Clinical Studies

Primary Bone Lymphomas Thought to Be Osteomyelitis Urgently Demand a Rapid Diagnosis in Bone Pathology

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Abstract. *We describe in detail three cases of primary bone lymphoma (PBL), initially treated as osteomyelitis of unknown etiology. These cases show which difficulties can occur with diagnosing this entity and highlight the urgent need for rapid diagnostic results in the field of bone pathology. Case 1: A 22-year-old man with the very rare diagnosis of precursor B-lymphoblastic lymphoma in the tibia (previously published). Case 2: A 13-year-old boy with an anaplastic large cell lymphoma of the "os pubis". With initial diagnosis pointing to multifocal osteomyelitis, histology of the left iliac crest revealed a florid/chronic osteomyelitis. During clinical regression with a new osteolytic lesion, he received treatment for chronic recurrent multifocal osteomyelitis. Case 3: A 60-year-old man with an anaplastic large cell lymphoma of the right sacrum, accompanied by a putrid, florid/chronic osteomyelitis. At first, an incisional biopsy revealed a florid/chronic osteomyelitis-only.*

Primary lymphoma of bone constitutes 3% of primary bone tumors and 5% of extranodal lymphomas (or approximately 2% of all primary non-Hodgkin's lymphomas). Males are affected more frequently than females (male-to-female ratio is 1.8:1). Although lymphoma of bone is uncommon, all ages are affected, including children. Most patients are in the fifth to seventh decade of their life. Involved bones are those that normally contain red marrow. Common sites in decreasing frequency include femur, humerus, tibia, spine, pelvis, sternum, ribs, and bones of the skull and face. The etiology of bone lymphoma is unknown. Viral agents and immunosuppression are implicated in some cases. Primary lymphoma of bone has been documented as a post-transplant lymphoproliferative disorder in patients with immunosuppression. Bone has also been documented as a site for primary lymphoma in patients with AIDS. Rarely, patients with Paget's disease of bone may develop malignant lymphoma in the involved bone. However, these associations are not commonly documented and there are only a few case reports in the literature. Cytogenetic and molecular abnormalities are involved in the pathophysiology of many different types of lymphoma. These can be documented in the setting of primary bone lymphoma as well [for example: t(2;5)(p23;q35), seen in T-cell anaplastic large-cell lymphoma]. The most common presenting feature of bone lymphoma is bone pain, which occurs in 60-100% of patients. Other presenting features are palpable swelling or mass, and pathological fracture. Pediatric patients may present with functional deficits in involved limbs. Systemic symptoms (B-symptoms), such as weight loss, fever, and night sweats, are seen in fewer than 10% of patients in true stage IE (Ann Arbor staging system) lymphoma of bone. Regional lymph nodes may be involved in some patients, although this occurs more commonly in cases of bone involvement in patients with systemic lymphoma. Hypercalcemia is seen in some pediatric patients and has been associated with a poorer prognosis (2).

It is well-known that malignant lesions can be misdiagnosed as or arise from/accompany osteomyelitis (3). Neoplasia occurring in a sinus tract is a known complication of chronic osteomyelitis (4). There are only a very few such case reports in the literature regarding primary bone lymphomas (5-8). "Blum" *et al*. published a case series of three lymphomas masquerading as infection, out of which two cases presented as secondary bone lymphomas (9). "Bakshi" *et al*. recently reported three cases of anaplastic large-cell bone lymphomas in children, out of which two appeared as primary tumors. Due to the presentation, the differential diagnosis included small round cell tumors of childhood and osteomyelitis (10).

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Key Words: Primary bone lymphomas, osteomyelitis, bone tumors.

