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Ultrasound image of malignant bone tumors in children. An analysis of nine patients diagnosed in 2011–2016

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ultrasonography, power Doppler, bone tumors, bone destruction, elastography

Abstract

Introduction: The diagnostic process of bone tumors, including malignant ones, is based on conventional radiological methods, such as radiography and computed tomography, and with precise assessment of local advancement in magnetic resonance imaging. Ultrasonography is not included in the diagnostic algorithms as a tool suitable to detect this type of pathology. More and more frequent usage of musculoskeletal ultrasound in children as the first imaging method or, in some cases, as the only diagnostic method, makes it necessary to be familiar with sonographic presentation of bone tumors to suggest this diagnosis early enough and, after its verification, start treatment without a significant delay. Aim: The aim of this study was to determine changes in the sonographic image that might indicate a bone malignancy and suggest the need to extend the diagnostic process in this direction. **Material and method:** This article discusses 10 bone tumors in 9 children who had an ultrasound scan performed at the beginning of the diagnostic process before the histopathological diagnosis was established and treatment initiated. The assessment involved ultrasonographic features indicating the presence of a tumor. Results: In the group of 9 patients, 8 malignant bone tumors were diagnosed in ultrasonography and later verified histopathologically: 4 osteosarcomas and 4 Ewing's sarcomas. In one case, two bone tumors were detected in ultrasonography without specification of their nature (malignant/benign, primary/secondary). **Conclusions:** In the analyzed cases, ultrasonography enabled the correct diagnosis of a focal bone lesion, and in most cases (8/9) it presented an image that suggested its malignant nature and the necessity of further diagnosis and treatment.

Introduction

Bone tumors are principally diagnosed in radiography and computed tomography (CT), while local progression is precisely assessed in magnetic resonance imaging (MRI)[1,2]. Ultrasonography (US) is generally considered useful only in restricted cases, mainly for post-operative assessment[3], particularly in patients with prostheses that generate artifacts in CT and MRI, thereby hindering assessment, as well as for detection and monitoring of local complications of the tumor. Literature reports on its usefulness in the detection of bone tumors and on their US presentation are very limited[4]. This paper presents an analysis of malignant bone tumors detected on the basis of a US scan performed due to a clinical suspicion of a different pathology or at an early stage of a diagnostic process initiated due to the presence of a palpable local lesion. The aim was to determine abnormalities in the sonographic image that might indicate a tumor and suggest a need for an extended diagnostic process in this direction.

Material and methods

Of patients with malignant bone tumors diagnosed in the Department of Pediatric Radiology of the Medical University of Lublin in 2011–2016, we selected cases in which a bone tumor suspicion was made on the basis of a US examination that was performed for other clinical indications or was conducted at an early stage of a diagnostic process due to the presence of a palpable local mass before histopathological diagnosis was established. The study excluded patients with previously diagnosed disease in whom US was conducted for other purposes, e.g. to check for local complications, or patients during and after treatment, and patients with a radiological diagnosis of a bone tumor made by the same physician who conducted a US scan. The aim of such selection was to exclude cases where the knowledge of conventional radiological images could affect the analysis of US scans and create correlations between images. The total number of patients who met these criteria was 9 (5 boys and 4 girls, aged 12–15 years). Tab. 1 presents patient data and causes for ordering a US scan.

US examinations were conducted with the following scanners: Philips iU22 with linear probe L12-5, Siemens Acuson S2000 with linear probe L9-4 and Voluson 740 Expert with linear L12-6. All scans were performed by a single radiologist (T.M.) with long experience in musculoskeletal ultrasound imaging.

The examinations showed a lesion and its relationship with the bone. Pathological signs that could suggest the nature of the lesion were looked for. The images were analyzed in terms of: the presence of a tumor, its relationship with the bone, sonomorphology, accompanying bone destruction, abnormal calcifications and mineralization that could indicate periosteal reactions, periosteal pathology and the presence of a potential extraosseous mass. Moreover, tumor vasculature was also assessed in color and power Doppler, and, in some cases, its elasticity was evaluated in real time elastography (RTE). Also, additional signs that might indicate the malignant nature (e.g. tumor implants within the pleura, pleural fluid) were noted. When reliable measurements could be made, the three-dimensional size of the lesion was assessed. In most examined tumors, panoramic imaging was employed to evaluate the longest dimension.

The patients with a diagnosis of a bone tumor established in US were urgently referred to an oncologist and underwent further imaging examinations adequate for their pathology (radiography, CT, MRI).

Results

In the group of 9 patients, 8 malignant bone tumors were diagnosed in US and later verified histopathologically. These were 4 osteosarcomas (OSAs) and 4 Ewing's sarcomas (ESs). In one case (K.G.), two bone tumors were detected in US without specification of their nature (malignant/benign, primary/secondary).

