Case report

Gorham-Stout disease involving ipsilateral clavicle and scapula in a child – a case report focusing on imaging and histopathological features of this extremely rare condition

Marek Duczkowski[1], Piotr Palczewski[2], Michał Wagrodzki[3], Agnieszka Duczkowska[1], Teresa Klepacka[4], Agnieszka Szymborska[5], Anna Raciborska[5], Jarosław Czubak[6], Monika Bekiesinska-Figatowska[1]

[1]Department of Diagnostic Imaging, Institute of Mother and Child, Warsaw, Poland
[2]I Department of Clinical Radiology, Medical University of Warsaw, Infant Jesus Teaching Hospital in Warsaw, Warsaw, Poland
[3]Department of Pathology and Laboratory Medicine; Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland
[4]Department of Pathomorphology, Institute of Mother and Child, Warsaw, Poland
[5]Department of Oncology and Surgical Oncology for Children and Youth, Institute of Mother and Child, Warsaw, Poland
[6]Department of Orthopaedics, Pediatric Orthopaedics and Traumatology, Centre of Postgraduate Medical Education, Gruca Teaching Hospital, Otwock, Poland

Gorham-Stout disease (GSD) is a very rare entity of unknown etiology, characterized by excessive intra-osseous proliferation of blood or lymphatic vessels, resulting in progressive resorption of bone matrix and destruction of bone. To date we have found only seven published cases concerning fully confirmed GSD of the shoulder girdle bones in children. Our case concerns an 8-year-old boy with involvement of the left clavicle and scapula. The knowledge of imaging and histopathological features is crucial for establishing the diagnosis of GSD, therefore the exchange of experiences in this field is essential for improving the care of affected patients.

Key words: Gorham-Stout disease (GSD), child, shoulder girdle, case report.

Introduction

Gorham-Stout disease (GSD) is a very rare entity of unknown etiology, characterized by excessive intra-osseous proliferation of blood or lymphatic vessels, resulting in progressive resorption of bone matrix and destruction of bone [1]. It often presents as osteolysis of one or more adjacent bones, resulting in functional deficits and pain [2]. The disease was first reported by Jackson in 1838 and later characterised by Gorham and Stout in 1955 [1, 3]. The literature is inconsistent about the total number of published cases – ranging from 200 to 300 cases [4, 5, 6], of which we have found only 7 reports concerning fully confirmed involvement of the shoulder girdle bones in children [7, 8, 9, 10, 11, 12, 13]. The diagnosis of GSD is difficult and demanding and unfortunately often delayed for years. Both the radiologist and pathologist play an important role in the diagnostics of this disease.

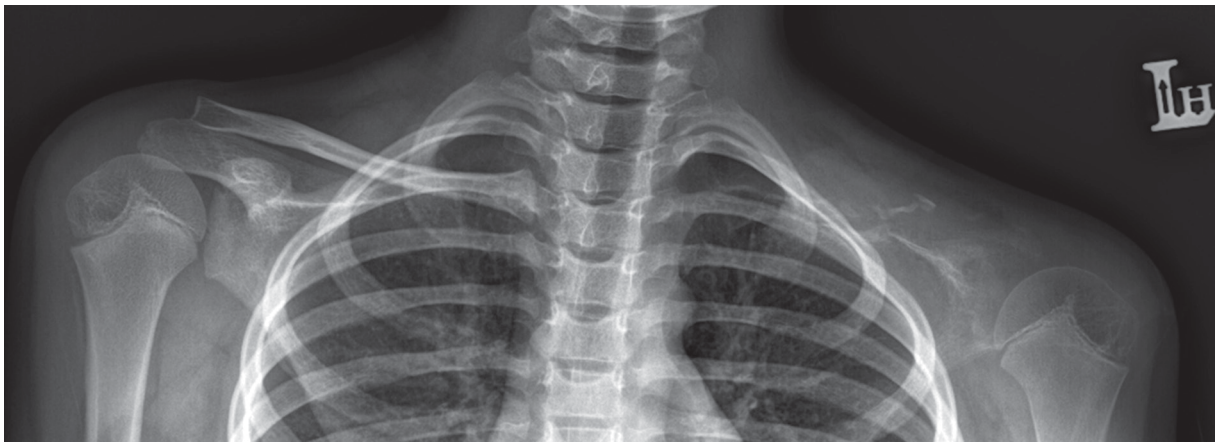

Fig. 1. Anteroposterior bilateral shoulder X-ray. Profound osteolysis and destruction of the left clavicle and scapula

