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Vanishing Bone Syndrome; A Diagnosis Dilemma: Report of a Rare Case and Literature Review

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Abstract

Gorham-Stout syndrome is a rare disease, which results in spontaneous bone resorption. Failure to proper diagnosis of this syndrome can lead to unnecessary bone surgeries. A 13 years old girl with right hip pain, limping, and proximal femur lytic lesions underwent three surgeries without the exact diagnosis. Surgical curettage, bone graft, and internal fixation failed miserably. According to the imaging studies and the biopsy results of bone lesions that showed lymphangiomatosis, accompanied by skin and spleen lesions, a rare presentation of the Gorham-Stout syndrome was diagnosed. Bisphosphonate treatment provides a significant recovery in her symptoms and imaging studies confirmed bone improvement.

Keywords: Gorham-Stout Syndrome, Lymphangiomatosis, Osteolysis

1. Introduction

Gorham-Stout syndrome (GSS) is a rare disease characterized by generalized or localized spontaneous bone resorption. At first, this syndrome was detected by Jackson in 12 years old boy in 1938. In 1955, Gorham and Stout presented a comprehensive definition of this disease introduced it as a degenerative bone disease (1).

The imaging of bone lesions could resemble aggressive bone tumors. The GSS diagnosis is based on clinical symptoms along with imaging studies and histopathological findings which can help to abandon other diagnoses (2). Also, this syndrome is a subgroup of idiopathic osteolysis based on Hardegger classification (3).

Despite the benign nature, the prognosis of this disease is unpredictable (4). Moreover, in some cases, it presents as a self-limiting pathological condition. A well-known presentation is a lytic lesion affecting one or multiple bones that can occur in any bone. However, it is more observed in the maxillofacial area and upper limbs (5, 6). The patients with GSS have a wide age range from 1 to 75. There is no relationship between the incidence of GSS and age, gender, and race (7). In the study of Hu et al. there was only one case with bone and soft tissue involvement (8). In other studies, low prevalence of bone lesions accompanied by skin and soft tissue lesions was reported (4). A simultaneous skin lesion is observed as lymphangiomatosis or hemangiomatosis in few of these patients; therefore, some authors used the term "invasive lymphatic vessel formation" to describe this disease.

Detection of this syndrome usually requires exclusion of other differential diagnoses, including aggressive bone tumors, rheumatoid arthritis, idiopathic osteolysis caused by nephropathy, osteomyelitis, and metabolic disorders (9). Failure to proper diagnosis of this syndrome can lead to unnecessary bone surgeries and unessential treatment. Various imaging modalities were used. Typical findings in plain radiography vary from focal radiolucency to disappearing a part of a bone, bone fragmentation, and fracture. MRI is considered a preferred imaging technique to detect this lesion. The most common findings of MRI consist of heterogeneous higher signal intensity on T1 and higher signal intensity on T2 (10). Also, MRI is more sensitive in detecting involvement of soft tissue and predicting the stage of the disease. Laboratory studies and hematologic tests are usually in normal ranges and can be used to rule out other diagnoses (10). A biopsy is mostly indicative of non-malignant hyperproliferation of small vessels (11). Hafez et al. proposed the diagnostic criteria for this disease, including angiogenesis, lack of cellular atypia or malignancy, lack of dystrophic calcifications, evidence of bone progressive resorption, lack of visceral involvement,

lack of ulcer development at the site of the lesion, and no evidence of infection (11).

2. Case Presentation

A 13 years old girl with right hip pain, which had initiated four years ago and a history of unsuccessful surgeries referred to our tumor clinic. There was a lytic lesion in the peri-trochanteric area of the right femur and follow up radiographs showed progressive bone resorption. Her doctor had performed an open biopsy and did a curettage and bone graft of the femoral lesion. The first pathologist hadn't found a characteristic finding or tumor-like cells. Four months after the primary biopsy, evidence of graft resorption was observed, the second surgery was done to prophylactic fixation with anatomical LCP plate.

When she returned to our tumor clinic, she walked with limping and she had Trendelenburg gait. Her radiography showed proximal femur anterior bowing and Varus deformity of femoral neck (Figure 1). The lucent areas were observed around a few screws, indicating device loosening. There was no clear periosteal reaction. Mildly elevated erythrocyte sedimentation rate (ESR) suggested the infectious loosening of the screws.

Radiography and CT scan showed few lytic lesions with a narrow transitional zone in the ipsilateral iliac wing and the acetabulum (Figure 1). MRI showed a signal change like liquid signal adjacent to the medial side of the right iliac wing (Figure 2). Ultrasound-guided needle biopsy of this lesion aspirated a liquid, which its biochemical quality was the same as lymphedema.