The histopathological examination revealed: 4 OSAs, 4 ESs and, in one patient (K.G.), 2 tumors identified as bone lymphoma (Burkitt non-Hodgkin's lymphoma, NHL-Burkitt).

Initials	Sex	Age	Year of examination	Tumor location	Cause stated on the referral
P.K.	M	14	2011	right tibia	local edema
D.C.	M	14	2012	left femur	persisting posttraumatic edema
Ł.A.	M	12	2012	10th right rib	abdominal pain
Z.K.	F	13	2013	left femur	joint edema
K.G.	M	12	2014	frontal bone/tibia	nodule in the frontal region/pain in the lower leg
P.S.	F	15	2014	left femur	tumor in the popliteal fossa
K.W.	F	13	2014	right femur	thickening in the thigh
D.M.	F	15	2015	right clavicle	suspicion of arthritis in the ACJ
P.B.	M	16	2016	7th left rib	shortness of breath

Tab. 1. *Patient data, tumor location and causes for ordering a US scan*

Initials	Location	Presence of a tumorous mass	Echogenicity	Homogeneity	Bone destruction	Periosteal separation	Periosteal reactions	Size	Vasculature	Elastography	Additional signs
P.K.	tibia	present	lower	heterogeneous	present	present	absent	5 cm	rich	mixed stiffness	regions of tumor mineralization
D.C.	femur	present	lower	heterogeneous	present	present	present	10 cm	rich	stiff	
Ł.A.	rib	present	lower	heterogeneous	present	invisible	invisible	11 cm	enhanced	not performed	infiltration of the soft tissues of the chest, pleural fluid
Z.K.	femur	present	lower	heterogeneous	present	present with loss of continuity	present	no data	rich	stiff	
G.K.	frontal bone	present	lower	homogeneous	present/ blurred cortical bone	present	invisible	4.5 cm	moderate	not performed	
G.K.	tibia	present	lower	homogeneous	slight/ blurred cortical bone	present	invisible	4 cm	rich	not performed	
P.S.	femur	present	lower	heterogeneous	present	present with loss of continuity	present	12 cm	rich	stiff	extraosseous tumor in the popliteal fossa, lymph nodes
K.W.	femur	present	lower	heterogeneous	present	present	present	8 cm	rich	stiff	
D.M.	clavicle	present	lower	heterogeneous	present	present	present	7 cm	rich	stiff	
P.B.	rib	present	lower	heterogeneous	present	invisible	present	15 cm	moderate	not performed	pleural implants, fluid

Tab. 2. *Morphological features of bone tumors in US*

In total, ultrasonography was used to evaluate 10 bone tumors. Their morphological features and US signs indicating their presence are presented in Tab. 2.

The most important common features for the whole group were: the presence of a pathological solid mass corresponding to a bone tumor (10/10) and low tumor echogenicity (10/10) (Fig. 1). In 8/10 cases, a tumorous mass was characterized by structural heterogeneity. The two cases of homogeneous echogenicity concerned two lesions found in K.G., diagnosed as bone lymphoma. Another feature common for the whole group was the presence of bone destruction (Fig. 2), but the two lesions diagnosed as bone lymphoma were characterized

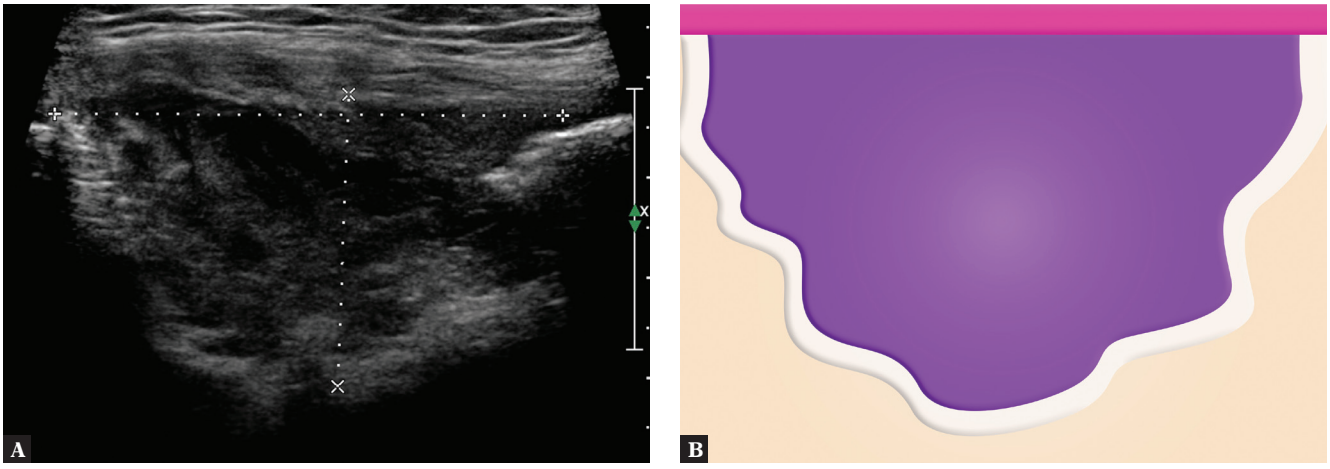


Fig. 1. *Patient P.K. Osteosarcoma. An osteolytic tibial defect of uneven outline filled with heterogeneous hypoechoic pathological tissue*

