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Case Report

The importance of computed tomography (CT) scans in the early diagnosis of Gorham-Stout Disease – A case report ☆

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ABSTRACT

Gorham Stout disease (GSD) or vanishing bone disease is an infrequent entity in clinical practice characterized by gross and progressive bone loss along with excessive growth of vascular and lymphatic tissue. Very little is known about the pathogenesis of GSD, which makes the diagnosis challenging. Due to the rarity of the disease, no treatment guidelines have been created yet. We report a case of GSD in a 53-year-old male patient. He presented with bone pain and initial imaging showed widespread osteolytic lesions in the cervical and mid thoracic spine, ribs, sternum, clavicles, scapula and humerus. Two percutaneous bone biopsies were performed, followed by an open spine biopsy of the L2 spinous processes for histological examination. Unfortunately, no diagnosis was established. Although, he was

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treated symptomatically, he kept enduring pain and presented again after seven months. His laboratory values were out of the normal range which prompted thorough investigations. New imaging and bone biopsy revealed multiple osteolytic lesions and vascular lesions with cavernous morphology. GSD was diagnosed after ruling out a neoplastic process and confirming the cavernous morphology with immunohistochemical stain. He was treated symptomatically with immunomodulators, bisphosphonates and supplements. Regular follow-up with a specialist was recommended. We hope this case will raise awareness of GSD in common clinical practice and shed some insight on its clinical presentation and the role CT and other imaging modalities play in the diagnosis of GSD.

Introduction

Gorham Stout disease (GSD) is a rare disorder characterized by proliferation of lymphatic and vascular structures within the osseous matrix associated with progressive osteolysis and bone resorption [1–5]. GSD affects patients of all ages; however, several studies suggest a higher prevalence among children and young adults, with no evidence of a sex or ethnic predilection [2–5].

The clinical picture of GSD generally includes pain, swelling, weakness and functional impairment of the affected region [2–5]. Patients may present with pathological fractures following minor traumas, having been asymptomatic up to that point [2–5]. Nevertheless, clinical manifestations are diverse, due to the broad spectrum of bones that may be involved. Involvement of the thoracic bones leads to the development of pleural and pericardial effusions and chylothorax [2–5]. Massive osteolysis can affect spinal and cranial bones, giving rise to neurological manifestations such as meningitis, paraparesis and paraplegia [2–5]. Patients may potentially present with osteomyelitis and subsequent septic shock as well [2]. Loose teeth, pain, facial deformities and obstructive sleep apnea are typical in patients with maxillo-facial involvement [2–4].

GSD is a diagnosis of exclusion and is established after other more common causes of massive osteolysis have been ruled out. Imaging modalities, namely radiography, bone scintigraphy, CT and MRI assist in the differential diagnosis. The definitive diagnosis is confirmed by careful histopathological examinations of bone lesions [2–4]. Despite its benign nature, the underlying pathological mechanisms implicated in the pathogenesis of GSD remain elusive, thus hindering the development of therapeutic options for these patients. Currently, management consists in pharmacotherapy, radiation and surgery [2–4]

Case presentation

A 53-year-old male patient presented to the Rheumatology Clinic with complaints of lower back pain. The patient reported back and chest pain, a feeling of general malaise, and restricted movements while walking during the last 3 years, but the pain had intensified in the last couple of months. He was under treatment for hypertension. His family history included a diagnosis of prostate cancer for his father and type 2 diabetes mellitus for his mother. He reported no alcohol consumption, no smoking and no known food or drug allergies. On physical examination, he reported pain during the flexion and extension of the neck, spine, elbows, knees and hands and during the internal and external rotation of the arms. No edema, hyperemia, or pain on palpation were present. He had a positive Lasegue and Minell sign, which suggested pathological changes on the level of L5 and the sacro-ileal joint. His complete blood count and blood chemistry panel was normal. On further investigation, multiple osteolytic bone lesions affecting the vertebral bodies were found along with a collapsed L5 vertebrae. A diagnosis of multiple myeloma was initially suspected. Two percutaneous bone biopsies were performed. The biopsied material showed no neoplastic changes with the presence of all three hematopoietic lines (myeloid, erythroid and megakaryocytic) with normal morphology and distribution. The myelogram was also normal. He was then admitted for an open spine biopsy, with the removal of the L2 spinous process for histologic examinations, which also failed to reach a diagnosis. He was discharged and referred to the Rheumatology Clinic, where he was treated symptomatically.