Whole body bone scan showed other active lesions in the first and ninth ribs. At the third surgery, we removed the internal fixation devices. There was neither sign of infection nor neoplastic tissue. Also, the surgical site cultures were negative. The pathologic evaluation of proximal femur showed vascular hyperproliferation without finding neoplastic cells or atypia. Abdominopelvic CT scan was normal except splenomegaly with multiple hypodense centers and heterogeneous spleen shadow. Two weeks after the third surgery, the patient came back with a new erythematous papulonodular skin lesion on proximal right thigh (Figure 3). Extensive lymphangiomatosis was observed in skin biopsy with negative culture. The second microscopic evaluation of bone tissue showed proliferation of thick-walled and thin-walled vessels with a lobular and diffuse architecture in a fibroinflammatory stroma. Destruction of bone trabecula was evident (Figure 4). Considering several negative bacterial cultures, healthy hematological tests, normal biochemical tests except mildly increased ESR, imaging studies and clinical appearances of bone and skin lesions, eventually, Gorham-Stout syndrome was diagnosed.

Therefore, we kept the patient under observation and oral bisphosphate treatment. Afterward, the lytic bone defects began to improve (Figure 5). Finally, the patient's symptoms decreased after four months and she could walk normally without limping. However, the patient complained about edema of the extremity and skin lymphangiomatous vesicles. The written consent was obtained from the patient's family.

3. Discussion

Gorham-Stout syndrome (GSS) is a bone vanishing syndrome manifested in the form of lytic bone lesions. The presence of intraosseous vascular proliferation can eventually lead to bone destruction. However, the etiology of this disease is still unknown.

According to the study of Gorham and Stout angiomatosis in vascular and lymphatic vessels is the main cause of bone destruction (1); this finding was proved in our patient. Ogita et al. suggested that the main pathogenicity of osteolysis is hemangiomatosis (12). Also, Young et al. proposed that osteolysis may be related to the underlying pathology leading to vascular dysplasia (13). The study of cellular and hormonal mechanisms by Hirayama et al. revealed that sensitivity of osteoclast precursors to blood factors is elevated in GSS with enhanced osteoclast formation that leads to an increase in osteoclast creation (14). Moller et al. reported that osteolysis following GSS occurred by increased activity of osteoclasts (7).

In our patient radiography, we observed bone resorption in the femur and the ipsilateral ilium. GSS, not only demolished her proximal femur but also resorbed bone grafts after the first surgery. Contrary to the finding of Hafez et al., the GSS also invaded the soft tissues of this patient, including the skin and spleen. It was a rare finding in Hu et al. study (8). Several tissue cultures abandoned osteomyelitis. Biochemistry test results ruled out the possibility of endocrine diseases, and finally, GSS diagnosis was approved due to the angiogenesis in both bone and skin biopsy specimens.

Several treatments, including surgery and radiotherapy, have been proposed for this disease (15, 16). Surgical methods for GSS treatment include: (1) resection in expandable bones, (2) resection and reconstruction with endoprosthesis or bone graft (15); however, bone graft reconstruction is limited due to graft resorption, similar to what happened to our patient. Suggested pharmacological methods for GSS patients include bisphosphonates (16) and alpha interferon (15). Recently, a new treatment