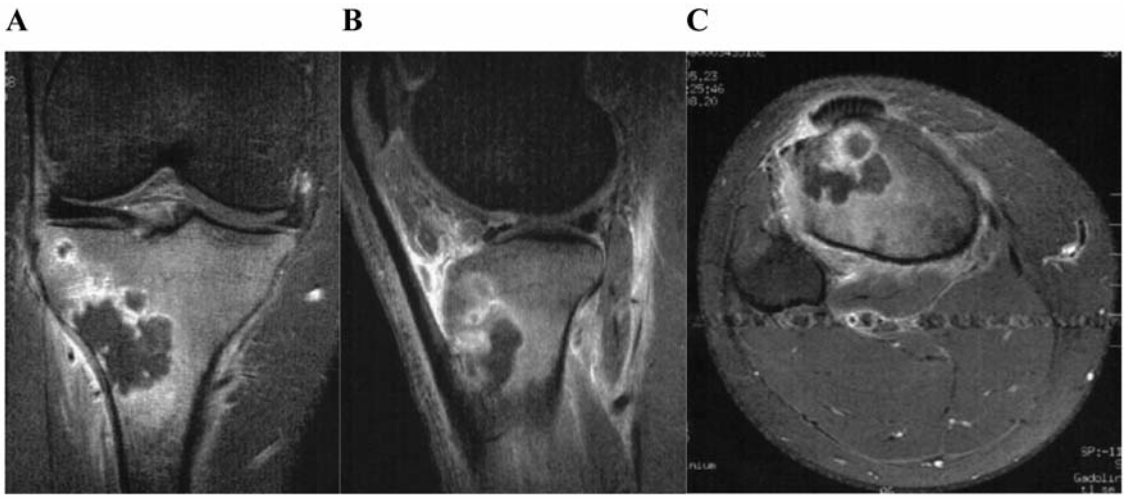

Figure 1. *3-Tesla-(MRI): Coronal (A), sagittal (B), and transversal (C) T1-weighted images after "i.v."administration of gadolinium-DTPA (Magnevist, Schering, Berlin) and fat saturation, showing proximal right tibia with an irregular, lytic lesion with rim-like contrast-enhancement and intense periostal reaction.*

Case Reports

"Case 1". A 22-year-old man began to have spontaneous pain and swelling of the right knee. Suspecting tendonitis at the insertion of the patellar tendon, he was treated at another hospital with non-steroidal, anti-inflammatory drugs (NSAIDs). This treatment relieved some, but not all, of the symptoms. Three months later, the patient presented to the clinic in our Department complaining of pain involving the right proximal tibia, including the musculature in this area, when he did weight-bearing activities. He also reported occasional pain at the region of interest, even while at rest. He had magnetic resonance images that showed an irregular, lytic lesion involving the proximal tibia (Figure 1).

The physical examination at this time revealed some pain on palpation of the right, proximal, lateral tibia without any other signs of inflammation. The examination of the right knee joint was unremarkable. Significant laboratory studies included: leukocytes 4.6×10^3/μl (normal $4.5\text{-}11\times10^3$/μl), C-reactive protein (CRP) 2.2 mg/dl (normal 0-1.0 mg/dl); and erythrocyte sedimentation rate (ESR) 31/60 mm (normal 1-13 mm/h). A bone scan was performed which demonstrated accumulation in all three phases at the region of interest, consistent with acute inflammation. No other foci were noted. Due to the morphology on the MRIs, osteomyelitis of the right proximal tibia was suspected. A debridement with application of local antibiotics was carried out. No microorganisms were isolated from cultures of the debrided material. Grossly, the debrided material consisted of multiple fragments measuring 5.5 cm in aggregate. Microscopically, the lesion exhibited highly concentrated lymphoid infiltration, areas of necrosis, and foci of bone destruction and remodeling. The lymphoid infiltrations were partially follicular and focally accompanied by foam cells. Immunohistochemical stains were positive for (CD10), CD20, CD34, CD45, CD79a, CD99 (MIC2), (BCL2), and terminal deoxynucleotidyl transferase (TdT). High proliferative activity (greater than 95%) was demonstrated with the antibody MIB1, detecting intramuscular positivity for the Ki-67 antigen (Figure 2). Based on these results, the diagnosis of precursor B-lymphoblastic lymphoma (B-LBL) was made.

"Case 2". This 13-year-old child complained of progressive pain in both hips and the left leg in August 2011. He was admitted to the University Hospital for Children in September. Fever of 39˚C two days before admission was reported. The physical examination of the hips showed intense pain on internal rotation in 90˚ flexion, and in abduction, with pain to palpation of the medial joint on the left side. Minimal pain on internal rotation in 90˚ flexion was found on the right side. Initial laboratory studies revealed a normal leukocyte count, CRP of 2.4 mg/dl, and an ESR of 65/115 mm. Significant serological findings included an increased anti-staphylolysintiter of 4.0 (normal: <2.0). Screening for infectious organisms, including microscopy, polymerase chain reaction (PCR) and culture for "Mycobacterium tuberculosis", was negative. Immunological studies including C3, C4, ANA, Hep-2 were negative. The initial anterior to posterior radiograph of the pelvis showed an unclear lesion with a sclerotic rim penetrating the growth plate of the right femoral head (resembling a ganglion or a longstanding inflammatory change) and a second unclear lesion with a sclerotic rim in the left iliac crest. MRI showed contrast medium enhancement in the right femoral head, the