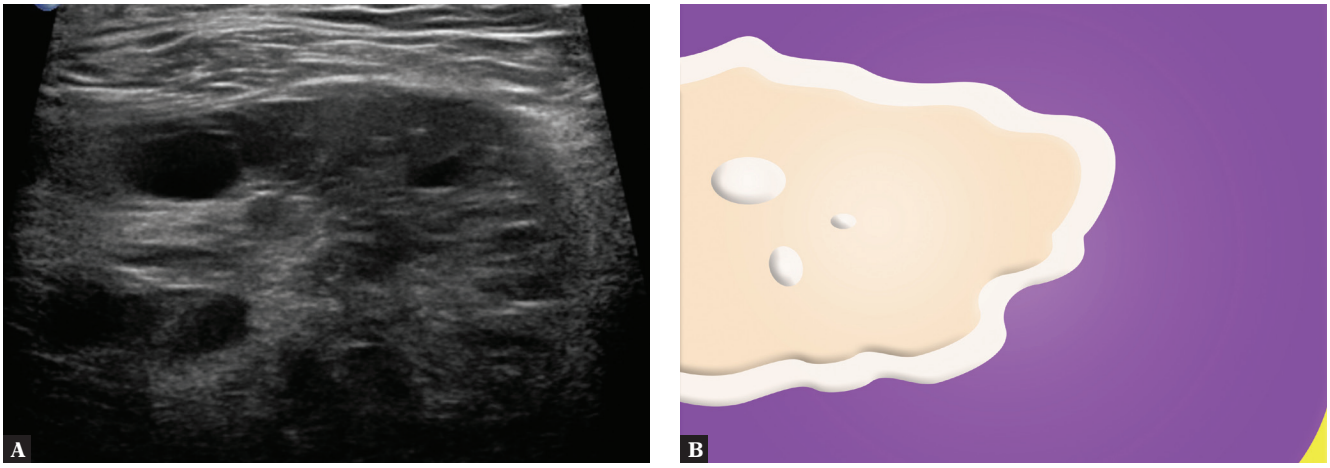


Fig. 2. *Patient D.M. Ewing's sarcoma. A pathological tumor mass emerging from the end of the shoulder clavicle with visible clavicle destruction: uneven bone outline and partial penetration of the ultrasound wave to the infiltrated bone*

by subtle bone destruction in the form of blurred cortical outline. The remaining tumors presented images of bone destruction with its visible defects (8/10). In 8/10 cases, there were signs of marked separation of the periosteum. Two cases in which this phenomenon was not clearly visualized refer to two Ewing's sarcomas originating from the ribs (Ł.A., P.B.).

By analogy with radiography, periosteal reactions, which are characterized by high specificity in detection of malignant bone tumors, were also assessed in US. Mainly two types of abnormal reactions were looked for: separation of newly emerged subperiosteal bone (a sonographic equivalent of the Codman triangle) as well as mineralization and calcifications perpendicular to the long axis of the bone (an equivalent of spiculated periosteal reaction of the "sunburst" type) (Fig. 3). These lesions were detected in 6/10 cases.

The size of the tumors in the longest axis ranged from 5 to 15 cm in the group of pathologies diagnosed as osteosarcoma and Ewing's sarcoma. In the two tumors classified as lymphoma, the greatest were their longitudinal dimensions: 4.5 cm and 4 cm. In one case (Z.K.), the tumor size was not noted.

All tumors exhibited enhanced, at least moderate, vasculature, frequently with chaotic distribution of vessels, which were the most numerous on the periphery of the pathological masses (Fig. 4).

In some cases, there were additional sings that unambiguously suggested a malignancy. As for Ewing's sarcoma of the ribs: P.B. had numerous tumor implants in the parietal pleura and a significantly increased amount of pleural fluid, while Ł.A. had chest infiltration, an extraosseous mass in the costophrenic recess with signs of infiltration of the diaphragm and liver, and increased amount of pleural fluid. Moreover, P.S. had an extraosseous mass in the popliteal fossa with enlarged lymph nodes; moreover, areas suggesting hemorrhagic cysts occupying a part of the tumor were noted within the extraosseous mass.