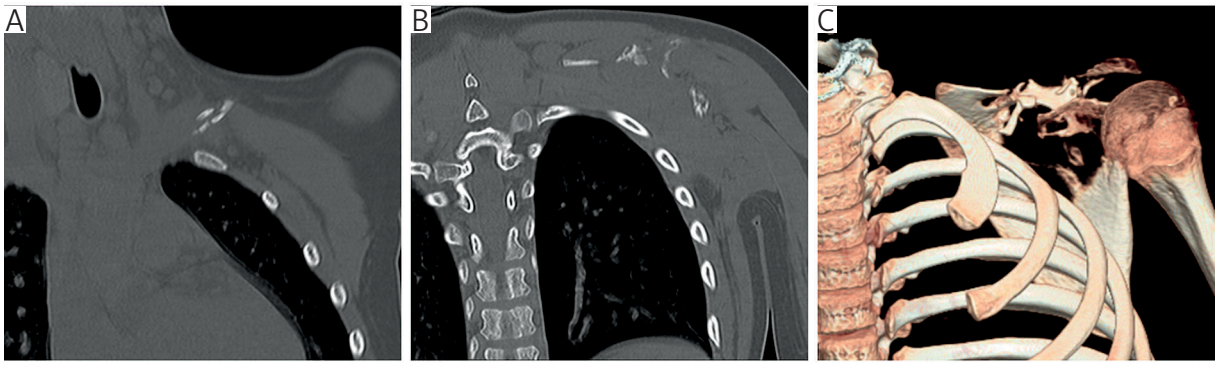

Fig. 2. Left shoulder computed tomography (CT) scan, coronal multiplanar reconstruction (MPR). Massive osteolysis and fragmentation of the clavicle (A) and scapula (B). 3-dimensional (3D) reconstruction (C)

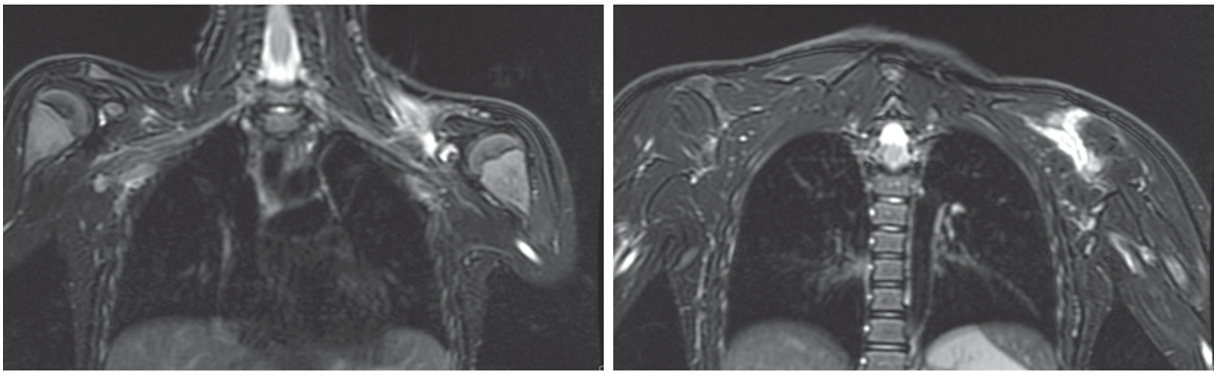

Fig. 3. Bilateral shoulder magnetic resonance imaging (MRI), Dixon/T2 water-only images, coronal plane. High signal intensity of the left clavicle and coracoid process of the left scapula (A), of the remaining affected parts of the scapula (B); surrounding soft tissues hyperintensity (A, B)

