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Case Report

CASE REPORT

Gorham Stout disease: a case report from Syria

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Abstract

Gorham-Stout disease (GSD) is a rare entity that destroys the bone matrix resulting mainly in osteolysis, pain and pathologic fractures among a broader clinical picture. We report a case of a 60-year-old female with a sudden discovery of pathologic fractures in the pelvis and the absence of the left femoral head. On biopsy, no cellular atypia was found, instead disturbed bone formation with prominent vascularity with scattered foci of necrosis & osteolysis, which lead to the diagnosis of GSD. Possible differential diagnoses were discussed and excluded. The patient was put on Bisphosphonate that led to a relative improvement in the symptoms. This disease needs a more thorough investigation to identify the key cause, what is beyond the scope of this report.

INTRODUCTION

Gorham-Stout disease (GSD or vanishing bone disease, is a rare benign condition characterized by the destruction of bone matrix and the proliferation of vascular structures resulting in massive osteolysis of the bone [1]. Gorham and Stout presented the entity for the first time as a single disease with a varying localization through a large case series [2]. The disorder can appear in any age group, but it generally presents in the second and third decades of life without displaying a clear gender, race or geographic predilection [2, 3]. Although GSD can affect any bone in the body, the most commonly involved bones are the maxillofacial region, upper extremities bones and the femur [1]. The clinical picture varies Localized pain is the most common symptom, while other symptoms include swelling, weakness, pathologic fractures and limb-function impairment [4]. The entity also involves adjacent soft tissues and skin [1].

While osteolysis has many other commoner causes, the differential diagnosis should be carefully made to exclude these causes before declaring the case as GSD. The differential diagnosis for osteolysis incorporates infection, cancer, inflammatory and endocrine disorders, and other diseases as well [1].

CASE PRESENTATION

A 60-year-old Caucasian female was reported with a history of heavy smoking (30 packet year), 20 years of medically treated hypertension, partial thyroidectomy and familial history of osteoporosis (in the mother). The patient suffered 6 months earlier from an insignificant trauma. The patient was admitted to the hospital for a dysfunctional left lower limb characterized by pain in the left knee with difficulty walking and standing. The complaint developed to pain in the left hip worsening on

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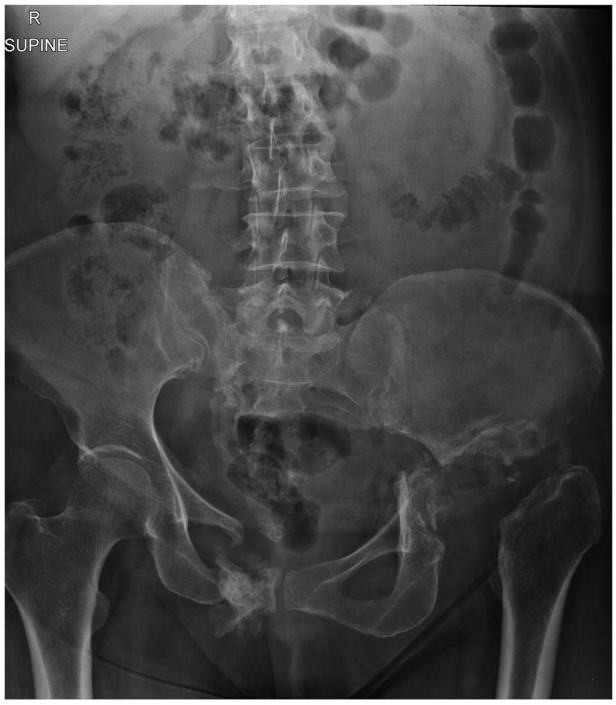

Figure 1: Pelvic X-ray showing the detachment of the right pelvis with a clockwise rotation of the coronal plane.

movement, not responding to analgesics, radiating to the medial surface of the left lower limb down to the toes, accompanied by a limping gait and crackles in hip and knee joints. On exam, her left limb was 2 cm shorter than the right with a swelling of the posterior lateral surface of the right hip.

