

SERIAL LYMPHOSCINTIGRAPHIC FINDINGS IN A PATIENT WITH GORHAM'S DISEASE WITH LYMPHEDEMA

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ABSTRACT

Gorham's disease is a rare disorder characterized by vascular, "lymphangiomatic" and/or "hemangiomatic" lesions in bone and surrounding soft tissues. Associated lymphedema has not been reported and clinical evolution is unpredictable. Plain radiographs, CT, MRI, and occasionally bone scintigraphy, are used to detect the bone and soft tissues changes. Biopsy is a major component of the diagnostic process. We report the findings of serial lymphoscintigraphy in a young boy with a polyostotic Gorham's disease associated with lymphangioma of the thigh and lower limb lymphedema. In this patient, lymphoscintigraphy was useful for diagnosis and follow-up of primary lymphedema. It provided valuable information concerning the occurrence, location, and progression of lymphatic lesions in both bone and soft tissues.

Keywords: Gorham's disease, lymphangiomas, lymphoscintigraphy, SPECT/CT

Gorham's disease (GD) is a rare musculoskeletal disease characterized by the uncontrolled proliferation of blood vascular or lymphatic capillaries within bone and surrounding soft tissue (1-2). GD is associated with massive osteolysis. In contrast to multicentric carpo-tarsal osteolysis for which a

genetic mutation was identified, there is actually no report suggesting a genetic predisposition to GD (3). Relation between osteolysis and hemangiomas was suggested by Gorham and Stout in 1954 (4). Lymphatic malformative nature of GD could be the primary cause of extensive osteolysis (5). Various terms like Gorham's disease, Gorham-Stout syndrome, massive osteolysis, and vanishing bone disease have been used to describe this disorder (1). More cases are described in early adulthood and the disease usually starts in a single bone and extends to the adjacent bones and soft tissues. Approximately 200 cases have been reported to date (6).

Imaging methods, particularly radiography, computed tomography (CT), and magnetic resonance imaging (MRI), show evidence of bone involvement; additionally, CT and MRI have been utilized to evaluate soft tissues changes (7-10). Bone scintigraphy may show increased or decreased isotope uptake in the affected bone (7-8,10). GD needs to be distinguished from other causes of osteolysis, and the final GD diagnosis is made by biopsy and immunochemistry with D2-40 (marker of lymphatic endothelium) (11).

We present a case of GD with lymphedema documented with lymphoscintigraphy. To the best of our knowledge, this is the first report in the literature of abnormal lymphoscintigraphic findings in GD.