Case presentation

We report the case of an 8-year-old boy with the involvement of the left clavicle and scapula. The patient had a 2-month history of pain and limited range of motion in the shoulder joint, resulting in inability to raise the arm. The symptoms were preceded by a low-impact trauma on a trampoline. An X-ray performed at an outside institution two months after trauma revealed extensive osteolysis and destruction of the left clavicle and scapula (Fig. 1). The patient was referred with the suspicion of malignancy to the Institute of Mother and Child in Warsaw – a national reference center for children with bone tumors, where advanced imaging, laboratory tests and biopsy were performed. Low-dose computed

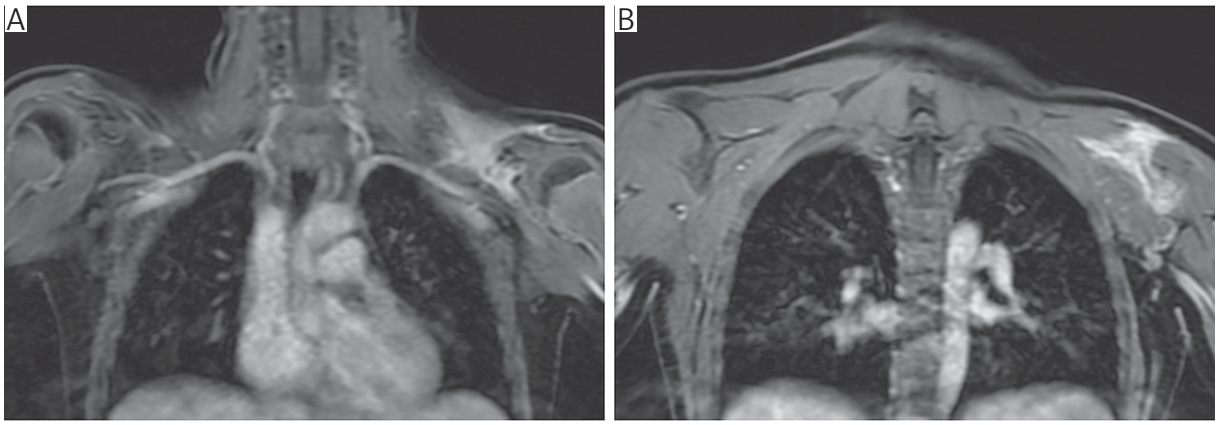

Fig. 4. Bilateral shoulder MRI, Dixon/T1 water-only post-gadolinium images, coronal plane. Intense enhancement of the left clavicle and coracoid process of the left scapula (A), of the remaining affected parts of the scapula (B); intense enhancement of the surrounding soft tissues (A, B)

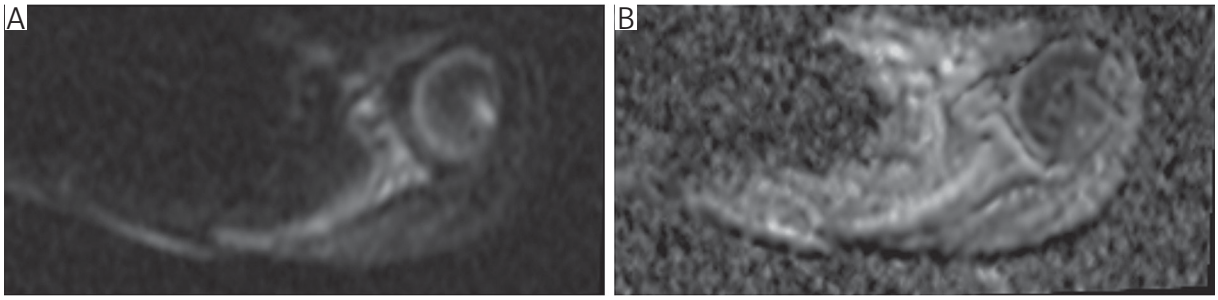

Fig. 5. Left shoulder MRI, diffusion-weighted imaging (DWI), axial plane. High signal intensity of the scapula on DWI (A) without restricted diffusion on apparent diffusion coefficient (ADC) map (B)

