CASE REPORT

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Gorham-Stout's disease in the metatarsus: a case report

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Gorham-Stout disease (GSD) is a rare disease occurring in the bone tissue and is characterized by spontaneous, progressive resorption. The etiology and treatment of the disease remains unclear. This article presents a 53-year-old male patient diagnosed with GSD in the 3rd and 4th metatarsal of his right foot.

Key words: Gorham-Stout; metatarsal; phantom bone.

Gorham-Stout disease (GSD), also referred to as phantom bone, massive osteolysis, lost bone disease, acute spontaneous bone absorption and hemangiomatosis, is a very rare disease resulting in massive osteolysis. While the etiology is unknown and the age of onset is variable, it is most commonly seen in younger patients. No genetic transmission or gender-based differences have been found. Gorham-Stout disease causes progressive destruction and resorption in the bone structure and is characterized by typical radiologic findings, typical clinical patterns and semi-specific histological findings.[1] Histological examination reveals proliferation (angiomatosis) in the small thin walls of the artery or lymphatic vessels and local osteoclastic hyperactivity.[1,2] Massive osteolysis spreading to the adjacent tissues and disrupting the anatomical integrity of the bone is present in radiology.[3,4]

Gorham-Stout disease was first described by Jackson in 1838. Clinical and pathological characteristics of the disease were described by Gorham and Stout in 1955 in a study with 24 patients.[1,3,5] The writers reported that local angiomatosis caused by massive osteolysis was the result of changes in the osteoclastic and osteoblastic activity balance. They also asserted that local angiomatosis proliferation and the beginning of osteolysis might be triggered by trauma in cases with a history of minor trauma.[3]

This aim of this article was to review GSD, a very rare disease with an unknown etiology and unpredictable prognosis, in light of the literature.

Case report

A 53-year-old male patient was admitted to our clinic with complaints of difficulty in walking and pain in the right foot for approximately one year. Pigmentation increase in the foot dorsal and keratotic lesions were observed in the physical examination (Fig. 1a). Metatarsals were sore and sensitive with palpation and metatarsophalangeal joint movements were painful and limited. Prior to admission, the patient's medical history included no treatment except antibiotherapy and topical steroids requested by dermatology for skin lesions and no previ-

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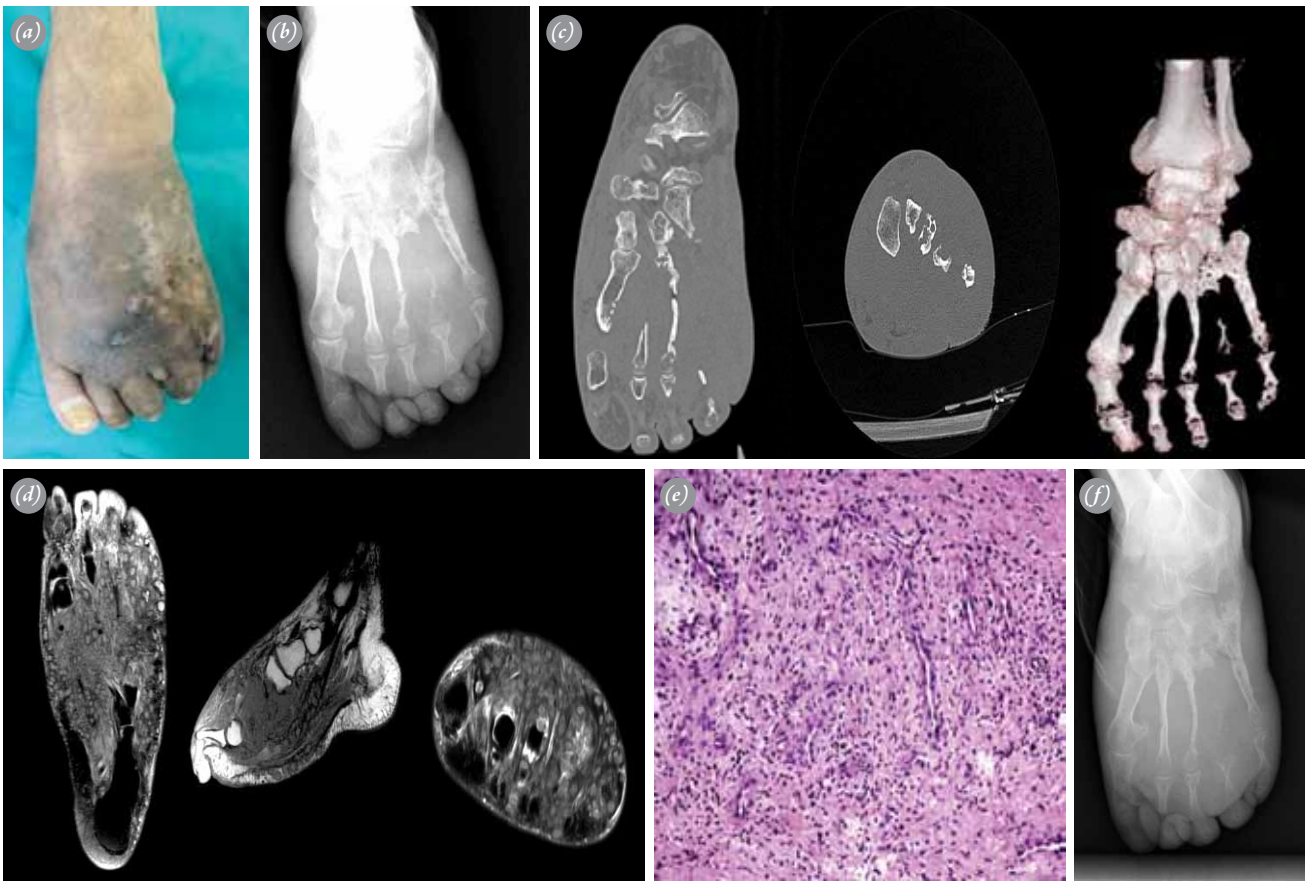

