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Scientific letters

Dalbavancin treatment of prosthetic knee infection due to oxacillin-resistant *Staphylococcus epidermidis*☆

Tratamiento con dalbavancina de infección protésica de rodilla por Staphylococcus epidermidis *resistente a la oxacilina*

Infections associated with prosthetic joints are a serious health problem which require multi-disciplinary surgical and medical management. The situation may be complex in the case of allergy, resistance or contraindications to commonly used antibiotics if there are no alternatives. Dalbavancin may be an option but up until now no cases of prosthetic infection treated with this antibiotic have been published, according to the PubMed (years 2000–2017) database with key search words of: dalbavancin and prosthesis. A late reported case of prosthetic infection caused by *Staphylococcus epidermidis* and treated with dalbavancin is described.

We report the case of a woman aged 55 with a history of chronic kidney disease, short bowel syndrome, the carrier of a central venous catheter for total parenteral long-term nutrition and who had a knee arthroplasty in 2009. After 7 years she presented with signs of prosthetic knee infection. Complete removal of the prosthetic knee and the implantation of a spacer impregnated with vancomycin and gentamicin was carried out. In the samples obtained during the procedure *S. epidermidis* was isolated, with the minimum inhibitory concentration (MIC) for each antibiotic as described below: vancomycin sensitive (MIC $\leq$ 1), daptomycin (MIC $\leq$ 0.5) and linezolid (MIC $\leq$ 1); resistant to cotrimoxazol (MIC > 2/38), clindamycin (MIC > 2), oxacillin (MIC > 4) and levofloxacin (MIC > 4). Due to the chronic kidney disease, we believed it correct not to use vancomycin, and a treatment with daptomycin in monotherapy was selected for 10 days. When the moment for sequential therapy was reached, the oral alternative with elevated bioavailability was linezolid, which was not used as its complete absorption could not be ensured due to the short bowel syndrome. In order to protect the catheter required for parenteral nutrition and avoid a prolonged hospital stay, outpatient treatment with dalbavancin was administered when its sensitivity by ETEST® (MIC $\leq$ 0.047) was made known and in accordance with the recommendations from the Spanish Medicine Agency.[1] A first dose of 1000 mg iv was administered followed by a weekly dose of 500 mg iv for 3 weeks. Two months after becoming asymptomatic and with no signs of infection or organ failure, reimplantation was carried out with continuation of empirical antibiotic treatment until negative obtainment of a total of 5 intraoperative cultures was made from the bone-prosthesis interphase, spacer and synovial fluid. Nine months after follow-up the patient continues in complete remission.

Infection associated with prostheses is one of the most serious complications of arthroplasty. The estimated rate of infection for knee arthoplasties in our environment is between 2% and 3%, with the staphylococcus bacteria being responsible for around 65% of cases.[2,3] Combined therapy based on the extraction of prosthetic material, together with antimicrobial treatment obtains healing rates of around 80%.[4] Dalbavancin is a parenteral antibiotic of the lipoglycopeptide group, with good action and penetrability in tissue compartments and demonstrates good bacterial activity compared with the majority of gram positive organisms.[5] The susceptibility of dalbavancin compared with negative coagulase staphylococcus is around 100%.[6] Dalbavancin has been assessed *in vitro*, with acceptable results in biofilms generated by staphylococcal infections, although there not enough evidence with regard to prosthetic joint material.[7,8]

In our case, with regard to dosing, the recognised recommendations used for treatment of acute skin and soft tissue infection in adult patients were used. This is the only indication which has been approved up until now.[9] Unlike other antimicrobials where association with rifampicin has proven to be effective, its use in combined therapy does not appear to have been confirmed by the available scientific data which has supported it up until now, and for this reason monotherapy was chosen as therapy.[7]

To conclude, and as a result of this experience, dalbavancin could be used as an alternative in the treatment of oseoarticular infections caused by gram positive bacteria in the event of no other efficacious antimicrobial alternatives existing.

