Acute Osteomyelitis as a Complication of Varicella

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Varicella is a common viral infection in children. Most children recover without sequelae. Skin and soft tissue infections are common complications; pneumonia and encephalitis less common; and skeletal complications are rare. Acute osteomyelitis is one of the serious complications and should be considered in any child who has pain in a limb or joint after an episode of varicella (13). Prompt evaluation and adequate systemic antibiotic therapy may prevent the spread of infection and loss of life or limb. We report two cases of osteomyelitis as a complication of varicella, the first one (in Norwegian) was published earlier (7).

Case Report 1

A previously healthy 18-month-old boy with a 5-day history of varicella infection was hospitalized due to rapidly increasing general symptoms of illness. Body temperature at admission was 39.8°C. Some degree of local lymphadenitis was found in his right axilla, and movement of his right arm made him cry intensely. On admission, WBC was 19.9 \times 10^9/l (6–18 \times 10^9/l) and C-reactive protein (CRP) 133 mg/l (<5 mg/l), whereas other biochemical parameters were normal.

By 1 day after admission, a diffuse edema had developed in his right shoulder. CRP had risen to 236 mg/l and blood cultures were positive of group A betahemolytic streptococcus (GABHS). As osteomyelitis was clinically suspected, bone scintigraphy was performed using \(^{99m}\)Tc-methylene diphosphonate (MDP). The scintigrams showed increased activity in the right humerus diaphysis (Fig. 1A), and antibiotic therapy was started immediately (penicillin G and dicloxacillin i.v.). Radiograms of the right humerus performed on the second day after admission did not demonstrate any pathological changes.

A second bone scintigram performed after 6 days (Fig. 1B) showed significantly increased activity in the right humerus diaphysis. Follow-up radiograms after 10 days showed irregular osteolytic lesions and periosteal reaction in the proximal metaphysis and proximal part of the diaphysis coherent with osteomyelitis (Fig. 1C). The patient received 2 weeks of intravenous antibiotics and subsequently 4 weeks of per oral penicillin. Clinically, the boy improved rapidly and could be dismissed from hospital after 17 days. Except for a slightly increased sedimentation rate, all biochemical parameters were normal at that time. Follow-up radiograms after 1, 2, and 5 months showed slowly normalizing conditions. On the final radiogram after nearly 6 months, no pathological changes or signs of sequelae could be demonstrated.

Case Report 2

A previously healthy 6-year-old girl was hospitalized with fever and pain in her left knee and calf. One week earlier she had an outbreak of varicella, and the pain in her extremity started 1 day after the varicella outbreak. The day before admission to
Fig. 1. A. Scintigram the day after admission to hospital shows increased uptake of $^{99m}$Tc-MDP in the right humerus diaphysis (arrowheads), consistent with osteomyelitis. B. Scintigram 6 days after admission shows increasingly pathological uptake of $^{99m}$Tc-MDP in the right humerus (arrowheads). Uptake in the middle and distal part of the humerus might be due to reactive hypermia. C. Radiogram of the right humerus 10 days after admission shows irregular bone mineralization and structure in the upper part of the lateral humerus diaphysis (arrowheads) consistent with osteomyelitis. Less marked changes are seen on the medial side of the metaphysis.
hospital she had been diagnosed with GABHS tonsillitis and treatment with peroral penicillin was started. She could not use her painful extremity. Initial tests showed CRP 32 mg/l and sedimentation rate 46 mm/h. Other biochemical parameters were normal. Repeated negative blood cultures were negative.

Radiograms of the left leg at admission did not demonstrate any pathology. Magnetic resonance imaging (MRI) showed edema in the bone marrow of the lateral tibia metaphysis and of the medial femur condyle due to bone marrow edema (arrowheads). There was also some hydrops in the knee (Fig. 2A, B). Initial bone scintigraphy with $^{99m}$Tc-MDP demonstrated increased activity in the proximal

Fig. 2. A. Initial MRI, coronal T1W image of the left knee. Edema in the bone marrow of the lateral tibia metaphysis causes loss of fat signal (arrowheads). B. Initial MRI, coronal STIR image of the left knee. Increased signal in the lateral tibia metaphysis and of the medial femur condyle due to bone marrow edema (arrowheads). C. Scintigram shows increased uptake of $^{99m}$Tc-MDP in the lateral tibia metaphysis (arrowhead).
tibia (Fig. 2C). No certain osteomyelitic changes could be seen at any point on plain radiographs.

The girl was treated with 2 weeks of intravenous and 3 weeks of per oral cloxacillin. The pain in her left leg decreased rapidly after the treatment was started; after 2 weeks of antibiotics she had no symptoms. Repeated radiograms 1 month after admission showed very moderate changes in the femur diaphysis. A second scintigram performed 3 weeks later was normalized.