Fig. 1. **(a)** Clinical view of the patient's foot. **(b)** Anteroposterior radiograph of the patient's foot. **(c)** Computed tomography image of the patient's foot. **(d)** MR image of the patient's foot. **(e)** Hemangiomatous vascular pattern and mid-level mixed type inflammatory cell infiltration in fibroconnective stromal tissue (H&E, x100). **(f)** Postoperative 1st year AP radiograph of the patient's foot. [Color figure can be viewed in the online issue, which is available at www.aott.org.tr]

ous radiological examinations were requested. Foot radiographs revealed massive osteolysis in the 3rd and 4th metatarsals and thinning in the 2nd and 5th metatarsals (Fig. 1b). Laboratory tests (total blood count, biochemistry, sedimentation and CRP) results were normal. A biopsy was planned due to the suspicion of GSD, in addition to massive osteolysis, frequently caused by tumors and chronic infection. Foot MRI and CT and PA lung, thoracolumbar and pelvic radiographs were taken for screening and diagnostic purposes (Figs. 1c and d). Under operation room conditions, an incision was made to the dorsal of the 4th metatarsal and the lytic area was curetted. Microscopic examination of the removed material revealed osteolysis accompanied by hemangiomatous proliferated vessels in fibroconnective stromal tissue compatible with GSD (Fig. 1e). There were no malignant findings or growth in the culture sample. In light of these findings, the patient was diagnosed with GSD and treatment options were explained. The patient did not accept radiotherapy and surgical options. A single dose of intravenous bisphosphonate (zoledronic acid; Aclasta 5 mg/100 ml) was administered by infusion. Follow-up was performed at 3-month intervals after treatment. At the end of the first year, the patient reported a significant decrease in pain. Radiographs revealed healing of the fracture line in the 2nd metatarsal diaphyseal and osteolysis did not progress (Fig. 1f).

Discussion

Gorham-Stout disease, otherwise known as phantom bone, massive osteolysis, lost bone disease, acute spontaneous bone absorption or hemangiomatosis, is a rare idiopathic disease causing widespread matrix loss seen with fibrosis tissue of the bone and thin-walled vessel proliferation.[6] No endocrinological, metabolical, genetic transmission or gender-based associations or differences have been proved. The majority of cases are in children or in adults under the age of 40.[5,7]

Only 200 cases have been reported in the last 60 years. Although all bones in the body can be affected, the most commonly seen localizations are the skull

Table 1. Gorham-Stout cases with foot involvement in the literature.

Writers	Sex	Age	Involvement Region	Treatment	Family history	Trauma	Progression
Tookman et al.[10]	Female	52	Bilateral 1st IF joint and terminal phalanx	Calcitonin	None	None	Yes
Singh et al.[11]	Female	50	Right 2nd, 3rd, 4th metatarsals and 2nd proximal phalanx	Bisphosphonate	None	None	None
Bruch-Gerharz et al.[12]	Male	36	Left foot middle phalanx shafts	Radiation	None	Var	None
Al Kaissi et al.[13]	Female	10	Bilateral tarsal bone and pelvic region	None	None	None	None
Green et al.[15]	Female	22	Right tibial sesamoid	Eksizyon	None	None	None
	Female	20	Right 5th metatarsal	Eksizyon	None	Previous surgery	None

(18.3%), pelvis (17.7%), shoulder girdle (16.0%), lower extremities (14.9%) and upper extremities (11.4%). Occurrences in the spine, ribs and sternum have also been reported. Prognosis is poor and the mortality rate is high in patients with thorax involvement and chylothorax.[8,9] To our knowledge, only 6 publications have reported involvement in the foot.[10-15] Naranjo et al.[14] reported 3 patients in which primary idiopathic osteolysis had familial involvement. However, no other family history has been determined in other reports. Additionally, no mortality or progression has been reported, with the exception of the death of a 57-year-old female patient with multicentric involvement due to rib involvement, published by Tookman et al.[10] Foot involvement cases without familial involvement are shown in Table 1.

