontaneous absorption of bone, phantom bone, disappearing bone): its relation to hemangiomatosis. *J Bone Joint Surg Am* 1955;**37-a**:985–1004.
22. Heyden G, Kindblom LG, Nielsen JM. Disappearing bone disease: A clinical and histological study. *J Bone Joint Surg Am* 1977;**59**:57–61.
23. Young JW, Galbraith M, Cunningham J, Roof BS, Vujic I, Gobien RP, Liebscher L, Butler WM, Fudenberg HH. Progressive vertebral collapse in diffuse angiomatosis. *Metab Bone Dis Relat Res* 1983;**5**:53–60.
24. Wang W, Wang H, Zhou X, Li X, Sun W, Dellinger M, Boyce BF, Xing L. Lymphatic endothelial cells produce M-CSF, causing massive bone loss in mice. *J Bone Miner Res* 2017;**32**:939–50.
25. Devlin RD, Bone 3rd HG, Roodman GD. Interleukin-6: a potential mediator of the massive osteolysis in patients with Gorham–Stout disease. *J Clin Endocrinol Metab* 1996;**81**:1893–7.
26. Hirayama T, Sabokbar A, Itonaga I, Watt-Smith S, Athanasou NA. Cellular and humoral mechanisms of osteoclast formation and bone resorption in Gorham–Stout disease. *J Pathol* 2001;**195**:624–30.
27. Möller G, Priemel M, Amling M, Werner M, Kuhlmey AS, Delling G. The Gorham–Stout syndrome (Gorhamös massive osteolysis). A report of six cases with histopathological findings. *J Bone Joint Surg Br* 1999;**81**:501–6.
28. Korsic M, Jelasic D, Potocki K, Giljevic Z, Aganovic I. Massive osteolysis in a girl with agenesis of thyroid C cells. *Skeletal Radiol* 1998;**27**:525–8.
29. Hagendoorn J, Padera TP, Yock TI, Nielsen GP, di Tomaso E, Duda DG, Delaney TF, Gaissert HA, Pearce J, Rosenberg AE, Jain RK, Ebb DH. Platelet-derived growth factor receptor-beta in Gorham's disease. *Nat Clin Pract Oncol* 2006;**3**:693–7.
30. Hammer F, Kenn W, Wesselmann U, Hofbauer LC, Delling G, Allolio B, Arlt W. Gorham–Stout disease—stabilization during bisphosphonate treatment. *J Bone Miner Res* 2005;**20**:350–3.
31. Hopman SM, Van Rijn RR, Eng C, Bras J, Alders M, van der Horst CM, Hennekam RC, Merks JH. PTEN hamartoma tumor syndrome and Gorham–Stout phenomenon. *Am J Med Genet A* 2012;**158a**:1719–23.
32. Li MH, Zhang HQ, Lu YJ, Gao P, Huang H, Hu YC, Wang Z. Successful management of Gorham–Stout disease in scapula and ribs: a case report and literature review. *Orthop Surg* 2018;**10**:276–80.
33. Thompson JS, Schurman DJ. Massive osteolysis. Case report and review of literature. *Clin Orthop Relat Res* 1974;**103**:206–11.
34. Lata J, Sharma R, Parmar M. Massive osteolysis of hemimandible: a case report. *J Maxillofac Oral Surg* 2009;**8**:381–3.
35. Franco-Barrera MJ, Zavala-Cerna MG, Aguilar-Portillo G, Sánchez-Gomez DB, Torres-Bugarin O, Franco-Barrera MA, Roa-Encarnacion CM. Gorham–Stout disease: a clinical case report and immunological mechanisms in bone erosion. *Clin Rev Allergy Immunol* 2017;**52**:125–32.

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