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Acute Systemic Toxicity in a Patient After a Single Dose of Diclofenac

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Non steroid antiinflammatory drugs (NSAIDs) have been known to be a cause of acute hemolytic anemia, acute hepatic failure and acute renal failure for a long time. We report a 50 years old woman with lomber disc hernia who had been injected a single dose diclofenac sodium because of lomber pain and afterwards in 24 hour period observed deterioration in general health status. Her bichemical evaluation was consistent with acute hemolysis, acute hepatic injury and acute renal failure. After supportive therapy her general health status and biochemical parameters started to ameliorate and on the twentyfirst day of administration the patient was discharged with normal hematologic, liver and kidney parameters. It should be remembered by the clinicians that NSAIDs can cause multisystemic toxicities as hemolytic anemia, liver disfunction and kidney failure. Hence, immediate therapeutic interventions after the diagnosis can be life-saving.

Key Words: *Hemolysis, acute liver failure, acute renal failure, diclofenac.*

Bir Hastada Tek Doz Diklofenak Kullanımı Sonrası Gelişen Akut Sistemik Toksisite

Non sterid antienflamatuar ilaçlar (NSAİİ)'ın hemolitik anemi, karaciğer yetmezliği ve böbrek yetmezliğine neden olduğu uzun zamandır bilinmektedir. Bu yazımızda, lomber disk hernisi nedeniyle tek doz diklofenak enjeksiyonu yaptıran ve sonrasında genel sağlık durumu bozulan 50 yaşındaki bir kadın hastayı sunuyoruz. Hastanın laboratuar değerlendirmesi hemoliz, akut karaciğer ve böbrek yetmezliği ile uyumluydu. Yapılan tedavi sonrasında genel durumu ve laboratuar değerleri normale dönen olgu takibinin yirmibirinci gününde taburcu edildi. Klinisyenler NSAİİ'ların sistemik toksik etkileri olabileceğini akılda tutmalıdırlar. Çünkü tanı sonrası acil tedavi müdahaleleri hayat kurtarıcı olabilmektedir.

Anahtar Kelimeler: *Hemoliz, akut karaciğer yetmezliği, akut böbrek yetmezliği, diklofenak.*

Introduction

Non steroid antiinflammatory drugs (NSAIDs) have been known to be a cause of acute hemolytic anemia, acute hepatic failure and acute renal failure for a long time. Although these effects can be seen seperately, in some rare cases all of them can be observed in a patient sometimes in a serious manner (1). In this article we describe a patient with acute and serious autoimmune hemolytic anemia, liver and kidney insufficiency.

Case Report

A 50 years-old woman with lomber disc hernia had been injected a single dose diclofenac because of lomber pain and within 24 hours of drug injection her general health status deteriorated. Biochemical evaluation revealed serious anemia (hemoglobin: 6.9 g/dL, hematocrit: 14.3 %, erythrocyte sedimentation rate was 130 mm/hour, LDH: 4700 U/L, total bilirubin: 7 mg/dL, indirect bilirubin: 4.8 mg/dL). The liver enzymes elevated (AST: 1695 U/L, ALT: 787 U/L) and there was acute kidney failure (BUN: 85 mg/dL, creatinine: 5.7 mg/dL, uric acid: 9.8 mg/dL). Additionally direct and indirect Coombs tests were positive and INR was high (4.9). Because of the serious hemolysis at the beginning of the process we were unable to determine her blood group. She was anuric for more than 24 hours and in her physical examination we determined dehydration, acidotic respiration, paleness and icterus. After her admission to our clinic we immediately evaluated her status and started treatment. Simultaneously we started to infuze isotonic saline solution in order to rehydrate, and administered glucose, suitable amino acid solutions and fresh frozen plasma in order to support the liver. Patient received hemodialysis because of uremic state and risk of hyperkalemia in the immediate period and 5 more times during our follow up period. We also administered intravenous methylprednisolone 250mg/day after the first day of admission for the consecutive 3 days and oxygene inhalation by nasal canula. During our follow up, we infused a total 2 units fresh frozen plasma in the acute period. We were not able to infuse erythrocyte suspension since there was no chance to make

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cross-match because of the acute hemolysis. However, we started to administer erythropoetin beta 5000 U/day for 7 days and after the acute hemolytic period subsided, 4 units erythrocyte suspensions was transfused after successfull cross-match.

After the first 24 hours after the supportive therapy her general health status and biochemical parameters started to ameliorate and on the twentyfirst day of administration we discharged her with acceptable hematologic, liver and kidney parameters (Hemoglobin: 10 gr/dL, hematocrit: 30 %, BUN:40 mg/dL, creatinine: 2.2 mg/dL, SGOT: 27 U/l, SGPT: 14 U/l, LDH: 77 U/l).

Discussion

The most serious side effects of NSAIDs are hypersensitivity reactions like hematologic (aplastic anemia, trombocytopenia, agranulocytosis, hemolytic anemia), erythema multiforme and hepatitis (2-5). Multisystem toxicities including Coombs positive hemolytic anemia, acute liver failure and acute renal failure with acute tubular necrosis cases are also reported in the literature (1). Analgesics or sometimes contaminants of pharmacologic composition are reported to be the cause of acute hemolytic reactions generally by immunologic pathway (6). The mechanism of acute liver injury associated with NSAIDs is poorly understood, however a possible mechanism may be the interaction of NSAIDs' metabolites with some hepatocellular proteins. This interaction causes immunologic reactions and may produce hepatotoxicity in susceptible patients (7,8). The renal effects of NSAIDs especially in patients with varying degrees of kidney disfunction are generally due to altered hemodynamics because of the inhibition of renal prostoglandin production. This process can emerge as fluid and electrolyte imbalance, acute renal disfunction, nephrotic syndrome, interstitial nephritis or renal papillary necrosis (9).

In our patient, systemic toxicities including hemolytic anemia, elevation of liver enzymes and acute renal failure were all emerged after the administation of diclofenac. After cessation of this molecule and following supportive and therapeutic interventions, her general status and biochemical parameters recovered.

In conclusion, it should be remembered by the clinicians that NSAIDs can cause multisystemic toxicities such as hemolytic anemia, liver disfunction and kidney failure. Immediate treatment attempts after the early diagnosis can be life-saving.

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