left cranial iliac crest, and the left dorsal acetabulum, with involvement of the surrounding soft tissue and reaction of the hip joint similar to multifocal osteomyelitis. The main finding was at the left acetabulum. An ultrasound examination of the left hip showed minimal effusion in the joint. Aspiration of the left hip joint showed rare gram-positive cocci, but the subsequent culture was negative. A bone scan (^{99m}Tc-DPD) showed enhanced bone metabolism in the areas described above, without other findings. The histological finding of a probe excised under radiographic control in two planes of the left cranial ventral iliac crest was a partially florid/chronic osteomyelitis, with numerous granulocytes and plasma cells without suspicion of malignancy. Grossly, the examined material consisted of three fragments measuring 1, 1.5, and 3 cm respectively. Microscopically, viable bone tissue with lamellar layers, osteocytes in osteocyte lacunae, and osteoclasts attached to bony trabeculae could be seen. In focal areas, newly-formed fibrous bone was identified. Besides partially fragmented spongiosa, compact bone with attached periosteum was seen on other slides. Between spongiosa trabeculae, hematopoetic bone marrow was recognized and numerous granulocytes and plasma cells were found. Immunohistochemically, an increase of CD68-positive macrophages within the hematopoetic bone marrow was found. There were no S100- or CD1a-positive cells, and there was a slight increase of lymphocytes with mixed cell B- (CD20) and T-cell (CD3) infiltrates. The (NACE) reaction showed an increased percentage of granulocytes within the hematopoetic bone marrow, as well as an increased percentage of eosinophils. Repeated immunohistochemical staining showed an increase of macrophages (CD68-positive), increased granulocytes (chloracetate-esterasereaction) (Figure 3A), and negative staining for S100 and CD1a. There was no evidence of histiocytosis. Additional immunohistochemical staining (CD30) (Figure 3B) did not reveal any lymphomatous infiltrates.

Multiple blood cultures and intraoperative cultures were negative. With the assumption of an acute hematogenous bacterial osteomyelitis, several broad-spectrum antibiotics were administered until the end of October, without major changes regarding serum parameters of inflammation. The patient received five weeks of rehabilitation until December. After this treatment, while still receiving NSAIDs, he was able to walk without pain while using crutches at home.

During follow-up at the orthopaedic clinic in March, the patient complained of pain in the area of the lateral gluteal muscles on both sides after walking for long periods. On examination, he showed no signs of inflammation; pain on palpation in the right inguinal area and the symphysis; no pain on palpation at the greater trochanter on both sides; a negative Drehmann sign; and a full-range of motion without pain on both sides. A differential blood analysis remained negative. Significant laboratory studies included a leukocyte count of 9.8×10^3/µl, CRP of 0.5 mg/dl, and an ESR of ½ mm. Compared to the initial one, an a.p. pelvic x-ray showed new osteolytic lesions in the left inferior ramus of the "os pubis" without any other new alterations. The latest MRI revealed a slight progression on the left side with involvement of the ischiadic tuber, the inferior ramus of the "os pubis", as well as the pectineal and internal obturator muscle. The lesions in the right femoral head and the left iliac crest were no longer distinguishable. The subsequent bone scan (^{99m}Tc-DPD) showed intense activity in the left ischiadic and pubic bone along the inferior ramus of the "os pubis", without other foci. With the diagnosis of a (CRMO), therapy with azithromycin was started. The follow-up MRI four weeks later revealed clear progression of the above findings (Figure 4).

A probe excision of the left inferior ramus of the "os pubis" revealed an anaplastic large-cell CD30$^+$ (ALCL) lymphoma [(ALK)+ common variant], cytotoxic T-type, with a primary manifestation in the bone.

Grossly, the debrided material consisted of sturdy soft tissue measuring 4.5 cm in aggregate. Microscopically, closely packed, large blastic cells with some solitary central-nucleoli and some multiple-nucleoli were seen. Focally, the cytoplasm exhibited a plasmocytoid differentiation. Multiple mitoses and apoptoses, occasionally with a 'starry-sky'-like pattern, were recognized. Inflammatory infiltrates and necrosis were found. The tumor partially exhibited an almost plasmablastic, partially Burkitt-like differentiation, without typical Burkitt morphology. Immunohistochemically, the large blasts exhibited a clear membranous expression of the CD30 antigen (Figure 5A). The MIB1-proliferation index was very high, approximately 95% (Figure 5B). There was no expression of CD3, CD20, CD79a, kappa, lambda, CD5, BC16, CD10, and CD23. The tumor cells expressed the BCL2-oncoprotein. Additional immunohistochemical stains showed that the CD30-positive tumor cells overexpressed the ALK-1 protein and stained with an (EMA) antibody. The tumor also exhibited at least a weak CD4 expression (Figure 5C). A consult from a different Institute of Pathology confirmed the diagnosis of an ALCL of the cytotoxic T-type (TIA+).

