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Case Report

Gorham-Stout syndrome with cervical involvement treated with radiotherapy: a case report

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ABSTRACT

Gorham-Stout disease (GSD), vanishing bone or phantom bone disease, is an uncommon disease whose etiology is uncertain and its pathophysiology poorly understood. This syndrome is characterized by the spontaneous destruction of the bone matrix associated with massive osteolysis and proliferation of lymphatic vascular structures in the affected areas. In the present article we present a case of GSD in a 10-year-old male patient with osteolytic lesions affecting the skull base, including the occipital bone, the petrous portion of the temporalis and clivus, as well as the vertebral bodies from C1 to C5. This syndrome should be suspected when there is bone pain that does not subside with analgesic treatment. An initial study with an x-ray will help us infer the disease in search of a bone deformity. The treatment depends on the characteristics of the lesion, the best being surgery with radiotherapy.

Key words: Gorham-Stout Syndrome; bone resorption; vanishing bone massive; osteolysis.

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RESUMEN

La enfermedad de Gorham-Stout, o enfermedad del hueso evanescente, es una patología infrecuente cuya etiología es incierta y su fisiopatología poco conocida. Este síndrome se caracteriza por la destrucción espontánea de la matriz ósea asociada a osteólisis masiva y proliferación de estructuras vasculares linfáticas en las zonas afectadas. El presente artículo reporta un caso de enfermedad de Gorham-Stout en un paciente masculino de 10 años con lesiones osteolíticas que afectan la base del cráneo, incluyendo hueso occipital, la porción petrosa del temporal y clivus, así como los cuerpos vertebrales de C1 a C5. Este síndrome se sospecha cuando existe dolor óseo que no cede con tratamiento analgésico. Un estudio inicial con una radiografía nos ayudará a sospechar la enfermedad en busca de una deformidad ósea. El tratamiento depende de las características de la lesión, siendo la mejor, la cirugía con radioterapia.

Palabras clave: Síndrome Gorham-Stout; resorción ósea; osteólisis; hueso evanescente.

INTRODUCTION

GSD is a rare disease characterized by progressive spontaneous bone resorption with massive osteolysis and proliferation of vascular structures in the affected areas; its etiology remains unknown, there's no hereditary pattern identified.[1] This disease is often seen in young adults with no sex predilection. It was first described in 1838 and again in 1872 by Dr. Jackson. However, it was not until 1955 that Dr. Gorham and Stout defined it as a specific ontological syndrome. There are just a few cases reported worldwide.[2] The clinical presentation is related to the bone affected being scapula (26%), jaw (15%) the most affected, also skull and pelvic cursing with pain, local inflammation and progressive deformity.[3] The diagnosis is based on histological findings characterized by progressive osteolysis with associated angiomatosis of blood and lymphatic vessels,[4] the treatment remains in discussion with a combination of pharmacotherapy, radiotherapy and surgery due to an unknown cause.[5] Mortality increases when osteolysis affects the spine, ranging from 6% to 50%.[6]

CASE REPORT

A 10-year-old male was brought by his parents for medical evaluation for referring pain in the cervical region during the last two months. The pain initially had a moderate intensity (referred with a score of 7/10) and was exacerbated by cervical mobilization and limited range of motion. Days after, the pain increased in intensity, until reaching a score of 10/10. He was treated with non-steroidal anti-inflammatory drugs, without obtaining an effective response. The patient has no medical, personal or psycho-social history of importance.

During the medical examination only pain was found on cervical mobilization during flexion, extension and bilateral rotation movements, predominantly posterior.

A non-contrast computed tomography of the cervical spine and skull showed extensive lytic lesions in the form of osteoporotic patches involving part of the sphenoid bone, clivus, temporal and left occipital bones, and the cervical vertebral bodies from c1 to c5 (Figures 1-2). Paraclinical examinations, blood cytometry, blood chemistry and urinalysis showed no changes. Only alterations in serum electrolytes were observed (Table 1).

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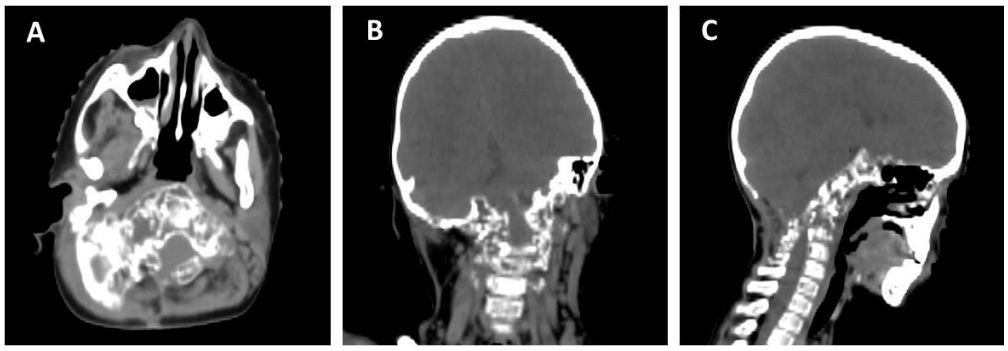