After 7 months, his symptoms persisted and he presented again to the clinic. His complete blood count (CBC) was normal, with elevated levels of C-reactive protein (CRP) equal to 11.48 mg/l (less than 5 mg/l).

His blood chemistry panel showed normal values of glucose and liver enzymes, but abnormal levels of renal parameters: a creatinine level of 139.8 μmol/L (53-124 μmol/L), urea of 13.76 mmol/L (1.6-7.5 mmol/L) and uric acid of 706.4 μmol/L (150- 428 μmol/L). Further tests showed elevated levels of anti-TPO antibodies of 77.76 IU/ml (less than 35 IU/ml) and ALP of 338 IU/L (20-140 IU/L). The levels of PSA, TSH, PTH, serum calcium, phosphorus and calcitonin were within normal limits. He was then referred to a nephrologist.

A renal ultrasound revealed an expansion of the renal sinus more prominent on the left side, with some parenchymal loss and the presence of multiple hyperechogenic formations. His GFR varied between 44-54 ml/min/1.73 m^3. A diagnosis of chronic renal failure and bilateral nephrocalcinosis was made.

A sample of his bone tissue was sent for a second evaluation. The specimens contained bone tissue that consisted of cortical and spongious bone. The spongious bone was consid-

erably restructured with the trabeculae were configured irregularly. In the fibrosed medullary cavity there were numerous sinusoidally configured, thin-walled vessels, which were lined by inconspicuous flat epithelia and contained erythrocytes. Macrophages were transformed into foamy cells. There was no inflammatory cell infiltration, no nuclear and cell atypia. As shown in Figure 1, the CT scan revealed multiple osteolytic lesions were seen throughout the entire cervical and middle thoracic spine, numerous ribs, bilateral scapulas, bilateral clavicles, bilateral humerus, and the sternum.

Overall, the pathologist concluded that it was a vascular lesion with cavernous morphology. The histopathology examination, in addition to the imaging findings, suggested a cystic skeletal angiomatosis with extensive manifestations in the spinal vertebrae, in the ribs, sternum, extremities and possibly also the base of the skull, that was further supported by immunohistochemistry, as well. A neoplastic process was ruled out.

A diagnosis of Gorham-Stout disease, also known as Vanishing Bone disease, was made. The patient was given symptomatic treatment (Thalidomide, Xarelto, Decortin, Ibandronate, Allopurinol, Calcium, Vitamin C, Vitamin K and Ibuprofen) and was recommended to have regular follow-up with the specialist.

Solid oval-shaped vertebral lesions or spherical with external expansion are demonstrated in spinal canal, narrowing of the spinal canal and recesses (neuroforaminal spaces). Such lesions are presented indiscriminately, such as in vertebral c (green arrows), d (blue arrows), sternal, costal (red arrow, e, pelvic and two proximal femurs. Right femur with massive osteolysis (white arrow, e), where osteosynthetic metal and hyperdense mass are found in bone defect (synthetic material implanted) (blue arrowheads, e, f).

Discussion

Gorham-Stout disease, also known as Vanishing bone disease, is a rare pathological entity, with only a few hundred cases reported in literature. It mainly affects the maxillo-facial region, the upper extremities, the clavicle, ribs, vertebrae, the pelvis, as well as cranial bones [1–3]. It is characterized by massive osteolysis and osseous resorption, associated with an abnormal non-neoplastic proliferation of vascular and lymphatic tissue [1–5].

The condition arises sporadically. A familial, inherited pattern, as well as environmental predisposing factors, have not been established [2].

To date, the pathogenesis of the disorder remains to be elucidated, but several hypotheses have been put forward to explain the pathological mechanisms involved in the bone resorption and neoangiogenesis processes. Gorham and Stout, who were the first to delineate it as a distinct disorder, hypothesized that a preceding traumatic event triggered the osteolytic process, which was subsequently aided by local factors such as changes in the pH, active hyperemia and changes in mechanical forces [3,4].