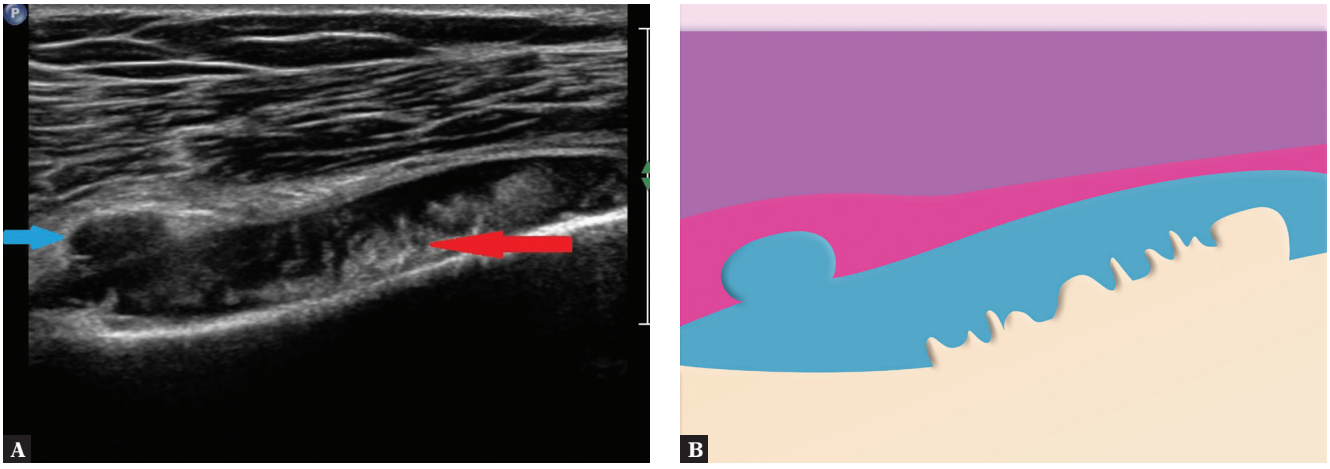


Fig. 3. *Patient Z.K. Osteosarcoma. Femoral tumor. A subperiosteal pathological mass with visible hyperechoic reflections indicating neoplastic mineralization with a tendency to their radial arrangement (red arrow). On the left side of the image, one may notice visible features of tumor invasion in the periosteum with a slight hypoechoic nodule (blue arrow)*

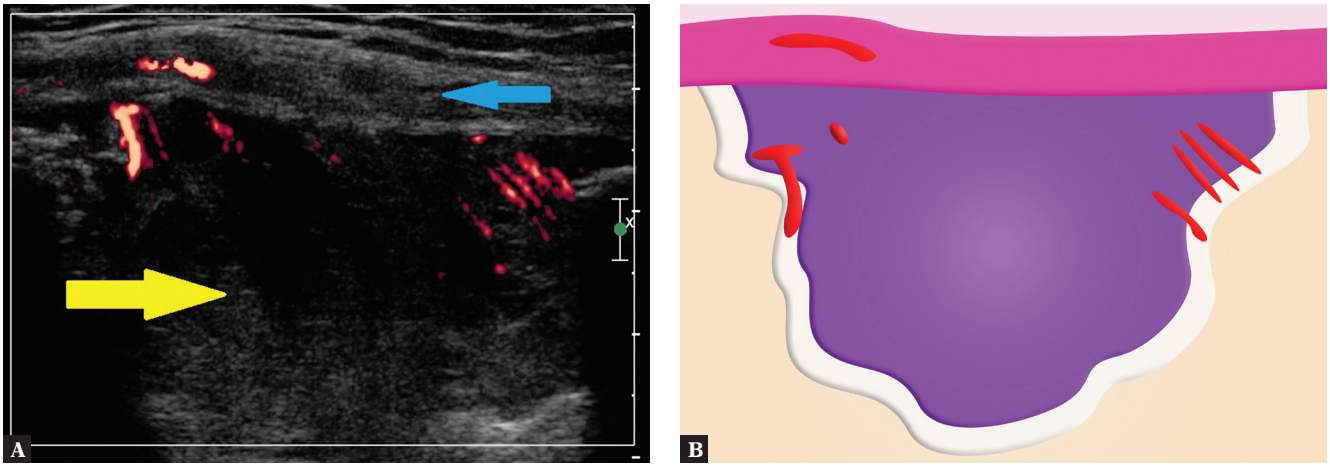


Fig. 4. *Patient P.K. Osteosarcoma. An osteolytic lesion of the tibia, as in Fig. 1. Power Doppler imaging shows numerous vessels on the periphery of the lesion, thereby confirming the tissue nature of the pathological mass that occupies the bone defect (yellow arrow). Additionally, one may notice thickening, edema and hyperemia of the periosteum (blue arrow)*

Elastography was conducted in 6/10 cases. In 5/10 cases, the lesions appeared entirely as blue on elastograms, which attested to their considerable stiffness. In one case (P.K.), the stiffness of the lesion was mixed, and the part of the tumor that showed greater solidity on the elastogram (blue) was also characterized by higher echogenicity.