FIGURE 1. Computed tomography images taken before radiation therapy treatment. This figure shows three examples of computed tomography images obtained for radiation therapy planning. In axial view (**A**) we can observe a large osteolytic lesion over the petrous region of the temporal bone and the left occipital bone. The coronal view (**B**) shows osteolytic lesions of predominantly petrosal form bilateral with extrusion to the vertebral bodies of C1 and C2. The sagittal image (**C**) shows extensive osteolytic lesions in the clival region and the center of the occipital bone extending to the vertebral bodies and spinous apophysis of the first vertebrae.

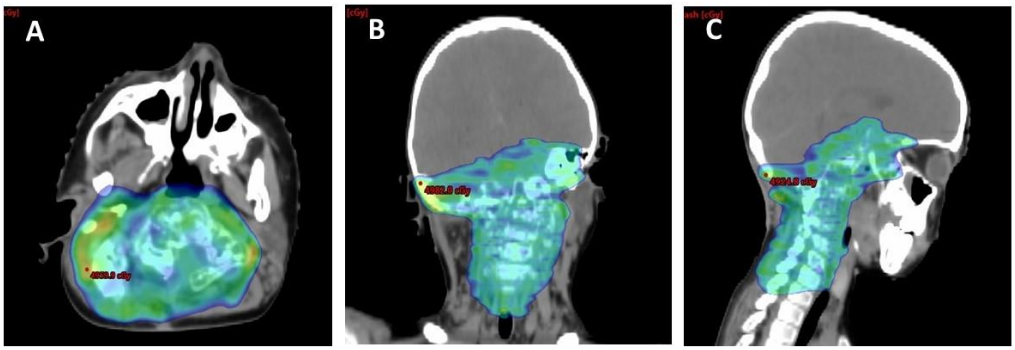

FIGURE 2. Radiation therapy planning. This figure shows three examples of CT scan axial (**A**), coronal (**B**) and sagittal images (**C**) used for radiation therapy treatment. The dose distribution is shown in wash color on the target volume in the three images.

TABLE 1. Serum electrolytes

Electrolyte	Test during clinical approach	Test after three months follow-up	Age-specific reference values
Sodium	138 mEq/L	141 mEq/L	135 – 147 mEq/L
Potasium	3.7 mEq/L	4.2 mEq/L	3.4 – 4.7 mEq/L
Chlorine	108 mEq/L	102 mEq/L	96 – 106 mEq/L
Calcium	11.3 mg/dL ↑	9.9 mg/dL	8.8 – 10.8 mg/dL
Magnesium	2.4 mg/dL	2.2 mg/dL	1-6 – 2.4 mg/dL
Phosphorus	5.3 mg/dL ↑	4.4 mg/dL	2.7 – 4.5 mg/dL
During the clinical approach, laboratory studies showed mild elevation of serum total calcium, serum calcium and phosphorus levels which decreased to normal values after medical treatment for three months.			

The pediatric neurosurgery department obtained a biopsy of the bone lesions taken from the vertebral body of C5 which were described by the pathology department as osteolytic lesions with angiomatous vascular proliferation of benign characteristics, without presenting cellular atypia or osteoblasts. In addition, a possible infectious disease was ruled out.

The neurological surgery department analyzed the case and decided not to perform surgical treatment due to the extension and deep location of the lesions. The patient was referred to our institution to be treated with radiotherapy (RT) and medical treatment with bisphosphonates.

RT was performed in Varian CLINAC iX equipment, with a total dose of 45 Gy in 25 fractions of 1.8 Gy per day, using a volumetric technique for beam modulation (VMAT) (Figure 2).

As for medical treatment, calcitriol capsules 0.25 mg every 24 hours and calcium carbonate pills 500 mg every 24 hours were administered.

During the medical follow-up 3 months after radiotherapy treatment, the pain on cervical mobilization decreased in intensity to 3/10. In addition the following labs were obtained: creatinine 0.31 mg/dL, alkaline phosphatase 114 U/L, total calcium 10.2 mg/dL, phosphorus 5 mg/dL and magnesium 2 mg/dL. The disease remained stable until the first year of follow-up (Table 1).

Subsequently, the patient was sent back to his home for clinical and radiological follow-up in the coming months, which are pending.