"Case 3". This is a 60-year-old man with non-insulin-dependent diabetes mellitus and Wegener's granulomatosis, diagnosed nine years before. During Spring, the patient experienced progressive myalgias of the neck and shoulder musculature with B-symptoms, which always regressed with high-dose steroid treatment.

Although presenting with increased inflammatory serological parameters in June, no signs of re-activation of the Wegener's granulomatosis were found at another hospital. The patient received antibiotics for at least two weeks for pansinusitis and had pansinus surgery on the left side with plastic repair of the nasal septum. This was performed in July 2010. Histologically, no signs of

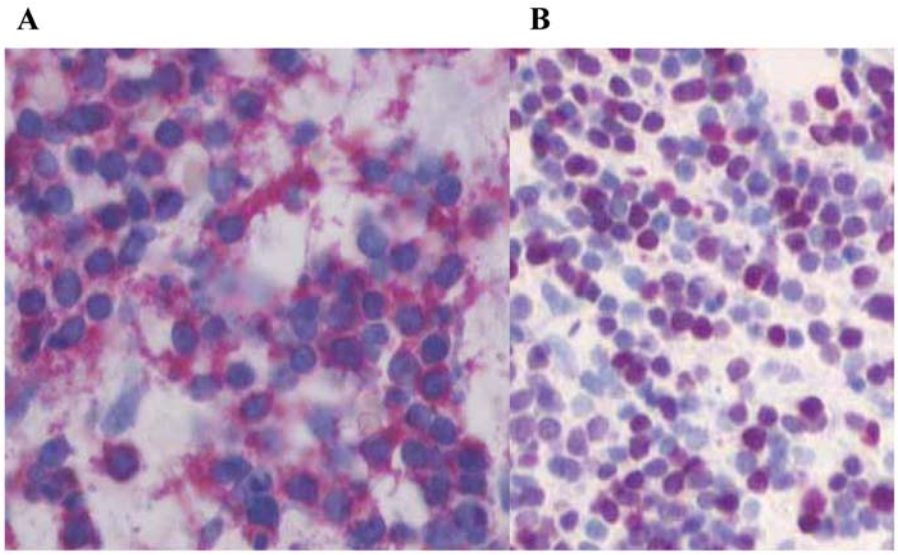

Figure 2. *Histology showing positive immunohistochemical staining for CD34 (A) and MIB1 (B).*

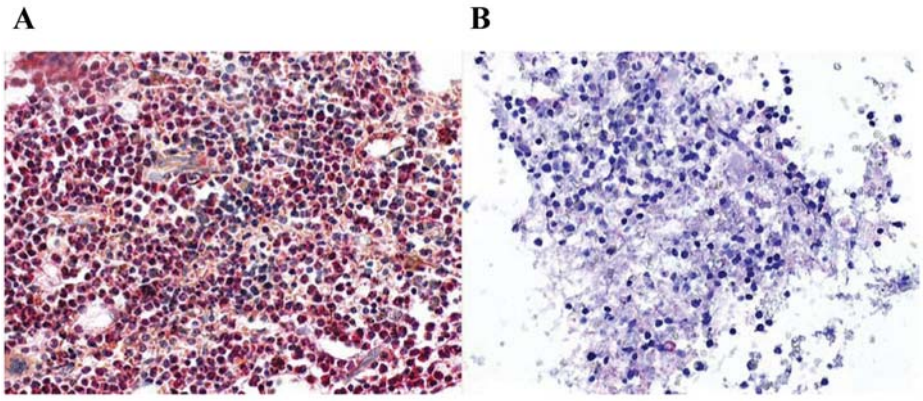

Figure 3. *A: Histology showing positive histochemical staining for naphthol (ASD) chloroacetate esterase (NACE). B: Histology showing a negative immunohistochemical staining for CD30. Original magnification ×20.*

Wegener's granulomatosis were found. During that summer, he was treated with low-dose steroids and 25 mg methotrexate/week and had no major complaints. In September 2010, the patient complained of pain with motion in the area of the right shoulder, right gluteal musculature, and the entire right leg, with B-symptoms and putrid secretion from the nose. This was accompanied by increased inflammatory serological parameters. After administration of fluorchinolones at another hospital, there was no longer secretion from the nose. The pain in the right gluteal area, accompanied by high inflammatory serum parameters, persisted with a moderate regression of both, while he was treated with an increased steroid dose, up to 50 mg/day. Blood cultures for bacteria were negative, and no other focus of infection was found. An a.p. x-ray of the sacroiliac joints was unremarkable. MRI of the pelvis with contrast revealed a lesion in the right "massa lateralis" of the sacrum with complete signal depression and without involvement of the sacroiliac joint or other findings. A bone scintigram showed multiple spots in this area.

