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SUCCESSFUL TREATMENT WITH MEZLOCILLIN OF A CHILD INFECTED BY PENICILLIN G–RESISTANT STAPHYLOCOCCUS AUREUS*

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The antibiotic treatment of gram-positive hospital infections has become a serious problem in recent years because of the unfavorable development of bacterial resistance, as in gram-negative infections. Therefore, resistance to antibiotics brings complex problems to the clinician during the treatment of infectious diseases.

Many useful semi-synthetic penicillin derivatives have been synthesized in order to overcome the gram-negative bacterial infections resistant to known antibiotics. Now, three new N-acyl derivatives of ampicillin have undergone extensive laboratory and clinical investigations: these are azlocillin, mezlocillin and piperacillin which are known as the ureidopenicillins[1-22].

It is reported that mezlocillin has a broad spectrum including both gram-negative bacilli and gram-positive cocci, except for the penicillin G-resistant Staphylococcus aureus[8,10,11,17,18]. Here we report a case with severe infection caused by penicillin G-resistant Staphylococcus aureus which could not be controlled by known antibiotics but in which our trial of mezlocillin treatment was effective in obtaining clinical improvement.

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Case Report

A 5-year-old boy was admitted to Hacettepe Children's Hospital with a three-day history of pain and swelling on the right hip and high fever. The physical examination and radiological findings revealed septic arthritis of the upper right femur. After purulent discharge was noted on the immediate joint, puncture penicillin G and gentamicin were started intravenously with doses of 500000 U/kg/day and 5 mg/kg/day, respectively. Since penicillin G-resistant Staphylococcus aureus grew in the blood cultures and puncture material, an antibiotic regimen was arranged with methicillin (400 mg/kg/day) and gentamicin (original dose). When the patient had been on this treatment for 10 days, purulent pericarditis was noted and 700 cc of serohemorrhagic fluid was drained by pericardiotomy. Cultures of second blood and pericardial fluid revealed the same microorganism, which was resistant to methicillin. Therefore, cephalothin (150 mg/kg/day) was substituted for methicillin. On the twentieth day of treatment gentamicin was stopped and netilmicin was started since the cultures of third blood and swab from the mediastinum revealed Staphylococcus aureus resistant to gentamicin, methicillin and cephalothin. Although sensitive antibiotics had been used for a long time, lung infection, pneumothorax, pericarditis and mediastinitis developed and penicillin G-resistant Staphylococcus aureus grew on each culture of blood and swab from the mediastinum. Since we had failed to control the infection, mezlocillin (75 mg/kg, three times a day) was started in place of cephalothin. It was used with netilmicin for seven days. Mezlocillin was then continued alone since netilmicin had in the meantime been found to be ineffective. On the fourth day of mezlocillin, a dramatic clinical improvement with absence of fever was noted. Several blood and swab cultures revealed no growth during the mezlocillin treatment. At the end of 15 days with mezlocillin the mediastinum was closed. Ten days after closure of the mediastinum mezlocillin was discontinued. Subsequent cultures revealed no bacterial growth, and the patient was discharged in good health.

Discussion

The problem of staphylococcal infections has become increasingly serious in recent years[23]. This is particularly true for patients in hospitals. Staphylococcal septicemia and pneumonia with various complications give rise to clinical symptoms of major importance. The well-known resistance of many types of staphylococci to penicillin is caused by penicillinase, which is able to inactivate penicillin by hydrolysis. A severe staphylococcal infection should be assumed to be caused by penicillinase-positive microorganisms until proved otherwise. Therefore, the preferred drug for initial therapy would be one of the penicillinase-resistant penicillins. It might be used alone or with one of the aminoglycosides that has some activity against penicillin-resistant S. aureus.

Mezlocillin has a broad spectrum of antibacterial activity against both gram-positive and gram-negative organisms[1-6,8-12,15-18]. In vitro studies have well established the efficacy of mezlocillin against gram-negative microorganisms including Pseudomonas aeruginosa, Klebsiella and Enterobacter species, and Escherichia coli[1-3,5]. Pharmacokinetic properties of mezlocillin have also been determined in different studies[4,6,7,13,14]. Although there is one report[12] related to experience with mezlocillin against staphylococcal infections, it has not been established whether the antibiotic has penicillinase activity or not. There have also been reports that mezlocillin has no antibacterial effect on penicillin G-resistant Staphylococcus aureus[1,3,4,10].

It is quite surprising that although the organism responsible for the infection in our case was penicillin G-resistant, improvement was obtained by mezlocillin treatment. As far as we can establish, it is the first case in the literature which responded to mezlocillin. In vitro and in vivo studies have shown that the effect of mezlocillin is increased when used with aminoglycosides[5,15-18]. In our case mezlocillin was used first in combination with netilmicin, but the latter was discontinued because of the development of resistance against it. Therefore, the clinical improvement may be attributable to mezlocillin alone.

Although there are a few reports regarding children[15-18], most of the in vivo experience with mezlocillin has been with adults[4,6,9-11,20-22]. Experience with both adults and children has shown that mezlocillin has a few side effects, but these do not necessitate interruption of treatment. These include mild diarrhea of short duration, mild allergic reactions, transient eosinophilia[6], transient proteinuria[7], mild pain on injection[9]; reversible leukopenia, hypokalemia and mild transient elevation of liver transaminases[10,15,17]; transient elevation of alkaline phosphatase[22]. We did not note any side effect attributable to mezlocillin in our case, despite the different antibiotic combinations which had been used. There was no liver or renal dysfunction nor any other disturbance that could be attributed to these combinations.

Although the encouraging data in the literature and in our case do not mean that mezlocillin provides activity against a sufficiently high percentage of various gram-negative bacteria and penicillin G-resistant Staphylococcus aureus so as to replace aminoglycosides in a therapeutic regimen for sepsis of unknown etiology or severe staphylococcal infections, they do indicate that mezlocillin might be safely used in specific conditions, as in our case.

Summary

A five-year-old boy with septic arthritis and purulent pericarditis caused by penicillin G-resistant Staphylococcus aureus which could not be controlled by different antibiotic combinations including penicillin, methicillin, cephalothin,

gentamicin and netilmicin was successfully treated with mezlocillin. Although it has been reported that there is no antibacterial effect of mezlocillin on penicillin G-resistant Staphylococcus aureus, mezlocillin therapy was effective in our patient.

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