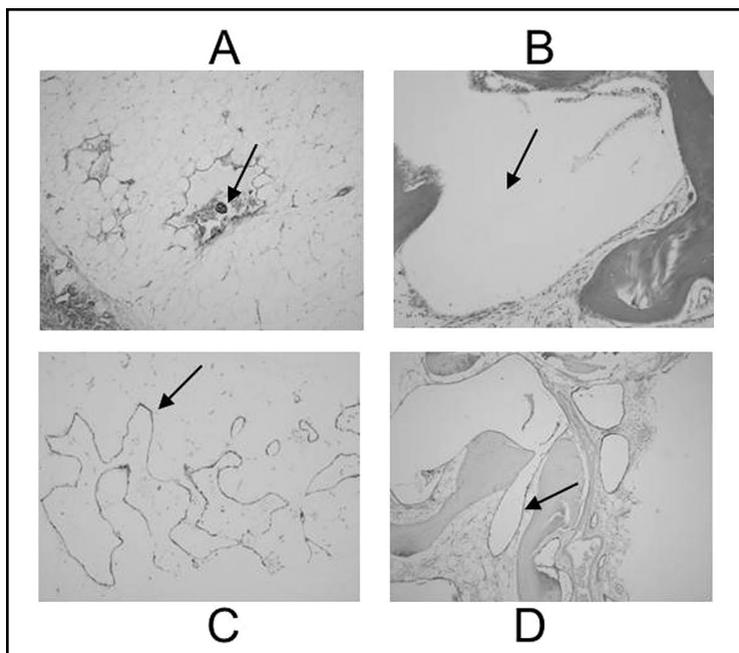


Fig. 1. (A,C): Biopsy of the thigh mass at age 3 with hematoxylin-eosin staining (A) demonstrating ectatic vascular cavities contain lymphocytic aggregates (arrow) and D2-40 immunochemical staining (C) highlighting vascular cavities lined by lymphatic endothelial cells (arrow). (B,D): Biopsy of ilium at age 3 with hematoxylin-eosin staining (B) demonstrating fibrosis surrounding cavernous cavities enlarging the medullar spaces (arrow) and D2-40 immunochemical staining (D) highlighting that vascular cavities are bordered by lymphatic endothelial cells (arrow).

CASE REPORT

A newborn male presented at birth with a mass in medial right thigh. Three years later, the thigh mass was unchanged, and the boy had a slight lymphedema of the right foot associated with limping. Histopathological findings of the thigh biopsy led to a diagnosis of lymphangioma with endothelial cells lining vascular spaces expressing D2-40 (Fig. 1-A,C). Radiography of right lower limb displayed heterogeneous dystrophy of bones. CT revealed multiple lacunar images within right tarsus and tibia. MRI showed altered signal intensity in right ilium bone marrow with hyperintense signal on T2 weighted images without gadolinium enhancement. At that time, only follow up was recommended.

At the age of six, the boy had a pathological fracture of proximal right tibia. Radiography revealed increased deminerali-

zation of right lower limb and ilium with presence of hollow spaces in the right ilium. Biopsy of ilium demonstrated within bone tissue large vascular lacunae bordered by cells expressing D2-40, and suggested for the first time the diagnosis of GD (Fig. 1-B,D). Lymphedema of the right foot extended to the leg. Lymphoscintigraphy was performed to investigate the lymphedema and also the lymphatic component of the lower limb lesions. ^{99m}Tc-labeled human serum-albumin nanosized colloid (Nanocoll*, GE Healthcare) was used. Thirty MBq were subcutaneously injected into the first interdigital space of each foot. Whole body imaging at 4 hours after injection showed on the right side a single inguinal node, a large accumulation of tracer in the thigh lymphangioma, foci delineating the distal femur and proximal tibia, and a large accumulation of tracer in the ankle. Tracer visualization of left ilio-