Nevertheless, recent research suggests that several elements including mononuclear phagocytes, multinuclear os-

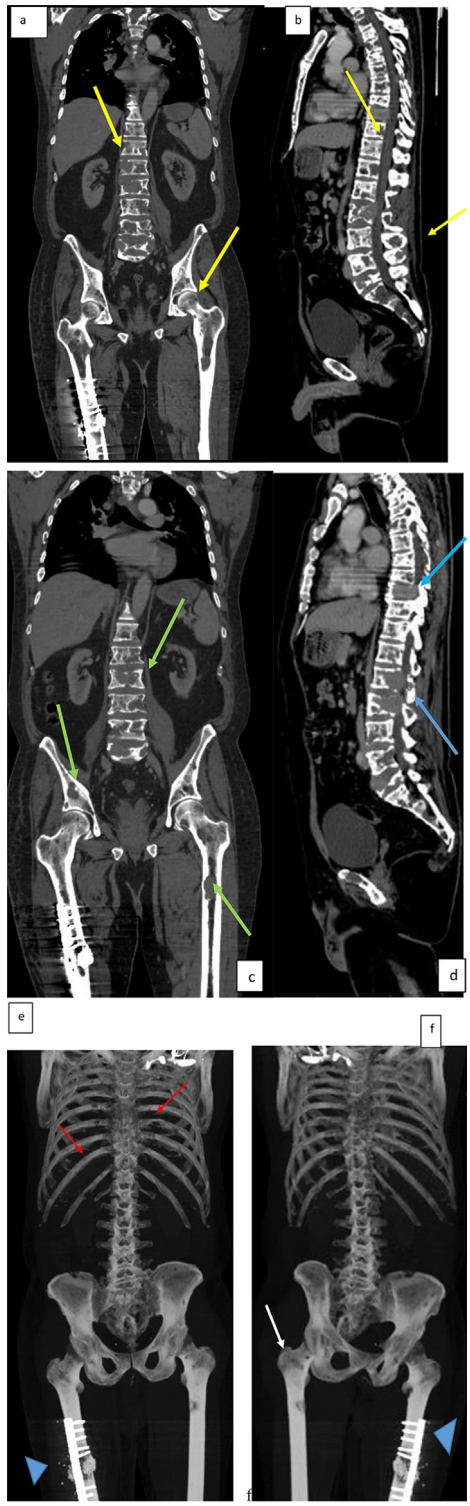

Fig. 1 – MPR (Multiplanar reformation) coronal and sagittal planes of a CT examination of bone structures, from the thoracic aperture to femoral distal metaphysis (A, B, C and D) and 3D (E, F), presenting numerous osteolytic lesions, with bone destruction, with solid tissue content in osteolytic lesions, where most of the lesions present with enhancement of contrast. (A, B, yellow arrows) (Color version of figure is available online)

teoclasts and the vascular endothelium are involved in the induction of massive osteolysis and development of a new network of vascular and lymphatic vessels. Moreover, studies show that precursors of these cells are more sensitive to humoral factors such as Interleukin-6 (IL-6) and Macrophage colony stimulating factor (M-CSF), promoting cell proliferation that leads to an increased number of circulating osteoclasts, increased osteoclastic activity and bone resorption, documented by elevated levels of CTX-1 (a marker of osteoclastic activity), in affected patients [2–6]. It has been noted that phagocytic and lymphatic endothelial cells from these lesions produce elevated levels of osteoclastogenic and angiogenic substances, promoting osteoclast proliferation and further contributing to the bone resorption [2–5].

Growth factors associated with lymphangiogenesis such as PDGF-BB and VEGF have been implicated in pathogenesis of Gorham-Stout disease, however additional studies are needed to shed light on their role [2,5].

Incidentally, there are theories that dysregulations in the production of calcitonin, a hormone synthesized by parafollicular cells (C-cells) in the thyroid gland with anti-osteoclastic activity, may play a role [2–4].

Histopathologically, the lesions are characterized by wide, capillary-like vessels with an abnormal slow flow and changes in the adjacent soft tissue, likely due to the extension of the lymphangiogenesis into the surrounding tissues [1,3,4]. It has been postulated that these structural qualities promote local hypoxia, that leads to an overproduction of hydrolytic enzymes, possibly instigating bone resorption [3,4].

Conclusion

We report a case of GSD that was not diagnosed in the initial stage. Due to the progressive nature of the disease, and lack of definitive treatment, understanding the underlying pathological processes is even more crucial. This case highlights the need for extensive research on GSD and the role imaging modalities, in our case CT scans, have to play in ensuring a timely diagnosis, thus preventing debilitating complications. As research advances, is it important we shift our focus on the development of a definitive treatment for GSD.

Patient consent

We obtained written, informed consent for publication from the patient.

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