Based on the analyzed cases, certain sonographic signs that may indicate a primary malignant bone tumor were distinguished.

Signs suggesting a malignant bone tumor in ultrasonography include:
1) a large bone tumor reaching over 5 cm in the longest dimension;
2) irregular bone destruction with unclear and blurred margins;
3) blurred and uneven cortical bone with signs of destruction;
4) periosteal abnormalities: separation, thickening and edema;
5) pathological mineralization—an image of "malignant" periosteal reactions;
6) rich vasculature;
7) a "hard" lesion in elastography;
8) a pathological extraosseous mass.

In all the cases of malignant bone tumors, several of the above listed signs occurred simultaneously.

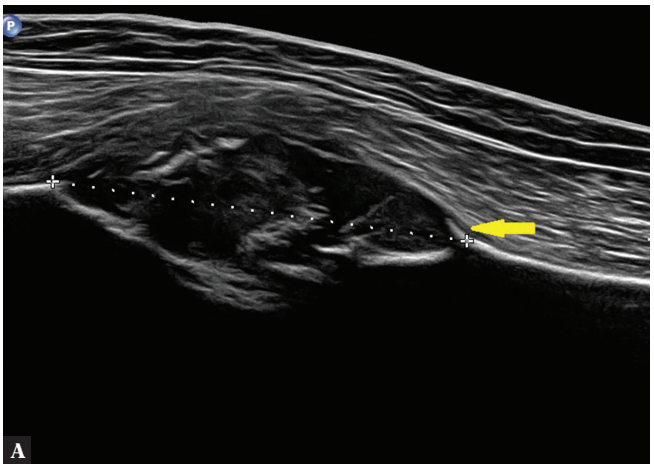
Discussion

The diagnostic process of bone tumors is based on conventional radiological methods, such as radiography and CT, which are used to detect the lesion and analyze its nature. Subsequently, MRI is conducted to evaluate local progression and detect potential complications[5,6]. General advancement of the disease is assessed with other methods, such as chest CT and scintigraphy.

Ultrasonography is not mentioned in diagnostic algorithms as a useful tool for early detection and diagnosis of these pathologies. It is mainly used in post-operative assessment, treatment monitoring and evaluation of local complications[3]. US is commonly believed to be helpful in the assessment of neoplasms and soft tissue tumors. It is frequently ordered as the first test in pediatric patients as it helps establish the final diagnosis of, for example, pseudotumors in many cases, thus limiting radiation exposure[7]. Various literature reports that provide evidence for high value of US in the assessment of musculoskeletal pathologies, such as bone erosions in the course of inflammatory diseases in rheumatology[8] and bone fractures[9], justify the claim that US might also be useful for the diagnosis of bone tumors.

The basic feature enabling visualization of a bone tumor in a US examination is cortical involvement or subperiosteal location of the lesion. All lesions visualized in this study exhibited these two features. Most malignant bone tumors are large at the diagnosis, exceeding 5 cm in the longest axis. Of all the described tumors, 7/10 exceeded 5 cm. In one case, the size of the tumor was not provided as it was difficult to measure, but it clearly extended beyond the probe's field of view. Such large lesions, exceeding the width of the transducer's head, may be overlooked in a US scan as a fragmentarily seen tumor might not be interpreted as a pathological tissue. In these cases, panoramic imaging may be helpful (Fig. 5)[4].

The assessment of the periosteum delivers important information. Pediatric US examinations enable the assessment of pathological separation of the periosteum in the case of inflammatory abnormalities in the course of osteomyelitis and fractures, showing also subperiosteal fluid collections and periosteal reactions[7,10]. In this work, periosteal separation was noted in 8/10 cases, while hyperechoic reflections in the periosteal region, corresponding with periosteal reactions, were seen in 6/10 cases. Two cases in which periosteal separation was not visualized concerned rib tumors, which might have



