The authors report a rare case of acute hematogenous osteomyelitis in a premature very low-birth weight infant caused by *Neisseria meningitidis*, a microorganism which occasionally causes arthritis, but is very rarely involved in bone infections. The strong teamwork of clinicians, the clinical microbiologist and the radiologist allowed the prompt formulation and confirmation of the clinical suspect (regardless of the paucity of symptoms and systemic signs), the rapid isolation of the microorganism and the prompt initiation of a specific therapy, thus obviating the need for a more invasive bone biopsy, which would have been hazardous considering the risks associated with an invasive procedure, and much higher in our case because of the young age of the patient and his prematurity. Moreover, this case confirms that early ultrasonographic examination may anticipate the diagnosis and the initiation of therapy in case of a clinical suspicion of acute hematogenous osteomyelitis, thus avoiding serious complications such as growth disorders or arrest, shortening or angular deformity, loss of motion and degenerative osteoarthritis. In accordance with what suggested in the literature, initial parenteral treatment followed early by oral antibiotics was chosen, with an excellent outcome.


Key words: Carrier; Hematogenous osteomyelitis; *Neisseria meningitidis*; Prematurity.

**Introduction**

Hematogenous osteomyelitis is predominantly a childhood disease; we report a case of acute hematogenous osteomyelitis (AHO) caused by *Neisseria meningitidis* (*N. meningitidis*), a microorganism which occasionally causes arthritis, but is very rarely involved in bone infections.

**Case report**

The patient was a premature twin boy born at 33 weeks of gestation and weighing 1290 g (very low birth weight); he was discharged 50 days after birth in apparently good conditions and weighing 2380 g.

At 64 days of age he was admitted again to the Neonatology Unit because of extreme irritability and pain in the left hip lasting 4 days, and a reported fever for 1 day, which had however subsided spontaneously. Physical examination showed limitation of active and passive motion and pain of the left hip, with an antalgic posture of the left leg in adduction and flexion; physical examination was otherwise unremarkable.

The erythrocyte sedimentation rate was 75 mm/hour, the white blood cell count 18 700/mm³ with 40% neutrophils and the serum levels of C-reactive protein 5 mg/dL (normal < 1 mg/dL). A radiogram of the hips was normal; ultrasonography showed a 12-mm thick juxtacortical hypoechoic collection adjacent to the left femoral metaphysis.

A blood culture was performed, and the child was immediately started on intravenous teicoplanin 30 mg/day and ceftazidime 300 mg/day.

Within 24 hours his clinical status had clearly improved. On the fifth day of hospitalization the blood culture grew *N. meningitidis* group B, which was sensitive to all tested antibiotics (including all cephalosporins), with the exception of gentamycin and kanamycin (intermediate sensitivity); thus, teicoplanin was stopped.

On the seventh day a complete recovery of the affected leg was observed; on day 15 ultrasonography showed no abnormalities, ceftadizime was stopped and he was put on oral cefixime 40 mg/day for 13 days.

A pharyngeal swab taken on day 22 was negative, the white blood cell count was 9300/mm³ with 28% neutrophils, and the C-reactive protein was 1.3 mg/dL.

Given the etiology of the infection, a pharyngeal swab was taken from all the close contacts of the patient, with his mother and twin brother being found to be asymptomatic naso-pharyngeal carriers of *N. meningitidis*. The twin was put on ceftriaxone, 240 mg i.v. for 1 day, and oral cefixime 40 mg/day for 5 days; this treatment eradicated *N. meningitidis*. However, the mother remained an asymptomatic carrier, despite multiple therapy with rifampicin 600 mg twice daily for 2 days, cefixime 400 mg daily for 7 days and pefloxacin 400 mg twice daily for another 7 days.
The father and the close contacts < 20 years were recommended prophylaxis with rifampicin 600 mg twice daily for 2 days.

Discussion

AHO after bacteremia characteristically affects the metaphysis of long, rapidly growing bones; it is almost always monoarticular and the femur is involved in approximately 30% of cases. The infection begins in the dilated capillary loops of the metaphysis adjacent to the cartilaginous growth plate, where: a) the blood flow becomes slow and turbulent enough to allow pathogenic bacteria to multiply and form abscesses; b) any obstruction results in small areas of avascular necrosis because of the terminal-type circulation; and c) the phagocytic lining cells are absent or functionally inactive.