In October 2010, the patient was transferred to our department for an incisional biopsy of the right "os sacrum". On admission, the patient had pain on intense palpation at the right sacrum, the leukocyte count was normal, CRP was at 16.4 mg/dl, and the ESR was at 88 mm. The patient was discharged without complications or major changes of the inflammatory serum parameters while awaiting the final pathology report. The report stated a partially florid/chronic granulomatous and necrotising inflammation with multiple calcified bone particles

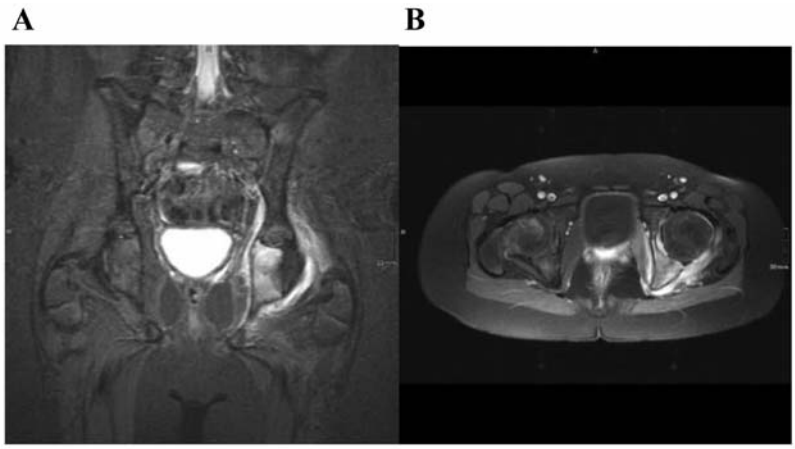

Figure 4. *3-Tesla-(MRI): Coronal T2 (A)-, and transversal T1 (B)-weighted image after "i.v."administration of gadolinium-DTPA (Magnevist, Schering, Berlin) and fat saturation, showing the progressive lesion on the left side with the punctum maximum in the involved ischiadic tuber.*

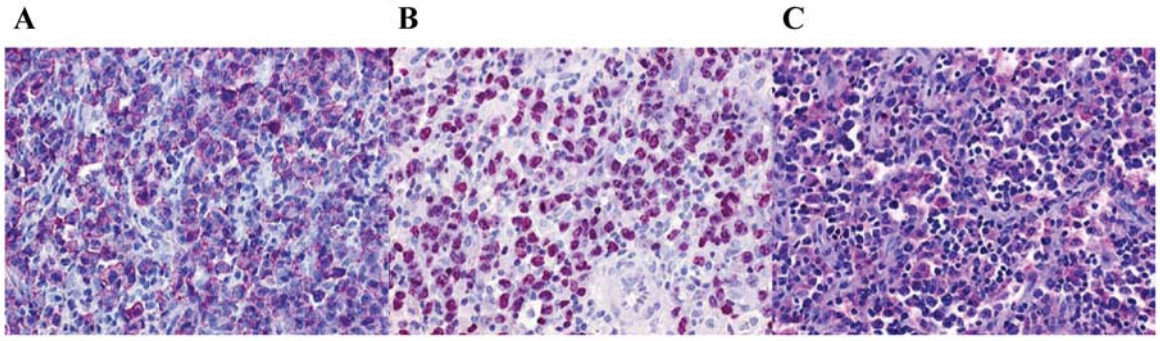

Figure 5. *Histology showing positive immunohistochemical staining for CD30 (A), MIB1 (B) and CD4 (C). Original magnification ×20.*

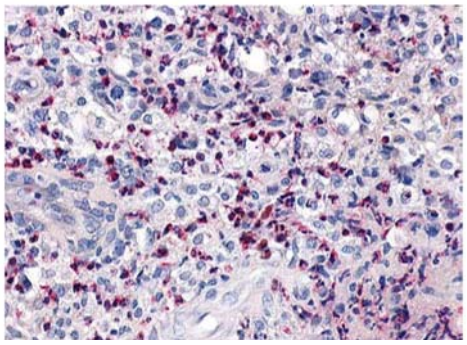

Figure 6. *Histology showing histochemical staining for naphthol (ASD) chloroacetate esterase (NACE). Original magnification ×20.*