Despite the lack of evidence on its etiopathogenesis, some writers have reported that the osteolysis causing local angiomatosis occurs due to changes in the osteoclastic and osteoblastic activity balance. It also has been asserted that local angiomatosis proliferation and onset of osteolysis can be triggered by trauma.[1,3,16,17] Papadakis et al. hypothesized that posttraumatic arterial hyperemia is responsible for bone resorption.[18] It also has been asserted that Gorham and Stout hemangiomatosis causes active hyperemia and increases local oxygen pressure and, in turn, proliferates bone destruction.[19] According to Young et al., endothelial dysplasia of the blood and lymphatic vessels causes osteolysis.[20] Möller et al. argued that a pathological defect in osteoclastic activity causes osteolysis.[9] Heyden et al. asserted that hemangiomatosis causes local hypoxia and acidosis along with the increase in hydrolytic enzymes.[21]

Gorham-Stout disease is diagnosed by combining radiological and histological findings and by ruling out metabolical, immunological, neoplastic, endocrinological, infectious reasons and inflammatory diseases. Disease is not accompanied by general symptoms. Most commonly seen symptoms are localized pain, thinning in the effected extremity, swelling and deformity,[9] Laboratory findings are nonspecific and increases in alkaline phosphatase and IL-6 levels have been reported.[7,22]

Computed tomography may be used to determine the biopsy area and extension of osteolysis in the bone. Angiography is not reliable as it cannot reveal the changes in pathological vessels, nor is scintigraphy due to variable accumulation of isotopes in the lesion area. On the other hand, MR is not helpful in diagnosis despite revealing increased intensity in T2-weighted images.[6,23-25] Radiography is the best method for diagnosis of the disease and reveals partial or complete loss of the area, sharpening and sclerosis in the remaining bony areas or lack of osteoblastic activity.[26]

Histological examination, despite incomplete characteristic findings, reveals osteoclastic activity dominated by angiomatous proliferation, edema and fibrous tissue in the bone tissue. However, osteoclastic activity is either minimal or not observed at all in some cases.[27] Because of this, histological findings must be supported by clinical and radiological findings. Histopathological and clinical criteria for massive osteolysis diagnosis were defined by Heffez et al. (Table 2).[28]

Table 2. Clinical and histopathological diagnosis criteria of massive osteolysis.

Clinical and histopathological diagnosis criteria of massive osteolysis[28]
• Positive biopsy for angiomatosis
• Lack of tumor and cellular atypia
• Lack of osteoblastic response or minimal response and lack of dystrophic calcification
• Local progressive resorption findings
• Non-expansive, non-ulcerative lesion
• No visceral involvement
• Osteolytic radiographic pattern
• Lack of hereditary, metabolical, neoplastic, immunogenic or infectious etiology

Other diseases such as tumors, rheumatoid arthritis, endocrinological diseases, infection, trauma, hereditary osteolysis, angioma of the bone and neurological system diseases which cause osteolysis must be taken into consideration in the differential diagnosis of GSD.[29]

Prognosis depends on complications such as neurological deficits and pleural effusion. A mortality rate of 15% has been reported, despite the fact that mortality is higher in patients with these complications. However, life span is not affected in patients with extremity involvement.[5]

Definitive treatment for GSD has yet to be determined. Treatments such as anti-osteoclastic treatment (bisphosphonates and alpha-2b IFN), radiation treatment and surgical treatment (endoprosthetic reconstruction, resection, amputation) are in use and the effectiveness of these treatments vary according to the patient's condition and severity of the disease.[5,30]

In medical treatment, treatment characteristics of agents such as Vitamin D, androgens, estrogens, magnesium, calcium, Vitamin B12, calcitonin, dactinomycin and somatotropin are regarded unsuccessful.[7,18] However, synergistic use of bisphosphonates and alpha-2b IFNs shows a strong anti-angiogenic effect and is considered to be the treatment method with the best results.[31-33]

Radiotherapy plays a role by sclerosing the proliferation of blood vessels and preventing their redevelopment. An approximate effective dose of 30 to 45 Gy has been reported, although some authors reported that best results were obtained with doses of 15 Gy in the upper extremities.[34-37] When applied in the early stages of the disease, success rates with radiation treatment increase. While osteolyzed bone regrowth is very unusual following radiation therapy, new bone formation has been reported in some cases.[21,38-40]

In surgical treatment, local resection or amputation of the affected bone, bone graft or prosthesis replacement is suggested. Surgical treatment is indicated in particular in cases in which the bone has a pathological fracture or widespread destruction. As prosthesis replacement and resection decreases the risk of repetitive bone resorption, these methods are preferred more than bone graft application.[30,35,41] Following bone graft application, Cannon[42] noted a high rate of graft resorption whereas Nemec et al.[43] reported a successful result in their patient who had complete acetabular involvement.

In conclusion, GSD is a rare disease with an unknown etiology that causes spontaneous progressive bone destruction in addition to vascular angiomatosis and osteoclastic activity increase. Due to differences in treatment protocols, differential diagnosis must be taken into consideration in cases where the tumor causing bone destruction and osteolysis is accompanied with infection, arthritis and osteolytic lesions.

Conflicts of Interest: No conflicts declared.

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