In neonates, the diagnosis of AHO may be missed, because of the paucity or even absence of systemic signs; local findings, such as edema, swelling, decreased motion of a limb and pseudoparalysis may be the only clue to the diagnosis. Definitive bacteriological diagnosis of osteomyelitis usually requires the isolation of the pathogen from the bone lesion. However, bone biopsy is a very invasive procedure, especially in an infant. Several series have demonstrated that a reliable diagnosis may be reached by obtaining blood for culture and sensitivities, since the paucity or even absence of systemic signs; local findings, such as edema, swelling, decreased motion of a limb and pseudoparalysis may be the only clue to the diagnosis.

Definitive bacteriological diagnosis of osteomyelitis usually requires the isolation of the pathogen from the bone lesion. However, bone biopsy is a very invasive procedure, especially in an infant. Several series have demonstrated that a reliable diagnosis may be reached by obtaining blood for culture and sensitivities, since blood culture is positive in about 50% of cases, and may obviate the need for a more invasive bone biopsy. Considering the young age of our patient and the risks related with an invasive procedure, much higher because of his prematurity, we decided not to perform a bone biopsy and to base our diagnosis and therapeutic strategy upon the data deriving from serial blood cultures and ultrasonographic examinations.

Our patient fulfilled two of the most important risk factors for developing AHO previously identified: birth weight < 2500 g and gestational age < 37 weeks.

In our case the localization of the infection reflects the data of the literature; some authors have suggested that the high frequency of long bone involvement in AHO is due to an increased exposure to minor non-penetrating trauma, which may result in hemorrhage or small vessel occlusion, leading to ischemia and necrosis, and providing an ideal environment for the localization of circulating bacteria.

It is well known that in the infant < 1 year some capillaries perforate the epiphyseal growth plate, and the infection may rapidly spread to the epiphysis, causing epiphysitis and pyoarthrosis; this may finally result in growth disorders or arrest, shortening or angular deformity, loss of motion and degenerative osteoarthritis. The absence of such complications in our case is to be attributed to the prompt recognition and treatment of the disease, despite a relatively non-specific clinical presentation and negative X-ray findings.

Indeed, the radiological signs of AHO do not usually appear before the 7th to 10th day of illness, while ultrasonographic recognition is often possible several days before the X-ray features of this disease become apparent. Our case confirms that early ultrasonographic examination may anticipate the diagnosis and the initiation of therapy in case of a clinical suspicion of AHO, thus avoiding late complications.

AHO generally requires high-dose parenteral therapy for 4 to 6 weeks; however, in case of a recent onset with timely identification of the responsible microorganism and a rapid response to the initial parenteral therapy, the total duration of parenteral treatment may be shortened and the patient switched to oral antibiotics for 14 to 25 days. The somehow surprising recovery of our child after only 24 hours of parenteral therapy encouraged us to try this option, with the excellent reported outcome.

The bacteria most often involved in neonatal AHO are Staphylococcus aureus, Escherichia coli and group B Streptococci; however, many other microorganisms, such as Proteus, Klebsiella pneumoniae, Enterobacter, Serratia marcescens, Pseudomonas and Salmonella spp., have been reported to cause bone infection in newborns.

The frequency of gram-negative organisms involved in AHO is increasing; Neisseria species are occasionally implied; Neisseria gonorrhoeae, Neisseria elongata and Neisseria sicca have been isolated in AHO (none of which in the neonatal population); N. meningitidis is very rarely involved in bone infections. N. meningitidis is isolated from the oro- or nasopharynges of 5% of infants; it causes two major diseases, purulent meningitis and fulminant meningococcemia, and other unusual forms of infection, such as pneumonia, pericarditis, endocarditis, arthritis, urogenital infections and acute abdominal disease combined with meningitis or septicemia or alone without systemic disease. A case of distal femur osteomyelitis caused by N. meningitidis type Y in a 14-year-old patient with inherited properdin deficiency has been reported; it is well known that subjects with inherited complement deficiencies are at greater risk for acquiring systemic meningococcal infections.

However this is, to our knowledge, the first reported case of AHO caused by N. meningitidis group B and the first N. meningitidis neonatal AHO; interestingly, osteomyelitis was the only presentation of N. meningitidis infection; immunodeficiency due to prematurity probably played a key role.

Why the twin brother, who was also N. meningitidis carrier and shared the same risk factors, did not develop...
Overt illness is open to discussion; as reported, we could speculate on the role of undetected minor trauma. The early identification of the pathogen involved allowed us to look for asymptomatic carriers to treat with standard therapy, and to perform antibiotic prophylaxis on close contacts. Such a strategy is in accordance with international recommendations\textsuperscript{14}.

In conclusion, \textit{N. meningitidis} should be added to the list of uncommon causes of AHO affecting newborns.

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\textbf{References}