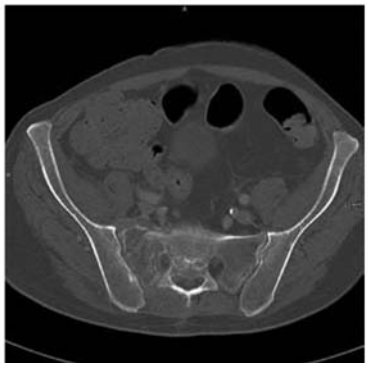

Figure 7. *Computed-tomography: Transversal image of the pelvis showing the progressive osteodestructive process in the right sacrum with a dense soft tissue formation, protruding into the small pelvis.*

consistent with osteomyelitis without an evidence of malignancy. Grossly, the examined material consisted of three pieces of tissue, 1.3×0.7×0.5 cm, 1.6×0.8×0.7 cm, and 1.2×1.0×0.6 cm, respectively; and two fragments measuring 0.6 cm and 0.4 cm in diameter, respectively. Microscopy: HE, naphthol ASD chloroacetate esterase (NACE) (Figure 6), immunohistologically the cells were positive for CD20, CD3, CD68, CK, CD1a.

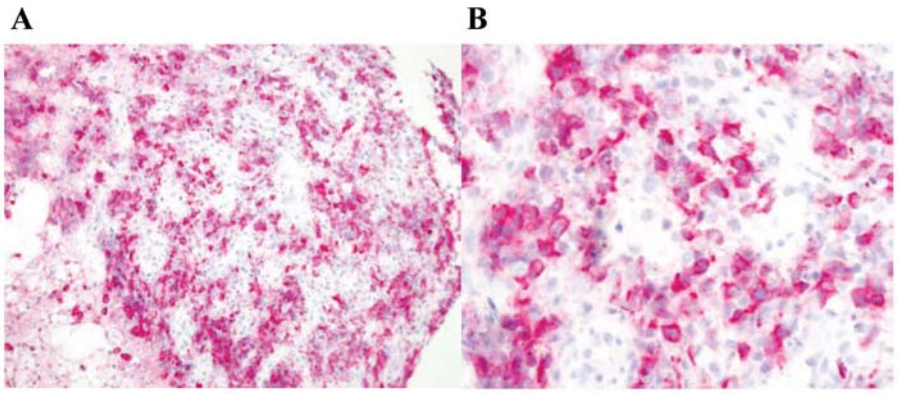

Figure 8. *Histology showing lack of immunohistochemical staining for CD30. Original magnification, A: ×20; B: ×30.*

Cultures for bacteria from the site of surgery were negative. A few days after discharge, the patient was admitted to a different hospital for treatment of suspected pneumonia. He was then transferred to the orthopaedic department in November because of persistent pain in the area of S1, sometimes radiating down to the right caudal dorsal calf. Treatment with two different broad-spectrum antibiotics resulted in no major change of the inflammatory serum parameter levels. The physical examination on admission showed normal, closed wound healing with the same level of pain on intense palpation as before. The a.p. x-ray of the pelvis did not show any bony erosive changes, and the x-ray of the thorax was unremarkable. An abdominal computed-tomography (CT) with contrast showed a 3.7×3.5 cm osteodestructive lesion in the right "os sacrum" without evidence of abscess formation and normal intra-abdominal organs. Under conservative treatment, including an intravenous antibiotic, the patient was discharged without pain and the recommendation to follow-up in six weeks. Inflammatory serum parameters still did not show any major changes, with the patient receiving 25 mg methotrexate/week, combined with a low dose of steroid (10 mg/d).

One week after discharge, the patient was re-admitted because of progressive pain in the gluteal area with suspicion of initial sepsis. He had pain on palpation at the right sacrum, a body temperature of 40˚C, and the only major change regarding the inflammatory serum parameters was a rising leukocyte count of 20.4×10^3/μl. A CT scan of the pelvis revealed a progressive osteodestructive process of the right sacrum (8×4 cm) with a dense formation of soft tissue protruding into the small pelvis (Figure 7).