Pelvic X-ray showed decreased bone density, a complete absence of the left femoral head, articulation of the left femoral neck with the iliac bone, regions of osteolysis in the right upper and lower divisions of the pubis and left sacroiliac articulation leading to the upward displacement of the right half of the pelvis accompanied by a small avulsion fracture on the anterior lower border of the twelfth thoracic vertebra (Fig. 1); then, CT and MRI revealed the complete absence of the left femoral head with cystic heterogeneous soft tissue in its place, and focal soft osteolytic tissue in the right upper and lower divisions of the pubis and in the right sacroiliac articulation (Figs 2 and 3); thus, radiological findings suggested degenerative changes.

Laboratory tests (Table 1) showed a decrease in vitamin D and Ca^{+2}, and DEXA revealed a decreased bone density (T-score = −3), and the Z-score to be estimated <−2 [based on NHANES database] [5]. The patient underwent surgery to exclude malignancy, and the biopsies from the femoral head were as follows: A segment showed highly vascular papillary formation covered by synovial cells with small nuclei and ill-defined boundaries, large clefts and scattered mononuclear inflammatory cell infiltrate. Another segment had soft tissues from a lytic lesion of the femur bone and revealed massive angiomatosis surrounded by fibrous connective tissue and residual lytic bone tissue (Fig. 4). No cellular atypia was noted within the examined specimens. Immune stains showed CD 34 positive proliferating blood vessel cells—Angiomatosis (Fig. 5). Later, a CD68 immunestain was negative; by then, the tissue remains were, however, predominantly necrotic. Other immunestains mentioned in literature (among others: TRAcP, Podoplanin and D2–40) as indicators of bone resorption and lymphatic-vessel-proliferation were unavailable. In conclusion, the pathologist stated the consistency of the specimen with aggressive osteolytic angiomatosis (GSD). The patient was provided with symptomatic treatment (anti-osteoclastic drugs [bisphosphonates], calcium and Vitamin D) along with walking aid support. The patient was kept under regular follow-up. Later, the pain reduced and the walking function improved.

Table 1: Lab test on admission

Test name	Result	Normal range
Complete blood count		
White blood cells	6.6 * 10^3/µl	5–10 * 10^3/µl
Neutrophils	69.1%	40–70%
Lymphocytes	24.5%	20–40%
Monocytes	4.2%	2–6%
Eosinophils	1.7%	1–6%
Basophils	0.5%	1–2%
RBCs	4.33 * 10^6/µl	4.5–5.5 * 10^6/µl
Hematocrit	11.6 g/dl	13–16 g/dl
RBCs MCV	78 fl	82–96 fl
RBCs MCH	26.7 pg	27.5–33.2 pg
RBCs MCHC	34.3%	31.5–35.5%
RDW	14.2%	0.0–16.0%
Platelets	325 * 10^3/µl	150–450 * 10^3/µl
Inflammation markers		
ESR	10 mm/h	0–20 mm/h
CRP	5.2 mg/l	<2 mg/l
Coagulation tests		
PT	13.2 s	11–13.5 s
INR	1.02	1–1.5
Blood chemistry		
Urea	18 mg/dl	10–50 mg/dl
Creatinine	1.2 mg/dl	0.7–1.36 mg/dl
Sodium	139 mmol/l	135–148 mmol/l
Potassium	4.2 mmol/l	3.5–5.0 mmol/l
Calcium (ionic)	2.31 mg/dl	4.5–5.6 mg/dl
Calcium (Total)	7.6 mg/dl	8.4–10.2 mg/dl
25-OH vit D3	17.5	30–80 ng/ml
Phosphorus	2.9 mg/dl	2.5–4.5 mg/dl
Glucose	98 mg/dl	70–110 mg/dl
Alkaline phosphatase	217 IU/L	100–290 IU/L
AST	50 IU/L	8–20 IU/L
ALT	31 IU/L	8–20 IU/L
Amylase	46 U/L	30–300 U/L

RBCs = red blood cell; MCV = mean corpusular volume; MCH = mean corpusular hemoglobin; MCHC = mean corpusular hemoglobin concentration, RDW = red blood cell distribution width; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; PT = prothrmbin time; INR = international normalized ratio; ALT = alanine transaminase; AST = aspartate transaminase.