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Human parechovirus sepsis induced coagulopathy in an infant☆

Sepsis por parechovirus humano que indujo coagulopatía en un lactante

The human parechovirsus (HpeV) is a member of the Picornaviridae viral family and has a fecal–oral route of transmission; it can cause nonspecific fever in adults. Cases of encephalitis/sepsis due to HpeV have been reported in infants.[1,2] One possible consequence of the viral infection is acute coagulopathy.[3] We hereby present the case of an infant with sepsis and coagulopathy who underwent the routine tests available at local level that could not confirm the source of infection. A larger virological study conducted at the national virology lab revealed infection due to HpeV. We recommend routine studies to rule out HpeV in infants with no obvious etiology of sepsis.[4]

One eight-week old infant without a significant personal history is assessed due to clinical manifestations of fever, irritability and diarrhea of one (1) day duration. The clinical examination shows one single blue macular exanthema on the infant's right thigh. The heart and respiratory rates are 220 beats and 50 breaths per minute, respectively. Temperature is 101.3 °F and the capillary refill time is over four (4) seconds – suggestive of poor peripheral perfusion and a situation of clinical sepsis. The additional tests conducted showed leukocyte counts of 4×10^9/l and CRP values of 23 mg/l, and lactate levels of 2.7 mmol/l. The INR was 1.5. Prothrombin time (PT) was 16.1 s (normal = 8.7–2.7), and the activated partial thromboplastin time (aPTT) was 67 s (normal = 8.7–2.7). The liver function tests showed ALT levels of 22 U/l; bilirubin levels of 7.1 μmol/l; ALP levels of 196 U/l; and GGT levels of 16 U/l, all within normal ranges. A complete screening for sepsis including lumbar puncture; blood cultures; urine cultures; and coprocultures was conducted followed by the administration of a triple empirical antibiotic therapy (amoxicilin, gentamicin, and cefotaxime) and due to an inadequate peripheral perfusion, boluses of crystalloid solutions are administered too. On day two, the diarrhea gets worse with presence of swelling in the infant's lower limbs and scrotum areas. The controls reveal that the APPT extends over 100 s. The preliminary results from the blood, fecal and urine samples tested negative and the lumbar puncture confirmed glycorrhachia levels of 2.9 mmol/l and proteinorrhachia levels of 0.29 g/l.

We conducted X-rays of the chest and the abdomen and pelvic and cranial ultrasound scans and they all looked normal. We added teicoplanin to the antibiotic therapy to treat possible MRSA due to the local epidemiological situation of a higher incidence rate of infections due to MRSA. The fact that there was no improvement following the multiple antibiotic therapy and that the active source of infection could not be identified was suggestive that the etiology of sepsis could be viral. For a more in-depth study, the samples collected were sent to the national virology lab where unlike the procedures conducted at hospital standard labs, the CRP testing to rule out the presence of HpeV is routine. On day three, the fever stops. The CRP tested positive for HpeV RNA in fecal, pharyngeal, blood, and CSF samples. On day four, the patient's vital signs went back to normal and the antibiotic therapy was withdrawn. The patient was discharged from the hospital on day eight.

The clinical presentation of HpeV goes from a self-limited fever disease to sepsis with high mortality rate.[5] The pathogenesis that leads to coagulopathy in infections due to HpeV is different from that of disseminated intravascular coagulation (DIC). In the DIC, the tissue factor is released after vascular damage, or after the cytokine release. The DIC PT and aPTT are extended; the fibrinogen level is high, normal, or even reduced, and there is a rapidly decreasing plateletcrit. According to the diagnostic algorithm for the DIC created by the Scientific and Standardisation Committee on Disseminated Intravascular Coagulation that takes all the aforementioned parameters into consideration, scores ≥5 have 97 per cent specificity and 91 per cent sensitivity in the diagnosis of DIC. Our patient scored 1 only, with normal platelet and fibrinogen levels during the course of the sepsis.[6] This made us consider the possibility of a viral etiology as the cause of the clinical manifestations. The takeaway message here is that one situation of sepsis that does not improve with multiple antibiotic therapy or extended aPTT without use of fibrinogen concentrate should make the physician think of a viral infection. There are many viruses that can cause this activation of endothelial cells, which may activate the blood coagulation cascade, inducing the expression of the tissue factor. This is a multifactor process also mediated by the molecule-leukocyte adhesion. Similarly, the edema secondary to the inflammation leads to the activation of the intrinsic blood coagulation cascade. This has been the case of our patient's pattern of coagulation with PT and INR peaks on day 2, and aPTT peaks on day 4.

Since it is not studied on a routine basis, the true incidence of HpeV is unknown. One retrospective study of 5396 infants showed that 1 per cent of the infants hospitalized in the neonatal intensive care unit suffered from an infection, 39 per cent of whom tested positive for enterovirus or parechovirus.[7] Although there are not many clinical guidelines on the management of HpeV, the detailed monitoring of the patients' vital signs and organic functions is necessary to plan adequate support therapies, since cases of rapid progression of encephalitis or sepsis may be fatal. The rapid systematic study of the HpeV RNA through CRP testing could mean achieving the diagnosis within six (6) hours after hospital admission and thus limiting the use of unnecessary antibiotics.[8]

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