Exploration, incision, and drainage with antibiotic implant application at the ventral process were performed. Inflammatory scar tissue and some cloudy fluid were found, but there was no typical putrid fluid or abscess. A few days later, after there was no change regarding clinic and serum parameters, a second CT scan of the pelvis was performed and did not show any changes. During revision surgery, putrid-looking fluid was found behind a membrane at the ventral sacrum. Incision, drainage, and antibiotic implant application followed. Postoperative regression of serum parameter levels to a CRP of 10.7 mg/dl and a leukocyte count of 21.6×10^3/μl were seen. A few days later, a rise in serum CRP to 21.4 mg/dl and a leukocyte count of 24.3×10^3/μl became evident. A CT scan of the pelvis and abdomen showed a drainage tube in place and bilateral pleural effusions. Meanwhile, all intra-/postoperative cultures (including of blood and a central line) were negative. The histological result from the revision procedure did not confirm putrid inflammation. It showed hemorrhagic, infarcted, mature adipose tissue. Grossly, the debrided material consisted of two soft tissue fragments measuring 2 cm in diameter. Microscopically, mature, lobular adipose tissue, containing large caliber vessels was seen. In some places, large, fresh hemorrhage with neutrophils was seen in the same area. An anti-granulocyte bone scintigram (686 MBq ^{99m}Tc) did not show any focus of inflammation, with low storage in the L1 lumbar vertebra and the "os sacrum". A debridement of the right lateral sacrum "*via*" a dorsal approach was performed. The histology showed an anaplastic, large-cell CD30$^+$ lymphoma (ALK/Ki1-lymphoma) accompanied by putrid, florid/chronic osteomyelitis. Grossly, the specimen consisted of multiple bone fragments with a total weight of 16 g and a diameter of 6.5×5×1 cm. Microscopically, a dense, predominantly neutrophilic infiltrate was observed in the bone marrow space. In addition, capillary proliferation in the bone marrow spaces and reactive osteosclerotic remodeling of cancellous trabeculae were present. Besides obviously abundant macrophages, blastic cell elements were seen, occasionally with irregular indented nuclei as well as prominent nucleoli. Immunohistochemical studies showed CD30$^+$ blasts (Figure 8) between the dense inflammatory infiltrates. There was no reaction for CD3, CD20, CD61,

CD34, BCL6, TdT, myeloperoxidase, S100 or vimentin. Additional immunohistochemical staining of the blasts was negative for EBV, LMP1, CD15, JCB, CD45, and ALK proteins.

Discussion

The criteria for a diagnosis of primary bone lymphoma (PBL) were established by "Guidici" *et al*.: (a) on presentation, the patient demonstrates a primary focus in a single bone; (b) histological proof is obtained from the skeletal focus (not from a metastasis); and (c) the onset of symptoms of the primary skeletal lesion precedes the appearance of distant metastases by at least six months (11). The publication "Malignant Lymphoma" by "Mathur", updated 2005, states that the definition of primary lymphoma of bone continues to be debated. Most authors exclude disseminated or recurrent disease in which the bone is only one of many sites of involvement. To be considered primary lymphoma of bone, the following criteria should be met: Histological documentation of lymphoma in the bone; solitary bone lesion or multiple skeletal lesions with no prior involvement of lymph nodes or other lymphoid tissue; no lymph node involvement or involvement of regional lymph nodes; all of the above criteria were fulfilled in these three cases. Soft tissue extension from the bone lesion is acceptable, and the involved soft tissue may be sampled to document malignant lymphoma (2).

B-LBL, as in case 1, presenting as a solitary bone tumor is very uncommon. While lymphoblastic lymphoma (LL) comprises fewer than 5% of adult non-Hodgkin's lymphomas in the United States, approximately 90% of these cases are of the more common T-cell type. (6, 12). In one series of 25 cases of B-LBL, five (20%) of the patients had bone lesions, and of those, only two patients (8%) had solitary bone involvement (12). In a retrospective study of 131 patients with PBL by "Ramadan" *et al*., 103 (79%) had a diffuse large-cell lymphoma (DLCL) (13). A different study of 82 patients with PBL revealed approximately 80% DLCLs (14). "Horsman" *et al*., in a retrospective analysis of 37 patients with PBL, found 70.3% DLCLs (15).

Patients with solitary or multifocal B-LBL generally present with localized bone pain (6, 12, 16). This finding is similar to patients with any PBL, in which the presenting feature is bone pain in 60-100% of patients (2, 17). In the above mentioned study of 131 patients with PBL, one-third had disease in the long bones and another one-third had disease in the spine, out of which half presented with spinal cord compression (13). "Horsman" *et al*. also found in their study of 37 patients with PBL that the pelvis is the most frequently affected site (21.3%). The mean age of patients with B-LBL is 20 years (12), which is significantly older than the three patients with involvement of the tibia whose mean age was 6.3 years (16). The mean age of patients with PBL varies from 48-63 years (13-15). B-LBL and PBL can, as in these cases, present with a relatively long clinical prodrome, from months to over one year, and with an initially benign radiographic appearance (11, 16).