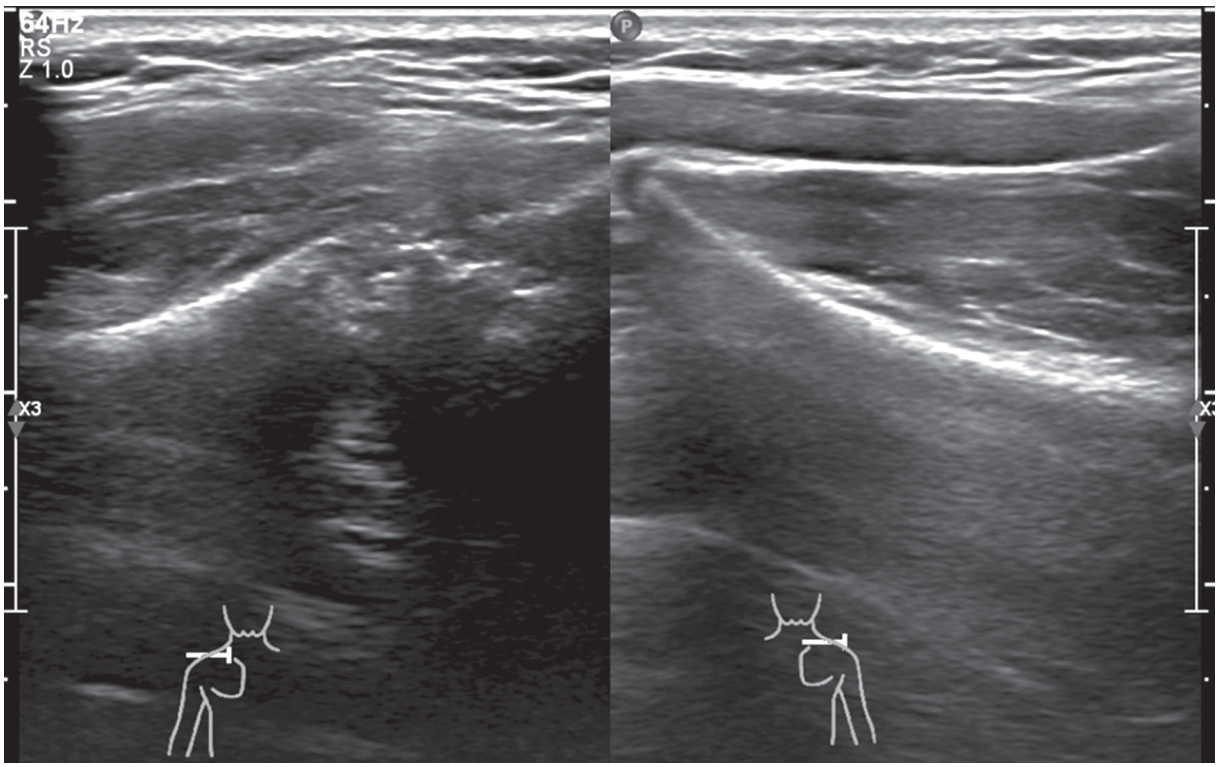

Fig. 6. Comparative ultrasound images on split view of the left and right scapula. Irregular margin of the left scapular spine (left image); normal margin of the right scapular spine (right image)