DISCUSSION

The mechanism of CGD is still uncertain and it is mostly bound to a hemangiomatosis or lymphangiogenesis activity [1, 6]. Possible theories range from bone resorption due to the effect of mononuclear osteoclasts.

Heffez *et al.* suggested eight diagnostic criteria for this syndrome [7], all of which apply to this case including a biopsy-proven angiomatosis and the absence of cellular atypia. GSD was

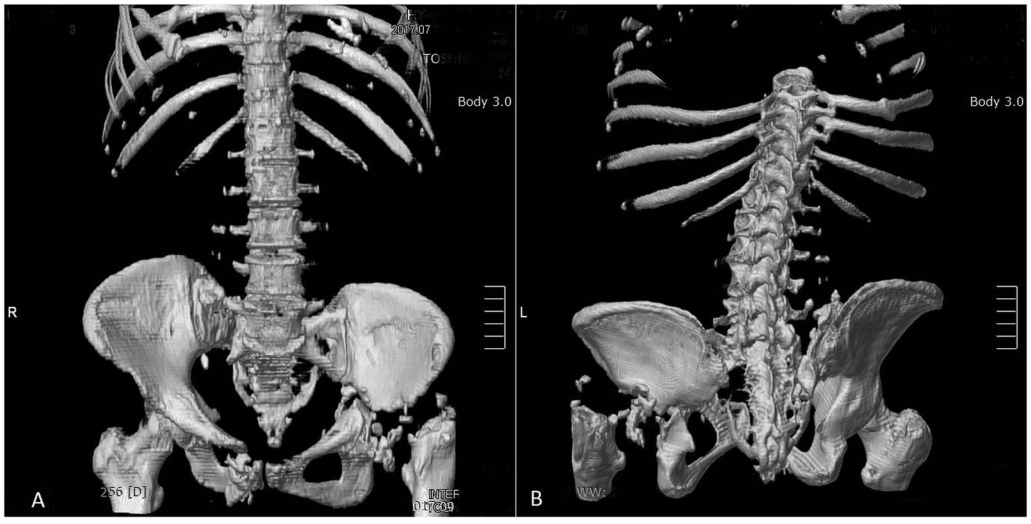

Figure 2: Pelvic 3D-constructed CT: (A) anterior section. (B) Posterior section. Both sections show a complete absence of the left femoral head.