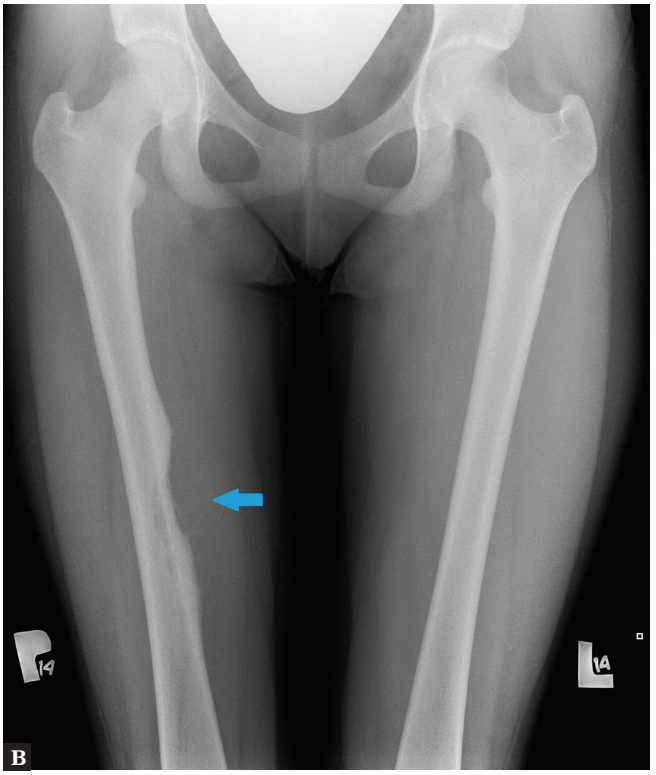
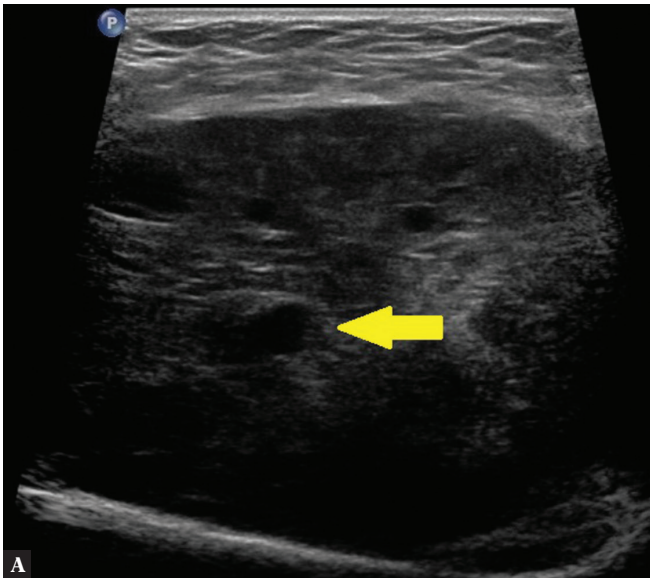


Fig. 5. *Patient E.W. Ewing's sarcoma. Femoral shaft tumor.* **A.** *Panoramic imaging helps assess the total longitudinal size of the tumor (8 cm) and more clearly shows the relationship of the lesion with the bone. In the distal part of the lesion, one can notice a sharp bone of the "rose thorn" morphology, which corresponds with the radiographic Codman's spur (yellow arrow). Uneven outline of the cortical bone adjacent to the bone.* **B.** *Radiography of the femoral tumor (blue arrow)*

been associated with their deeper location and restricted ability to visualize the periosteum. In two cases, periosteal abnormalities unambiguously suggested a malignancy: periosteal infiltration and the site of the loss of its continuity were visible. A sign that indirectly indicates the loss of periosteal continuity is the presence of a tumor component in soft tissues surrounding the bone; in one case an extraosseous tumor was located in the popliteal fossa (Fig. 6). When searching for pathological periosteal separation, it is recommended to carefully assess the boundary between the tumor and healthy bone as these lesions are the most visible in this location. As in radiography, one may notice the lack of clear delineation of a lesion from healthy bone (so-called broad transitional zone). In all cases, we also noted changes in the cortical bone indicating bone destruction. In G.K. with bone lymphoma, the severity of bone destruction was significantly lower and represented mainly by blurred



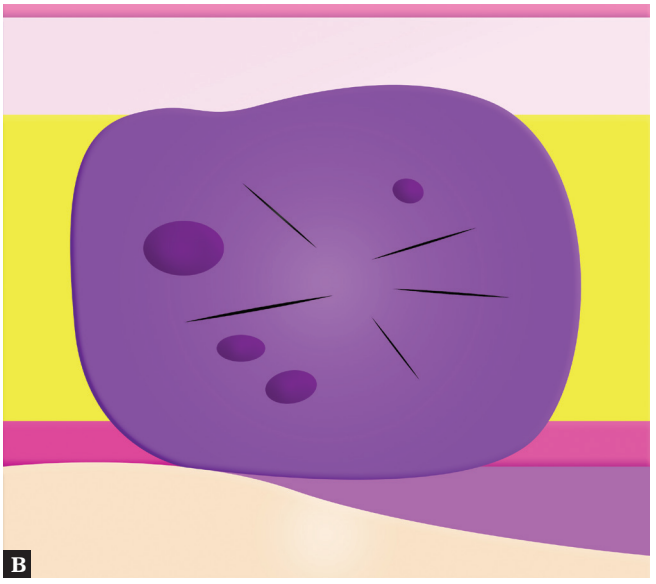


Fig. 6. *Patient P.S. Osteosarcoma. A tumor in the distal femur. An extraosseous mass in the popliteal fossa. Cystic areas within the tumor mass (yellow arrow)*