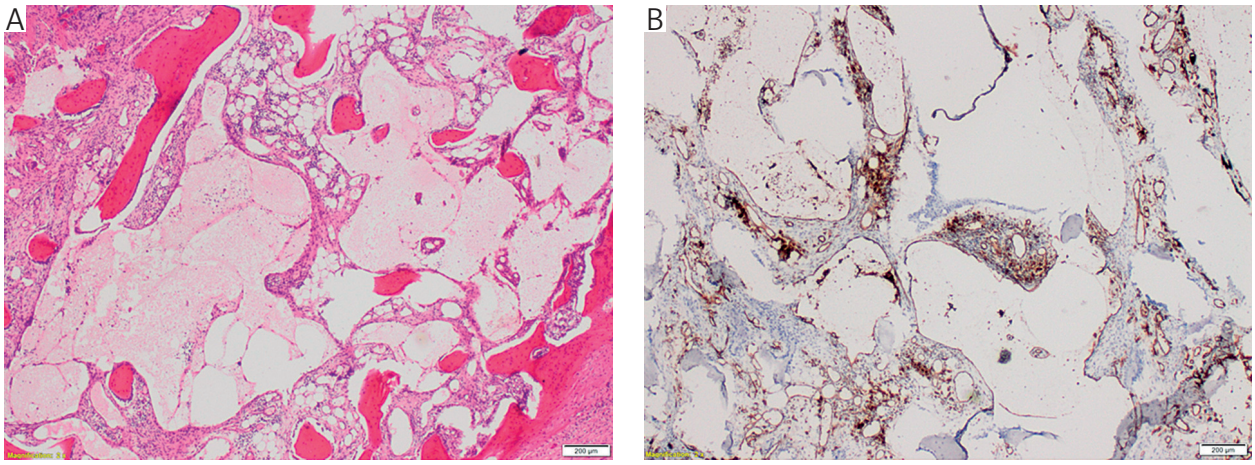

Fig. 7. Histopathology slides: hematoxylin and eosin (HE) staining and immunohistochemical (IHC) assay. Dilated thin-walled intraosseous vessels with cytologically bland endothelial lining (A). CD31 IHC assay [Dako, clone JC70A] outlines massive replacement of trabecular bone with vascular tissue (B)

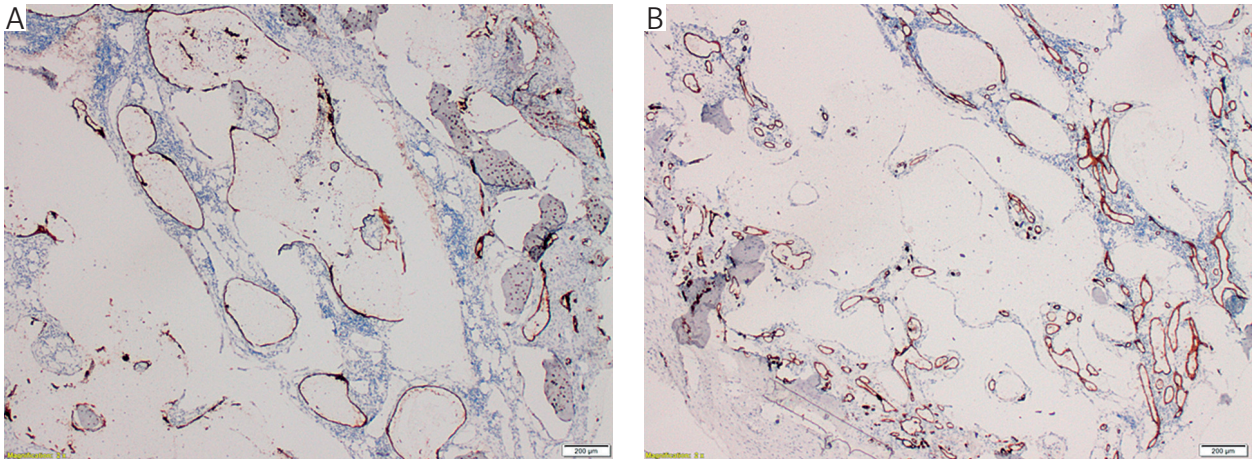

Fig. 8. Histopathology slides: IHC assays. Predominance of lymphatic channels in podoplanin IHC assay [Dako, clone D2-40] (A). CD34-positive blood vessels [Dako, clone QBEnd-10] (B)