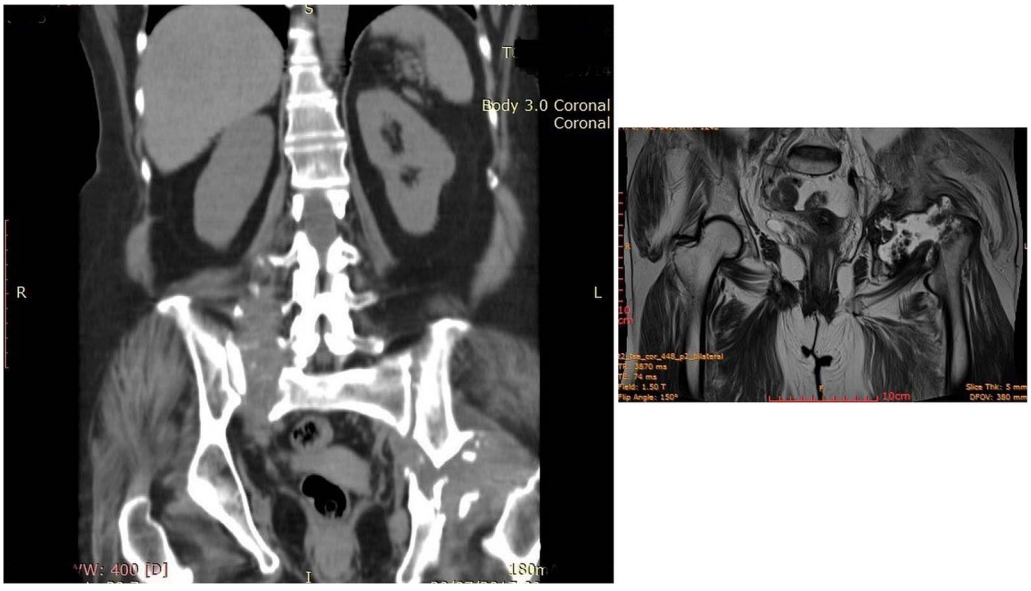

Figure 3: Pelvic MRI showing a complete absence of the left femoral head.

recently classified under lymphatic malformations by the ISSVA [8]. Unfortunately, proving the presence of a lymphatic activity and proliferation was unavailable; however, a pathology-proven angiomatosis and the absence of recognizable lymphatic vessels, which have distinct 'diffuse dilated lymphatic endothelial cells', are strong sufficient indications against generalized lymphatic anomaly and in favor of GSD [9]. The same reasoning applies in our case to all other lympahtic diseases.

Differential diagnosis to this entity spans an expansive range of possibilities. Negative renal and inflammatory markers exclude autoimmune, renal and infectious etiologies, whereas the family history weakens the probability of a hereditary cause (hereditary multicentric osteolysis is autosomal dominant). Neither neurologic symptoms nor malignant cells were detected what excludes the respective diagnoses.

Osteoporosis is common in postmenopausal women as opposed to GSD that tends to affect younger individuals, and it is also silent with pathologic fractures of the vertebral column and the hip and DEXA <-2.5 [10]. The presence of multiple foci of osteolysis and the angiogenesis on pathology tips the scales in favor of GSD.

The observed abundant hypocalcemia and the concomitant decrease in vitamin D levels would have led to osteomalacia, which is not compatible with the symptoms and the carried out investigations. A plausible hypoparathyroidism would not have caused this osteolysis, as the reverse—hyperthyroidism—is accused to be one of the causes.

Many therapies are suggested to address this disease, of which are Bisphosphonates that have been successfully used showing an anti-osteolytic activity [9].

