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CASE REPORT

DRESS syndrome due to antibiotic therapy of osteoarticular infections in children: Two case reports☆

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Abstract Osteoarticular infection in children frequently occurs before 10 years of age. Surgical drainage is sometimes required, whereas acute osteomyelitis can be treated with antibiotic therapy alone. The duration of antibiotic therapy varies, 2 weeks is sufficient for septic arthritis, whereas 6 weeks is often required for complicated cases. Some of these antibiotic drugs present direct complications with low clinical impact in certain individuals.

Hypersensitivity to these drugs causes different reactions in children. DRESS syndrome (Drug Reaction with Eosinophilia and Systemic Symptoms) is a severe and potentially life-threatening drug reaction. It is characterised by high fever, malaise, lymphadenopathy and skin rash. From a clinical perspective, these symptoms can lead to an exacerbation of the initial infectious process for which treatment was commenced.

The liver is the organ most often affected in DRESS syndrome associated with haematological changes, potentially similar to sepsis.

We present two cases of children with osteoarticular infections who developed DRESS syndrome after antibiotic therapy. Both patients made a complete recovery after cessation of the antibiotic drugs used.

PALABRAS CLAVE
Síndrome de DRESS;
Antibioterapia;
Niños. Infección ortopédica

Síndrome de DRESS como complicación de la antibioterapia en niños tratados por infecciones ortopédicas. A propósito de 2 casos

Resumen La infección osteoarticular en el niño es frecuente por debajo de los 10 años. El tratamiento consiste en la administración de antibióticos y en algunos casos tratamiento quirúrgico. El tiempo de antibioterapia varía, desde 2 semanas para las artritis, hasta 6 semanas en

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casos de osteomielitis más abigarradas. Algunos de estos medicamentos poseen complicaciones individuales directas con baja repercusión clínica.

Existen diferentes cuadros de hipersensibilidad a drogas descritos en la población infantil. El síndrome de DRESS consiste en una toxicodermia grave, que en ocasiones incluso puede comprometer la vida. Se caracteriza por fiebre elevada, mal estado general, adenopatías, y exantema. Desde el punto de vista clínico son síntomas superponibles a una exacerbación del proceso infeccioso previo por el que el paciente inició el tratamiento. Generalmente aparece afectación de órganos internos (sobre todo el hígado) y alteraciones hematológicas, que pueden hacer pensar en un cuadro séptico general.

Presentamos dos casos de infección osteoarticular bacteriana en niños que fueron tratados con antibióticos y que presentaron este cuadro. Ambos regresaron tras la retirada de la medicación antibiótica.

Introduction

Osteoarticular infection in children usually causes local pain, reddening, functional failure and often high fever in cases with septic arthritis and a lower fever in cases of acute or chronic osteomyelitis. Depending on the germ involved, patients may also present a skin rash and local lymphadenopathies.

The most common origin of osteoarticular infection in children is haematological. Generally, a respiratory or gastrointestinal germ crosses into the bloodstream and may colonise a distant joint or bone region. The initial treatment is based on administration of wide-spectrum antibiotics and surgical drainage in cases, which require it. The duration of antibiotic therapy varies depending on the specific infectious process, and may last for a long period. Some of these drugs entail specific direct complications with low clinical repercussion. These complications normally remit once the drug treatment is removed.[1]

Different cases of hypersensitivity to drugs have been described in children.[1–4] There is a severe type of toxicoderma, known as DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms),[2–4] which consists in the belated appearance of fever and malaise in patients treated previously for an infectious process. The first thought of the surgeon is usually a worsening of the initial symptoms and failure of the medical or surgical treatment. This syndrome is characterised by high fever, lymphadenopathies, exanthema, involvement of internal organs (particularly the liver) and haematological alterations, which occasionally may even compromise the life of the patient.

DRESS syndrome was first proposed by Bouquet et al.[5] in 1996. Even today, its diagnostic criteria and aetiopathogenesis are not well defined. It is clearly a case of family-related hypersensitivity to drugs. The compounds involved most frequently are anticonvulsants, antiretrovirals and antibiotics, which are the most relevant to orthopaedic surgeons (penicillin and derivatives, cephalosporins, sulphonamides, minocyclines).[6,7]

Symptoms usually appear between the 2nd and 4th week after the start of the osteoarticular infection treatment, with high fever (39–41 °C) being the initial symptom, and skin lesions appearing afterwards. Systemic involvement usually takes place 1 or 2 weeks after the onset of fever, with hepatic function being significantly compromised.[7]

The treatment consists in immediate suspension of the responsible drug. In cases of systemic involvement, the administration of systemic corticosteroids normally improves the symptoms and prognosis of the process.[7]

We present 2 cases of children who suffered bacterial osteoarticular infection treated with antibiotics and who presented these symptoms. The superposition of symptoms between a reactivation of infection and DRESS syndrome should make us pay very close attention to children who receive antibiotic therapy and present renewed fever, malaise, skin rash and lymphadenopathies. The different treatment of both cases should encourage us to learn about this syndrome.

First case

We present the case of a 7-year-old boy with no relevant history. He had been treated at another centre due to septic arthritis in his right knee through repeated arthrocenteses and intravenous antibiotic therapy (cloxacillin and cefotaxime for 14 days). The results of the analysis conducted at the time of admission included: leucocytes: $19.5 \times 1000/\mu L$ (neutrophils 75%, eosinophils 1.8%); haemoglobin Hb: 12.3 g/dL; haematocrit Hct: 36.3% and platelets: $469 \times 1000/\mu L$. The general biochemical analysis with normal hepatic enzymes was normal. C-reactive protein (CRP): 3.4 mg/dL.

Following an initial clinical improvement, after 7 days of admission he began to suffer fever with peaks of 40 °C. The analysis obtained after 11 days of admission showed a deterioration of hepatic function (GOT: 501 U/L, GPT: 555 U/L) and the haemogram (leucocytes $3200 \times 1000/\mu L$, Hb: 10.1 g/dL, platelets: $163 \times 1000/\mu L$).