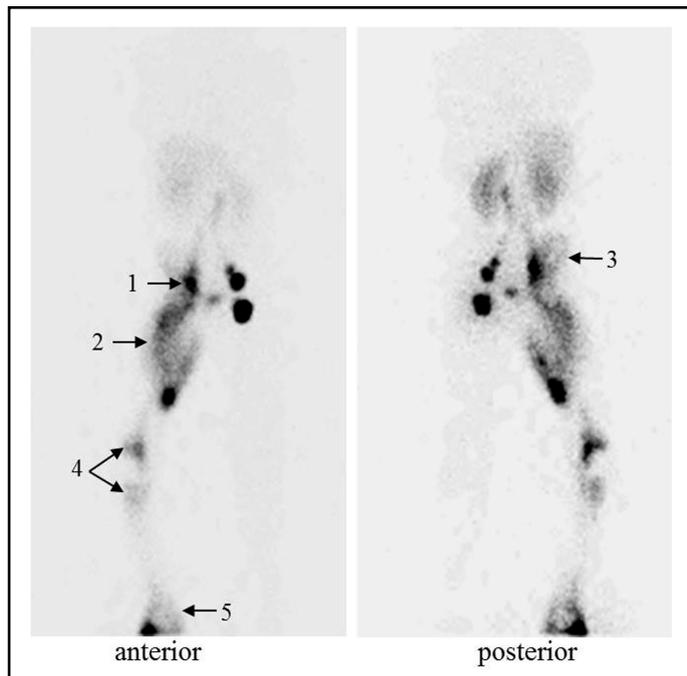


Fig. 2. First lymphoscintigram when the boy was 6 years old. Whole body imaging at 4 hours after injection shows on the right: one single inguinal node (arrow 1), a large tracer accumulation in the thigh (arrow 2) and in the right pelvis (arrow 3), foci drawing the silhouettes of the distal part of the femur and of the proximal part of the tibia (arrows 4) and a large tracer accumulation in the ankle area (arrow 5). The left side displays normal imaging of ilio-inguinal nodes.

inguinal nodes was normal. Lymphoscintigraphic findings were interpreted as hypoplasia of the right inguinal nodes and lower limb lymphangiomas (Fig. 2). The evolution was marked by a right tibia pseudarthrosis that justified iterative orthopedic treatments.

At the age of 9, the boy displayed significant inequality of the lower limbs. Lymphedema of the right foot involved the whole lower limb and was associated with recurrent erysipelas. A second lymphoscintigraphy using a hybrid gamma-camera was performed to follow the evolution of lymphatic abnormalities with the contribution of single photon emission computed tomography/computed tomography (SPECT/CT). Whole body imaging at 4 hours after subcutaneous injection of ^{99m}Tc albumin nanocolloid (35 MBq in each foot) was studied in comparison with the former

lymphoscintigraphy. It showed on the right side unchanged accumulation of tracer in the thigh, decreased inguinal node accumulation, increased accumulation in knee and ankle, and an additional accumulation in the medial part of the leg. On the left side, imaging identified additional popliteal nodes (Fig. 3-A). SPECT/CT that covered the lower part of the femurs and the legs located lymphatic spaces in the proximal tibia and internal muscular compartment of the right leg (Fig. 3-B). These findings were interpreted as worsening of lymphatic nodal hypoplasia, progression of lymphatic lesions in both bone and soft tissues, and a contralateral extension of primary lymphedema (12).

We previously reported the follow-up of this patient and the treatment of GD (13). The management of lymphedema was limited to antibiotic therapy and compression. Therapy with biphosphonates then tyrosine