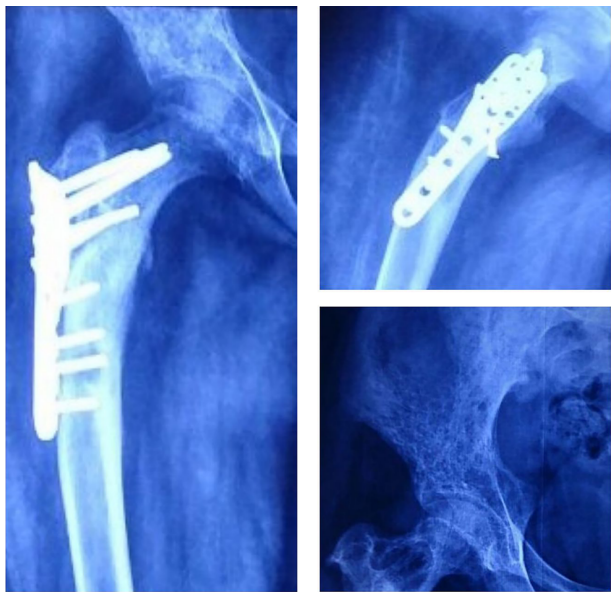

Figure 1. Bone osteolysis, pelvic involvement is shown

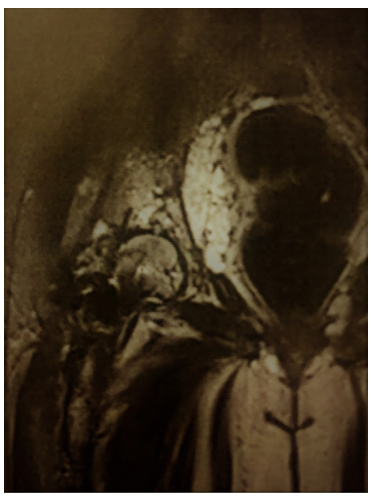

Figure 2. Pelvis MRI is indicated

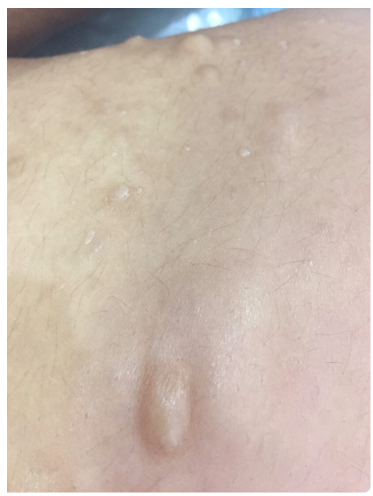

Figure 3. Papulonodular skin lesions on right thigh are evident

method has been introduced that applies monoclonal antibody against vascular endothelial growth factor (16).

Also, chemotherapy and local injection of Ok432 accompanied by considerable success in 50% of the patients (15). Our treatment with an oral bisphosphonate (alendronate 70 mg per week) for four months not only stopped the bone osteolysis but also improved her symptoms and bone quality.

Another notable point in this patient was unnecessary surgical intervention. These surgeries not only didn't help her treatment but also caused a femoral bone deformity and limping. In this regard, this issue could be prevented with sufficient knowledge of the disease.

3.1. Conclusions

According to our findings and literature review, it seems the previous criteria for this rare disease need a revision. The patient could have skin or visceral involvement.

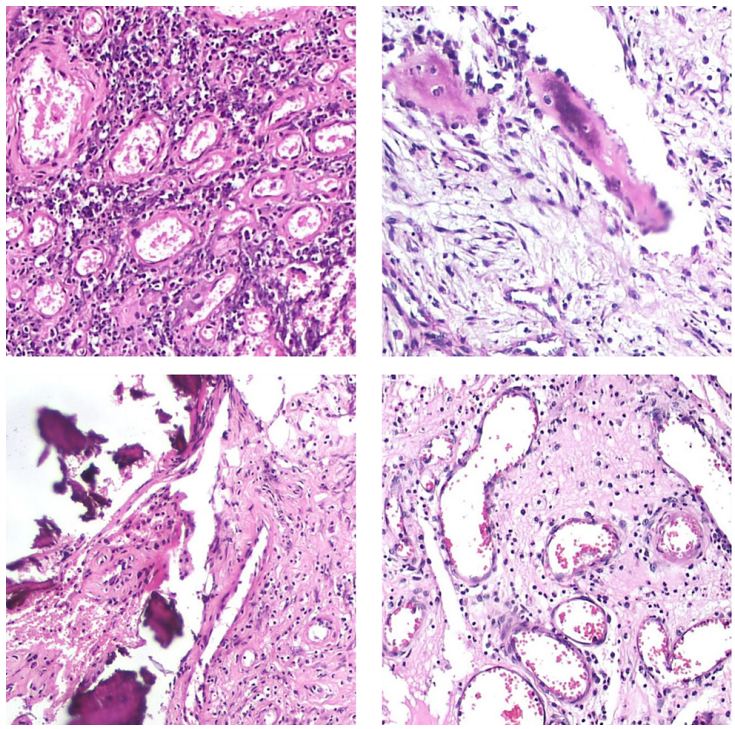

Figure 4. Microscopic examination shows proliferation of thick-walled and thin-walled vessels with lobular and diffuse architecture in a fibroinflammatory stroma. Destruction of bone trabecula are apparent in the sections

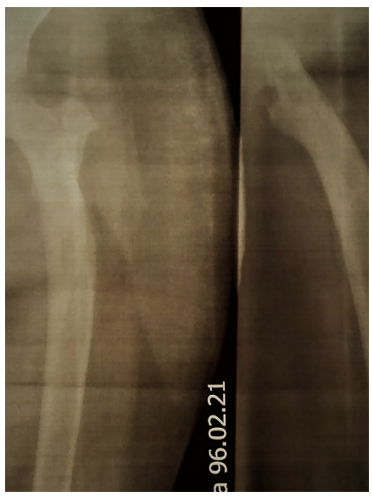

Figure 5. Bone improvement after medical treatment is shown

Furthermore, we have not a consensus on GSS treatment. Our experience showed due to less complication and easier handling, we can initiate GSS treatment with medication therapy.

Footnotes

Conflict of Interests: None declared.

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Patient Consent: The written consent was obtained from the patient's family.

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