DISCUSSION

GSD, also known as Gorham's disease, phantom bone disease, vanishing bone disease, progressive osteolysis, acute bone absorption, primary lymphangioma, and massive idiopathic osteolysis, is a rare disease. This syndrome is characterized by spontaneous destruction of the bone matrix associated with massive osteolysis and proliferation of lymphatic vascular structures. GSD does not have a gender or race predilection and generally affects individuals under the age of 40. Currently, only about 400 cases have been reported, with an overall mortality rate of 13%. Mortality increases when osteolysis affects the spine, ranging from 6% to 50%.[6,7,8]

The pathophysiology of this disease is multifactorial, involving genetic factors such as somatic mosaic mutations. The associated genes include PTEN (phosphatase and tensin homolog) which appears to be one of the first genes affected in this disease and whose mutation leads to the formation of malignant and benign tumors, TREM2 (triggering receptor expressed on myeloid cells 2), and TNFRSF11A (TNF receptor superfamily member 11a) which causes familial expansive osteolysis expansive and expansive skeletal hyperphosphatasia. Mutations in the KRAS pathway, which promote bone angiogenesis through signaling cascades, have also been reported.[9,10,11]

The clinical presentation of GSD depends on the location affected by the osteolytic process and is characterized by pain (the main symptom), edema, weakness, and impairment of the affected limbs, pathological fractures, neurological alterations, paralysis, respiratory failure, and, in some cases, death.[12,13] Our patient presented cervical pain of two months of evolution that increased until cervical mobilization was difficult and range of motion decreased.

There are different diagnostic criteria for GSD, with the main criterion being an osteolytic radiographic pattern, absence of dystrophic calcifications, absence of visceral involvement, and the presence of hereditary, neoplastic, metabolic, infectious, or immunological etiology. Radiologically, this disease manifests itself as intramedullary and subcortical radiolucent areas resembling "osteoporosis patches." It is an irregular and slow process, with local progression of concentric contraction in the affected bones. Bone regeneration does not occur even if the progression of osteolysis subsides. This leads to bone deformity and loss of bone mass, increasing the risk of pathological fractures. Clinical laboratory tests are not effective in this syndrome as they are usually normal, apart from alkaline phosphatase, which may be elevated in some cases. The main differential diagnoses of this disease include osteomyelitis, rheumatoid arthritis, hereditary multicentric osteolysis, hyperparathyroidism, and eosinophilic granuloma.[14,15] Non-contrast computed tomography of the cervical spine and skull of our patient reported extensive lytic lesions in the form of osteoporotic plaques that involved part of the left sphenoid, clivus, temporal, and occipital bones, and the cervical vertebral bodies from c1 to c5. The pathology service described C5 osteolytic lesions with angiomatous vascular proliferation of benign characteristics, without presenting cellular atypia or osteoblasts.

Regarding the treatment of GSD, different therapies are included, classified as surgical, medical, and radiation treatment. Surgical treatment is the preferred option for

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patients at risk of developing pathological fractures and involves resection of the affected bone and joint reconstruction with prostheses. Pharmacology treatment offers various alternatives, including the use of bisphosphonates to provide protection to the affected bone. Scientific evidence also suggests the use of vitamin D analogs, calcium, interferon-alpha-2b, androgens, and adrenal extracts to protect against osteolysis.[9] Radiation therapy is indicated for patients with long-standing, functionally debilitating instability that does not respond to medical treatment and who have large symptomatic lesions. Radiation therapy shows favorable results in 75% of cases but can have long-term complications, with the most common being growth restriction during schooling and the presence of radiation-induced secondary malignancies.[16] In the present case, the patient received RT treatment with a Varian CLINAC iX device, with a total dose of 45 Gy in 25 fractions of 1.8 Gy per day, using VMAT technique which has the objective to cause damage on DNA of irradiated cell seeking to stop the osteolytic and inflammatory process which seems to be the reason causing the pain and performance improvement. On the other hand, medical treatment given with bisphosphonates is not a therapeutic treatment but it is aimed to regulate calcium and phosphate serum values and its potential effects.

The progression of the disease is slow, and the prognosis is unpredictable. In the case of our patient, the subject continued medical follow-up 3 months later at his clinic.

CONCLUSION

GSD is characterized by massive osteolysis, mainly affecting the bones of the skull, shoulders and pelvic girdle. It is important to suspect the presence of this syndrome when there is bone pain that does not subside with analgesic treatment. An initial study with an X-ray will help us to infer the disease in search of bone deformity, and the computed tomography will help us to offer a timely diagnosis. Treatment depends on the characteristics of the lesion. Improving the quality of life of patients and offering a better prognosis. In our case, we describe the medical and surgical approach for our patient, and we also confirm what the most up-to-date literature reports on diagnostic and treatment methods in SDG. Offering a better quality of life to patients.

CONFLICT OF INTEREST

The authors declare there are no conflicts of interest.

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