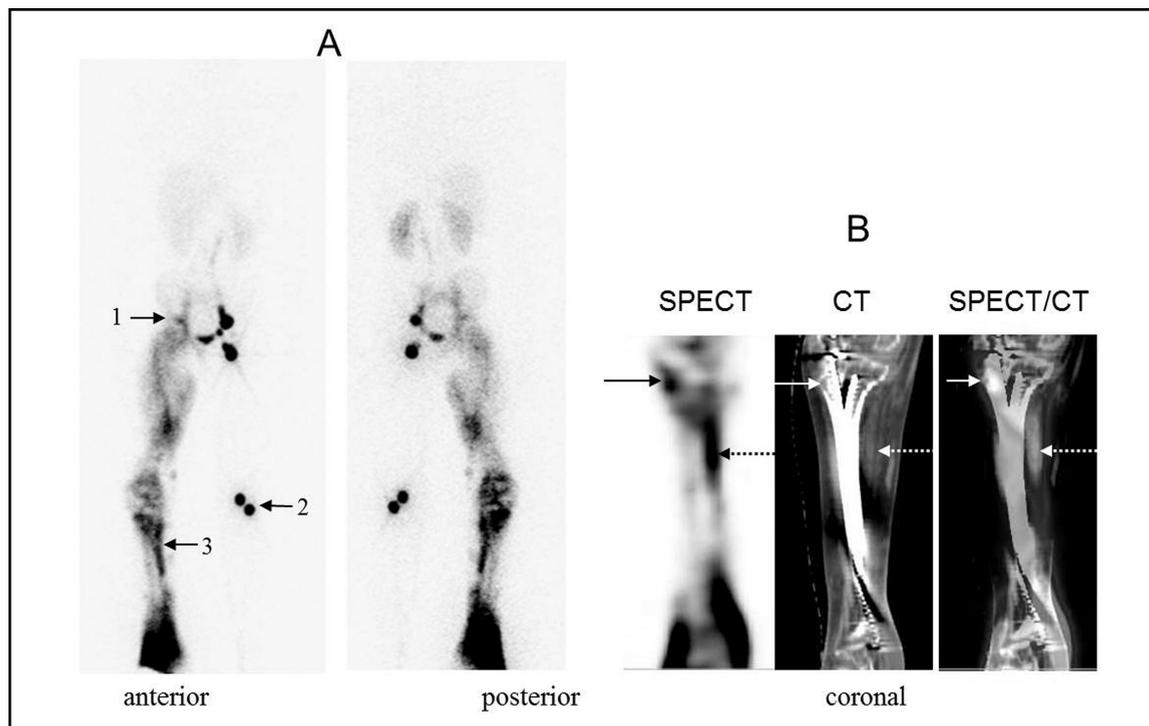


Fig. 3. Second lymphoscintigram when the boy was 8 years old. (A): Whole body imaging at 4 hours after injection compared with the former lymphoscintigram (Fig. 2) reveals that the accumulation of tracer in the right thigh is unchanged; there is a decreased accumulation of the right inguinal node (arrow 1) and left popliteal nodes (arrow 2); an increased accumulation in knee and in ankle; and an additional tracer accumulation area in the medial leg below the knee (arrow 3). (B): SPECT/CT coronal views clearly show lymphatic spaces in the proximal tibia (arrows) and internal muscular compartment of the leg (discontinuous arrows).

kinase inhibitor was administered without significant improvement. At the age of 11, followup found that femoral osteolysis had developed; the patient had a substantial lymphedema of the right foot; and he had trouble ambulating due to increased discrepancy in leg lengths.

DISCUSSION

GD is a rare vascular disorder which causes massive bone destruction. Osteolysis is due to proliferation of vascular elements and both hemangiomas and lymphangiomas are found with a variable predominance. These involve bone and sometimes soft tissues in the vicinity of the diseased bone. Lymphatic visceral involvement may also

occur, including chylous pleural effusion and chylous ascites (14).

To our knowledge, the association between GD and peripheral lymphedema has not previously been reported. Imaging modalities of conventional X-ray and MRI are currently used to evaluate the distribution of osteolysis and soft tissue involvement. We found in the literature a single report of lymphoscintigraphy in GD, however, it did not show any abnormality despite the presence of a chylous pleural effusion (1).

Herein we present a case of GD with lower limb bone osteolysis, thigh lymphangioma, and lower limb lymphedema, documented with two lymphoscintigraphies. An initial planar lymphoscintigram demonstrated hypoplasia of the right inguinal

nodes and lymphangiomatosis in the bone and soft tissues. Three years later, a second lymphoscintigram with SPECT/CT showed worsening of lymphatic hypoplasia with clear depiction of the localization and development of lymphangiomatosis. Furthermore, the presence of left popliteal nodes suggested a latent contralateral lymphedema.

In our case, lymphoscintigraphy contributed to diagnosis (nodal hypoplasia and latent contralateral lymphedema) and to lymphangiomatosis investigation. SPECT/CT allowed localization of dilated lymphatic spaces in the muscle and bone. We have recently demonstrated that SPECT/CT could contribute to the lymphoscintigraphic investigation of lower limb lymphedema (15). However, to our knowledge, only one other study has reported the use of SPECT/CT in the investigation of lymphedema (16).

Imaging modalities such as MRI and CT are currently used to investigate GD. However, lymphoscintigraphic imaging is the only modality that allows assessment of the lymphatic component in bone and soft tissues.

In conclusion, lymphoscintigraphy should be considered as a valuable imaging modality to investigate patients with GD.

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