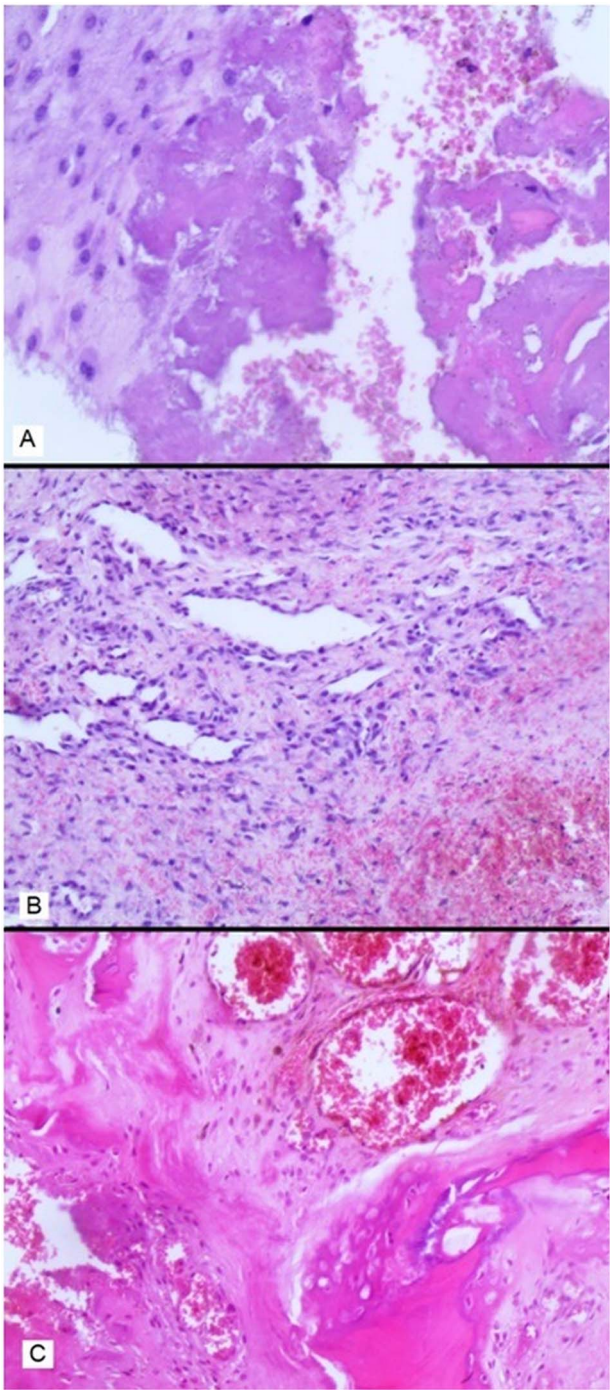

Figure 4: Microscopic photos (Hematoxylin and eosin stain ×100) showing scattered foci of necrosis & osteolysis (A), a replacement of bone by lobules of variable-sized vascular channels embedded in the cellular connective tissue (B), and proliferation of hemangioma-like blood vessels interspersed with broken trabeculae of lamellar bone (C) with no evidence of reactive bone formation.

CONCLUSION

This disease needs further investigation; however, we draw the attention to the possible coinciding hypocalcemia and vitamin D deficiency without osteomalacia and the possible occurrence in an older age group.

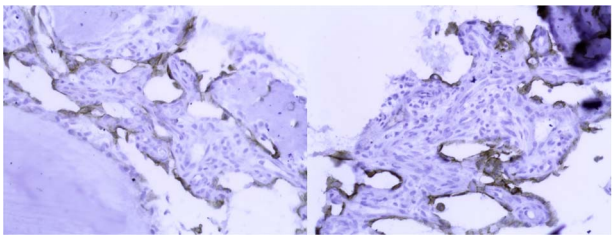

Figure 5: CD 34 positive in proliferating blood vessel tissue—Angiomatosis.

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None.

CONFLICT OF INTEREST STATEMENT

We declare no competing interests.

FUNDING

We declare no funding was applied.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not required.

PATIENT CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

GUARANTOR

Prof. Zuheir Alshehabi.

REFERENCES

1. Nikolaou VS, Chytas D, Korres D, Efstathopoulos N. Vanishing bone disease (Gorham-Stout syndrome): a review of a rare entity. *World J Orthop* 2014;**5**:694–8.
2. Malde R, Agrawal HM, Ghosh SL, Dinshaw KA. Vanishing bone disease involving the pelvis. *J Cancer Res Ther* 2005;**1**:227–8.
3. Mukhopadhyay S, Chattopadhyay A, Bhattacharya R, Roy U. Gorham's disease of mandible–a rare case presentation in pediatric patient. *J Indian Soc Pedod Prev Dent* 2016;**34**:180–4.
4. Dellinger MT, Garg N, Olsen BR. Viewpoints on vessels and vanishing bones in Gorham-stout disease. *Bone* 2014;**63**:47–52.
5. University of Washington. Bone densitometry [internet]. 2011. https://courses.washington.edu/bonephys/opbmdtz.html (15 September 2019, date last accessed).
6. Kiran DN, Anupama A. Vanishing bone disease: a review. *J Oral Maxillofac Surg* 2011 Jan;**69**:199–203.

7. 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.
8. ISSVA. Classification of Vascular Anomalies ©2018 International Society for the Study of Vascular Anomalies "issva.org/classification" (20 September 2020, date last accessed).
9. Ozeki M, Fukao T. Generalized lymphatic anomaly and Gorham-Stout disease: overview and recent insights. *Adv Wound Care (New Rochelle)* 2019;**8**:230–45. doi: 10.1089/wound.2018.0850.
10. Rosen H. Clinical manifestations, diagnosis, and evaluation of osteoporosis in postmenopausal women [internet]. *UpToDate*. https://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-evaluation-of-osteoporosis-in-postmenopausal-women? (15 September 2019, date last accessed).