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Case Report Open Access

Transient Cloxacillin Induced Agranulocytosis with Eosinophilia and Elevated IgE Levels

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Abstract

Cloxacillin is a commonly prescribed antibiotic for Methicillin-sensitive Staphylococcus aureus (MSSA) caused infections. We report a case of transient Cloxacillin induced agranulocytosis with eosinophilia and elevated IgE levels. Agranulocytosis is a life threatening condition, drugs are the most common cause and our knowledge and evidence of the relationship between drug use and agranulocytosis builds up and accumulates from case reports and observations. It is important to keep adding drugs to the list of potential causative drugs especially since monitoring blood count is simple and can be life saving.

Case Description

A previously healthy 50 year-old male was admitted for a non-traumatic septic arthritis of the left shoulder and vertebral osteomyelitis with MSSA positive blood and synovial fluid cultures. Clinical examination showed a red, swollen and tender left shoulder.

Trans-esophageal echocardiography was normal and showed no valvular vegetation. Complete blood count (CBC) showed leukocytosis of 28.900/mm^3 with 85% neutrophils and 0.9% Eosinophils. Platelets of 190,000/mm^3 and hemoglobin of 13.7 g/dl. Electrolytes and renal function were normal, albumin was 2.4 g/dl. Liver enzymes were normal except for elevated Gamma-glutamyl transpeptidase (GGT); 145 IU/ml. Prothrombin time (PT) and Partial thromboplastin time (PTT) were normal. C-reactive protein was 324 mg/L. A Gallium bone scan showed a positive uptake in vertebra T8 and in sterno-manibrio joint compatible with acute osteomyelitis. Intravenous treatment with cloxacillin was initiated at a dose of 2 gram four times daily. Cloxacillin was well tolerated with clinical and laboratory improvement, with normal CBC until day 21, when the patient was discharged for home intravenous antibiotic treatment.

As a part of patient's follow up in the outpatient clinic, blood tests on day 48 depicted:

1. Leukocytes 2900/mm^3, neutrophil count 0%, monocytes 26%, eosinophils 9% and lymphocytes 62%. Hemoglobin concentration and platelets count were normal.
2. GGT 192 (IU/ml), Alanine transaminase (ALT) 15 IU/ml and Alkaline phosphatase (ALP) 136 IU/ml.

The patient was admitted. He was free of symptoms. On admission he was well with no fever and no pathological findings on physical examination, chest X-ray and ECG. He denied taking any Over the Counter (OTC) drugs other than Paracetamol.

Cloxacillin was discontinued. Bone marrow biopsy showed mild hypocellularity with a decline in maturation in all cell lineages, a small focal increase in small T cell lymphocytes stained for CD3. There was no increment in B cell lymphocytes and no signs of malignant cells. Serum Protein electrophoresis showed normal immunoglobulin levels except for elevated IgE 2890 mg/ml (upper limit 183 mg/ml). C-reactive protein (CRP) was 3 mg/L.

Twenty-four hours after admission the neutrophils number raised to 400/mm^3, Liver function tests also returned to normal values after cloxacillin discontinuation.

Infectious or viral diseases like the reactivation of Herpesviruses can also manifest in leukopenia, agranolocutosis and Elevated IgE and are a part of our differential diagnosis but the absence of fever, normal CRP level and the quick recovery of the bone marrow after the discontinuatioan of the drug makes it an unlikely diagnosis.

Literature Review

According to the World Health Organization, an adverse drug reaction is defined as a noxious, unintended response to a drug that occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy or for modification of physiologic function [1]. Agranolocytosis is a marked and profound decrease in the number of granulocytes, or an absolute lack of granulocytes in circulating blood, typically resulting in a neutrophil count below 0.5×10^9 /L [2]. It is a dangerous and life threatening condition with the risk of sepsis and death [2-4].

Most cases (70-90%) of Agranolocytosis are caused by drugs, chemotherapy and non chemotherapy. Either the drug itself or one of its metabolites may be the causative agent [4-6]. Beta lactams and especially Penicillins have been reported to cause agranulocytosis since 1946 [7], and have been long associated with the inhibition of granulopoesis. It is thought to cause maturation arrest of myeloid cells and is usually reversible [8].

In a French monocentric cohort study on Drug induced Agranolocytosis (DIA) with 90 patients over 11 years (1990-2001), Antibiotics were the leading cause (25%) for agranulocytosis followed by anti-thyroid drugs (23%) and anti-aggregative platelet agents (16%). Among the antibiotics listed; Sulfamethoxazole, imipenem, amoxicillin/clavulanic acid and amoxicillin. Cloxacillin was not mentioned [9].

In MEDLINE search we found only three case reports of Oxacillin induced agranulocytosis between 1978-1982 [10-12].

The pathogenesis of drug-induced agranulocytosis is heterogeneous

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