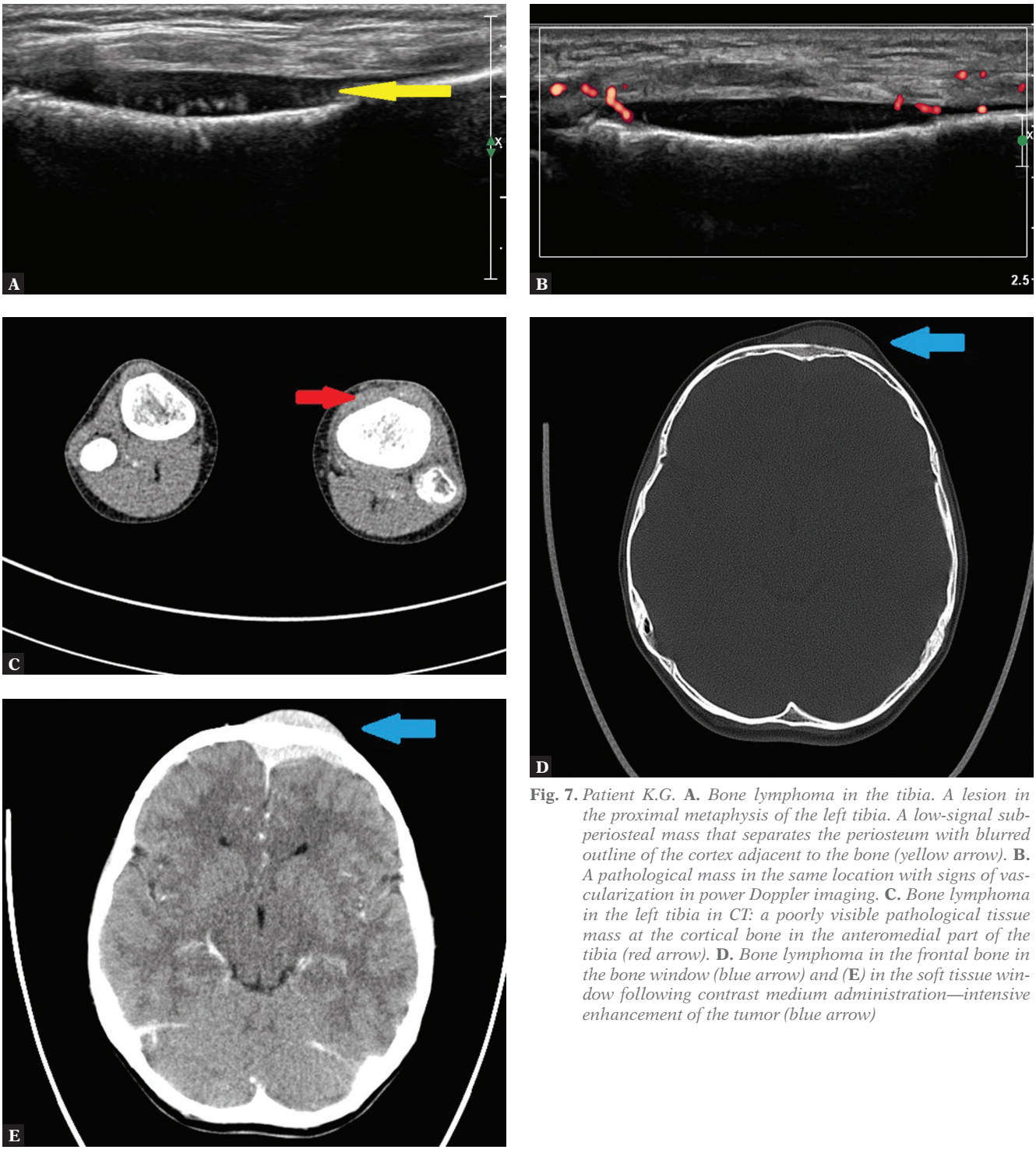


Fig. 7. *Patient K.G.* **A.** *Bone lymphoma in the tibia. A lesion in the proximal metaphysis of the left tibia. A low-signal subperiosteal mass that separates the periosteum with blurred outline of the cortex adjacent to the bone (yellow arrow).* **B.** *A pathological mass in the same location with signs of vascularization in power Doppler imaging.* **C.** *Bone lymphoma in the left tibia in CT: a poorly visible pathological tissue mass at the cortical bone in the anteromedial part of the tibia (red arrow).* **D.** *Bone lymphoma in the frontal bone in the bone window (blue arrow) and (***E***) in the soft tissue window following contrast medium administration—intensive enhancement of the tumor (blue arrow)*