Patients with B-LBL and PBL exhibit widely varied clinical presentations. Cases have been reported as mimicking chondroblastoma (11), chronic synovitis (17), monoarthritis (18), Ewing's sarcoma (16), fibrous dysplasia (12), and osteomyelitis (5-7, 9, 10). Although many imaging tests are usually applied when attempting to diagnose a lesion of this type, they may be non-contributory. Plain radiographs and CT scans are usually non-specific and demonstrate a lytic or sclerotic bone lesion (6, 16, 17). Early use of MRI may be helpful, and lesions will display high signal intensity on T2-weighted images (19). In most cases of this type, systemic symptoms are usually absent, and there are no clinical signs pointing to malignant lymphoma (17). Immunophenotypically, the neoplastic cells of B-LBL express TdT and B-cell antigens such as CD10, CD19, CD22, and CD79a (16). The combination of TdT, CD79a, and CD10 positivity is diagnostic of B-LBL (6).

Indications for surgical involvement by orthopedic surgeons for bone lymphoma most commonly fall into one of three categories: diagnosis, treatment of pathological or impending pathological fractures, and decompression of spinal canal compromise. At this time, no clear role for surgical debulking procedures or resection exists for PBL. In cases in which PBL is suspected, the surgeon must obtain fresh tissue for immunophenotyping, as well as for cytogenetic and molecular studies, where indicated (2).

Delays in diagnosis can have serious effects on the prognosis of a disease, in which the stage is considered the most important prognostic indicator (20). Therefore, it is essential to diagnose a lesion prior to leukemic spread or metastasis. Thus, in a patient with osteomyelitis-like symptoms and bone pain refractory to medical treatment, a thorough diagnostic work-up should be undertaken, and unusual neoplasms such as this hematopoietic malignancy should be considered in the differential diagnosis. Our cases are examples of why diagnostic delays can occur. In case 1, the MRI did not lead to the right diagnosis. In case 2, non-specific imaging findings of three different locations with a probe excision of one lesion, followed by a histology report stating florid/chronic osteomyelitis, led to the assumption that all three lesions represented the same entity.

The lesion of the iliac crest was chosen for the excision with respect to the principles of a diagnostic biopsy, including minimal soft tissue contamination (21). Clinical regression and a new osteolytic lesion accompanied by regression of two lesions, including the one of the excision site, led to a diagnosis of CRMO. The changes of histology in CRMO are not very specific and are not different from those expected in acute hematogenous osteomyelitis. Plain radiographs usually reveal non-specific features suggestive of osteomyelitis, such as

osteolysis, osteosclerosis, and new bone formation. As such, CRMO can indeed mimic primary bone tumors. Radioisotope bone scans can help to identify silent lesions. MRI scans are highly sensitive and of pivotal importance in disease monitoring. The diagnosis of CRMO is often made after the lesions and symptoms have persisted despite appropriate antibiotic treatment (21). In case 3, a patient with multiple comorbidities, a putrid, florid/chronic osteomyelitis in the area of interest was later on accompanied by PBL. It is suspected that a change of diagnosis in this patient occurred during the treatment phase in the hospital. By reviewing our cases, we have come to the same conclusions as "Blum" *et al*.: Surgeons should return to the basics of culturing all suspected tumors and obtaining a biopsy specimen of all presumed infections, even in instances of positive cultures or negative biopsy specimens. Significant worsening of symptoms in chronic osteomyelitis requires a thorough workup with appropriate imaging studies, and excision of an additional biopsy specimen (9). In addition, it is important to remember that if a surgical procedure is started without knowing the histological diagnosis and a surgeon is in doubt, a frozen section of the excised tissue is mandatory to avoid further delays and unnecessary procedures. This may not always be possible due to technical reasons, such as the de-calcification process of bony tissue for further preparation and microscopic examination. As mentioned, in cases of PBL, the involved soft tissue may be sampled to document for malignant lymphoma (2). Our cases help to strengthen the awareness of a possible change of diagnosis for a single entity and the possible co-existence of multiple different entities, even during an apparently effective treatment phase. This leads to the conclusion of there being an urgent demand for rapid diagnostic results in the field of bone pathology.

Conflicts of Interest

The Authors declare that they have no conflicts of interest.

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Received September 5, 2012
Revised October 9, 2012
Accepted October 11, 2012