tomography (CT) scan, performed in the native phase, confirmed massive osteolysis with bony fragmentation of the left scapula and of the ipsilateral clavicle (Fig. 2A–C). There was no evidence of chylothorax. Magnetic resonance images (MRI) acquired in standard sequences, in the native and dynamic post-contrast phases, revealed abnormal signal both in the affected bones and directly adjacent soft tissues, without the presence of any well-delineated mass. High signal on T2-weighted images (Fig. 3A, B) and post-gadolinium enhancement of the lesions (Fig. 4A, B) seemed similar to vascular structures; there was no restricted diffusion (Fig. 5A, B). On sonography the left clavicle and the scapular spine were fragmented (Fig. 6), while the surrounding soft tissue were moderately hypervascularized on color doppler. In our opinion all imaging findings spoke against primary or metastatic bone tumor. Taking into account the patient's age, history and osteolytic involvement of two adjacent bones of the shoulder girdle, the radiological suspicion of GSD was raised. Langerhans cell histiocytosis (LCH) and osteomyelitis (OM) were on our differential list, but considered less probable. All laboratory tests including C-reactive protein (CRP), lactate dehydrogenase (LDH) and alkaline phosphatase (ALP) were within normal range. An open biopsy of the scapular spine was performed. Bone samples were decalcified in 10% buffered ethylenediaminetetraacetic acid (EDTA – Mol-decalcifier, Milestone) in 37°C, fixed in 10% neutral buffered formalin, routinely processed, cut into 4-μm-thick tissue sections and hematoxylin and eosin (HE) stained. Immunohistochemical (IHC) assays were performed using Dako EnVision™ FLEX detection system. Histologically there was intraosseous proliferation of CD31-positive thin-walled vessels without cellular atypia of endothelial cells (Fig. 7A,B). IHC staining with D2-40 antibody revealed predominance of dilated lymphatic channels (Fig. 8A). CD34 expression outlined vascular capillaries

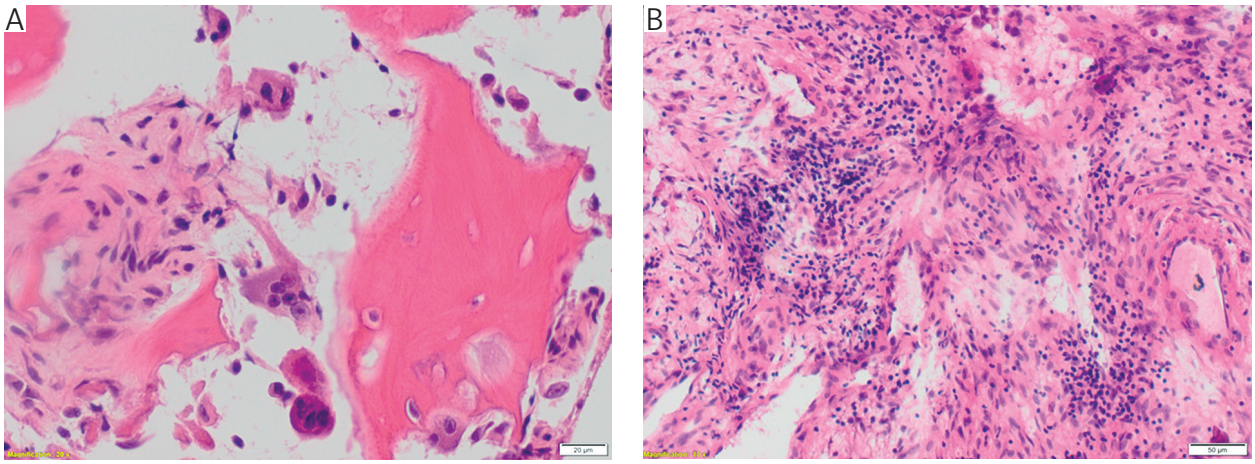

Fig. 9. Histopathology slides: HE staining. Osteoclasts at the edge of trabeculae of bone (A). Proliferation of fibrous tissue (B)

(Fig. 8B), suggesting dual nature of proliferating vessels. Trabeculae of cancellous and cortical bone were thinned and depleted in number with visible but not prominent osteoblastic reaction and scattered osteoclasts (Fig. 9A). Connective tissue proliferation with some lymphocytic infiltration was observed adjacent to vascular areas (Fig. 9B). OM was ruled out based on absence of neutrophils in inflammatory infiltrates and negative bacterial cultures. No histological signs of LCH were discovered. Histopathological findings in combination with imaging features, fulfilled the diagnostic criteria of GSD suggested by Heffez *et al*., in a patient with absence of visceral involvement and negative hereditary, metabolic, neoplastic, immunologic, or infectious etiology [14].