**Discussion**

Varicella is a common viral infection with an estimated complication rate of 2%, of which bacterial soft-tissue infections and pneumonia are the most common. Rarely, more serious complications, such as encephalitis, necrotizing fasciitis, abscesses, septic arthritis, and osteomyelitis, may occur (1, 11, 21, 25). To our knowledge, only 40 cases of osteomyelitis have been reported as a complication of varicella (1, 2, 5, 11, 15, 17, 21, 25). Usually, the metaphysis of the long bones is affected (9). The diaphysal affection in our first case is fairly usual. The dominant bacteria responsible for the infections were group A beta hemolytic streptococcus (23/40 cases); staphylococcus aureus was shown in 7/40 cases; unspecific streptococcus was reported in 1/40 cases; no bacterial growth was seen in 3/40 cases; and no report was available for the remaining 6/40 cases. The usual bacterial pathway is hematogenous, but continuous spread of bacteria from adjacent soft tissue varicella infection has been reported (2). The most common etiology of non-varicella-associated osteomyelitis in children is staphylococcus aureus (22). By contrast, there is a predominance of streptococci in osteomyelitis in connection with varicella. The association between varicella and invasive streptococci disease has several explanations. The varicella skin lesions provide a portal of entry for streptococci. The varicella infection might cause subtle alterations in the immune function, rendering the patient susceptible to streptococci. Confluence of peak seasonable activity of two infectious diseases (late winter and spring) is another hypothesis (3, 4, 18, 23).

Fever and other symptoms related to the affected area are normally seen within 2 weeks of onset of the varicella rash. The median age of patients with complicated varicella is as low as 2.9 years, and complications are mainly seen in males. Our cases are in concordance with the characteristics reported from other cases. Radiological changes seen in children with osteomyelitis after varicella are similar to those seen in other types of bacterial osteomyelitis.

Plain radiograph changes, such as cortical reaction and bone destruction, appear at the earliest after 1–3 weeks. More severe destruction with the formation of sequester is seldom seen in developed countries nowadays.

Bone scintigraphy with $^{99m}$Tc-MDP becomes positive within 24 to 48 h after the onset of symptoms (6, 8). This investigation should be performed preferably as a multiphase study with a flow phase, blood pool phases, and a delayed phase. The usual findings are increased regional activity in the affected bone in the flow and blood pool phases, and a more intense activity in the delayed phase. In previous non-violated bone, $^{99m}$Tc-MDP scintigraphy has a sensitivity of approximately 95%, the specificity being markedly lower. Scintigraphy of neonates has a lower sensitivity but reaches almost 90% (24). Sometimes a reduced uptake, a so-called cold scan, may be seen in osteomyelitis. This indicates a more virulent disease with reduced perfusion or even necrosis, and is an alarming sign (6). The abnormal diaphysal uptake of the right middle and distal humerus and in our first case could represent a reactive hyperemia distal to the primary lesion in the proximal end of the humerus (24). This possibility is supported by the fact that the plain radiograph only showed changes in the proximal part of the humerus.

MRI allows early detection of osteomyelitis, evaluation of the extent of involvement, and disease activity in cases of chronic osteomyelitis (14). Replacement of the medullary fat by bone marrow edema occurs during the very first days of the infection. The sensitivity of these changes is very high. Thereby, a negative MRI almost 100% excludes osteomyelitis. This is, of course, vital information for the process of diagnosing the condition. Marrow edema is an unspecific MRI finding; reported specificities for osteomyelitis ranging from 53% to 94% (14). Apart from marrow edema, other findings are periosteal elevation, subperiosteal fluid collection, bone destruction, and changes in surrounding soft tissue. Our routine protocols include T1 and STIR images. If an abscess is suspected, we include post-gadolinium T1W images. In addition, different protocols are used according to the specific needs of each patient.

Ultrasonography (US) has proven to be a valuable imaging modality when investigating osteomyelitis in children (15, 16, 19, 20). Imaging findings which might appear as early as 48 h after the onset of infection (12) are: periosteal thickening,
subperiosteal fluid/abscess, surrounding soft tissue changes and sinus tract formation. US also has the possibility of guided biopsy and aspiration and gives no ionizing radiation. The fact that the varicella-associated osteomyelitis occurs in young children whose periost has a loose cortical attachment and readily elevates (10) may indicate that US is an especially valuable modality in these particular cases (15). US has not yet been used in this context in our department.

In conclusion, osteomyelitis is a rare complication of varicella. However, it should be considered in any child who develops unexpected pain in a limb or joint during or after varicella infection. Successful treatment of osteomyelitis depends upon early detection. Thus, even a severe osteomyelitis generally resolves without sequelae. Radiologically, the varicella-associated osteomyelitis is similar to osteomyelitis of other causes, and the radiological evaluation should be the same. It is important to remember that conventional radiograms may remain normal for several days or even weeks. US may show periosteal changes after 48 h and bone scintigraphy and MRI normally show changes within 24 to 48 h after the debut of clinical symptoms.

References