cortical bone. This image could suggest permeative bone destruction, frequently encountered in this pathology[11]. The US signs presented above correspond with typical radiographic signs of bone tumors. Additional advantages of ultrasonography include direct visualization of a pathological tissue mass (10/10 cases) communicating with the bone and assessment of tumor vasculature by Doppler imaging (color Doppler and power Doppler) without the need to administer contrast media. In 8/10 cases of all osteosarcomas and Ewing's sarcomas, the pathological masses were heterogeneous and exhibited globally low echogenicity, frequently with areas of very low echogenicity (almost anechoic), suspected of being sites of necrosis/regressive lesions. In some cases, one could notice hyperechoic reflections, possibly corresponding with calcifications/ossification. As MRI, US is able to present morphologically diversified tumor components, e.g. cystic components, areas of necrosis or

hemorrhagic cysts, indicating the presence of a secondary aneurysmal bone cyst[11].

A case of two tumorous lesions in one patient (K.G.) requires a separate discussion. Both lesions presented a different morphology from the remaining tumors. They gave an image of subperiosteal infiltrations of markedly low but homogeneous echogenicity. They exhibited less pronounced features of local bone destruction, seen as blurred cortical outline. In this case, the final diagnosis was Burkitt non-Hodgkin's bone lymphoma which, compared with OSA and ES, is much rarer in the pediatric population and is characterized by a distinct biology, different radiological signs and multiple tumor forms, e.g. the presence of poorly pronounced bone destruction[11], as it was seen in our patient. In the case of the lesion located in the frontal bone, bone destruction and the tumor were both visible in CT. However, the other tumor, located in the tibia, showed no significant abnormalities in radiography and exhibited only slight changes in CT; they were much easier to detect thanks to the correlation with the previously conducted US examination. A significant difference from other tumors lies in the fact that other assessed lesions belong to a group of primary bone malignancies, while the two pathological masses in the course of bone lymphoma were probably of the secondary nature as involvement of other structures (e.g. the CNS) was also noticed in a short time and the disease was assessed as stage IV. However, because the malignancy was detected in this patient by bone manifestation, first in the frontal bone and then in the tibia, it was decided to include this case in the discussed group. The case is presented in Fig. 7.

The author is not familiar with any other reports about the use of elastography in the diagnosis of malignant bone tumors. Most lesions assessed in the study (5/6) were, as expected, highly stiff (Fig. 8). In one case, tumor stiffness varied; it was higher in hyperechoic areas in B-mode, which apparently results from greater mineralization of these parts of the lesion.

A small group of patients is a limitation of this study. On the one hand, this results from infrequent nature of primary malignant bone tumors, and on the other from narrow patient selection criteria adopted in this study (detection of a tumor in US or US with no prior knowledge of radiological and histopathological findings). It would be desirable to conduct further studies among a greater group of patients and to correlate US with other diagnostic methods.

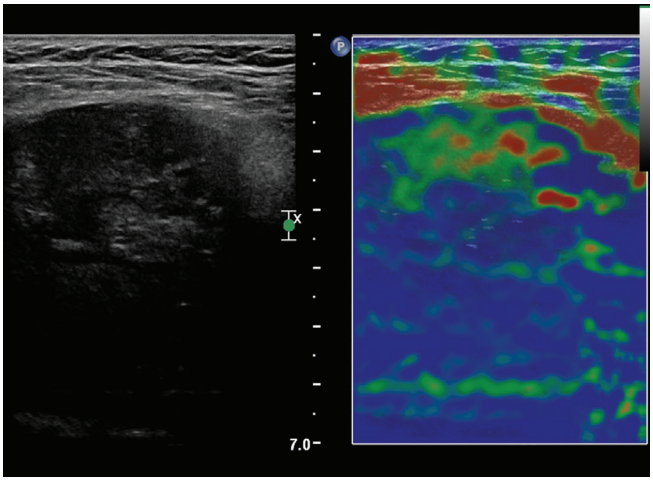


Fig. 8. *Patient P.S. Osteosarcoma. A tumor in the soft tissues of the popliteal fossa in elastography. The lesion coded in blue; a stiff lesion*

In the author's opinion, despite the low number of lesions described, their sonographic image is so characteristic that its presentation seems significant, even more so that medical literature on malignant bone tumors in ultrasonography is lacing and US examinations are commonly conducted in pediatric patients, frequently as the first tests. This may therefore aid in proper diagnosis. This is of particular importance especially if clinical pictures suggest a different background of lesions, e.g. inflammatory, which is quite typical of Ewing's sarcoma[12], or posttraumatic. Being familiar with US presentation of malignant bone tumors may help detect the pathology earlier.

Conclusions

In the analyzed cases, US enabled correct diagnosis of a focal bone lesion, and in most cases (8/9) it presented an image that suggested its malignant nature and the necessity of further diagnosis and treatment.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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