Discussion

To the best of our knowledge this is the eighth reported case worldwide, describing a child with fully confirmed GSD of the shoulder girdle bones. The cases reported to date include six boys from 8 to 17 years of age with focal lesions i.e. monostotic or limited to adjacent bones, as in our case, and a 5-year-old girl with multifocal, non-contiguous lesions involving the bones of the entire body, among them both clavicles and scapulas [7, 8, 9, 10, 11, 12, 13]. We have found three more reports, which in our opinion did not meet all diagnostic criteria of GSD, because a bone biopsy was either not performed or was not specifically mentioned by the authors [15, 16, 17]. Gorham-Stout disease is an extremely rare form of idiopathic osteolysis. Hardegger *et al.* proposed a classification of idiopathic osteolysis, composed of five types. Type 4 represents GSD, can occur in any part of the skeleton, at any age, is not hereditary and not associated with nephropathy [18]. The disease is most often seen in children and young adults, and is most common in bones that develop by intramembranous ossification such as bones of the shoulder girdle, pelvis, jaw, ribs and spine [14]. It is characterized by progressive osteolysis, self-limiting in some years [18]. Initially localized to one bone, the disease can gradually invade adjacent bones and surrounding soft tissues [13]. Most reported cases of GSD demonstrate monocentric occurrence. Rarely, more than one anatomic region is involved, separated by normal osseous structures [19]. The clinical course varies from spontaneous remission to fatal outcome with an overall mortality of about 13% [20]. The fatal outcome can occur in patients with vertebral involvement in the context of spinal instability or in patients with chest wall involvement complicated by chylothorax with a mortality reaching up to 52% [20]. Direct migration of dysplastic vessels into the thorax or the erosion of the thoracic duct are the suspected causes of chylothorax [21]. Gorham-Stout disease patients are commonly suspected upon imaging of malignancy or OM and the final diagnosis is often delayed for years. The differential diagnosis in children includes OM, neoplastic diseases such as LCH and Ewing sarcoma, endocrine disorders, e.g. brown tumor, and other rare conditions presenting with osteolysis, such as generalized lymphatic anomaly [22]. The exact pathogenesis of GSD is still poorly understood. Histologically it is characterized by extensive loss of bone matrix, primarily replaced by lymphatic and vascular tissue and at a later stage by fibrous tissue [23]. D2–40 expression is positive on IHC assays, with a sensitivity of 92.6% and specificity of 98.8% [5]. Criteria listed by Heffez *et al*. [14] are applied to establish the final diagnosis. Proliferation of lymphatic as well as blood vessels observed in our case indicates nonneoplastic process underlying GSD. Post traumatic hyperemia, local changes in pH levels, mechanical forces and elevated level of serum interleukin-6 were mentioned as possible causes for the angiomatous proliferation [1, 24, 25]. In accordance with findings reported by Devlin *et al*., Moller *et al*. and Hominick *et al*. [25, 26, 27], osteoclastic activity was

discovered in our case, suggesting a possible link between osteoclast-induced resorption of bone and vascular proliferation. The diagnosis of Gorham–Stout disease is difficult and demanding, particularly in the early stage. Imaging and histopathological features are crucial diagnostic criteria. Therefore the exchange of experiences in this field has a high priority for improving the care of the affected patients.

The authors declare no conflict of interest.

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Address for correspondence

Marek Duczkowski
Department of Diagnostic Imaging
Institute of Mother and Child
Kasprzaka 17A
01-211 Warsaw, Poland
e-mail: m.duczkow@gmail.com