

Albendazole-induced bicytopenia: case report

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Received: 11.12.2006 • **Accepted:** 19.01.2007

ABSTRACT

Echinococcosis is a parasitic disease which occurs due to cyst hydatid *Echinococcus granulosus* and occurs in the liver in 55-70% of cases. Cyst hydatid treatment can be performed in three ways: primary surgery, medical and PAIR (Puncture Aspiration Injection Reaspiration) treatment. Medical treatment can be applied with PAIR in order to decrease post-surgery recurrence and facilitate the treatment in repeating cases. The most commonly used agent in medical treatment is albendazole. The most common albendazole-induced side effect is elevated levels of liver enzymes. It rarely causes bone marrow toxic consequences. We present herein a case with albendazole-induced leukopenia and thrombocytopenia, which to our knowledge has never been reported in the literature.

Key words: Albendazole, cyst hydatid, leukopenia, thrombocytopenia

ÖZET

Albendazolun indüklediği bisitopeni: vaka sunumu

Kist hidatik *echinococcus granulosus*a bağlı oluşan ve %55-70 karaciğerde görülen paraziter bir hastalıktır. Kist hidatik tedavisi primer cerrahi olmak üzere, medikal ve PAIR (perkütan aspirasyon injeksiyon reaspirasyon) tedavisi olmak üzere üç şekilde verilebilir. Nüks eden olgularda, cerrahi sonrası rekürrensi azaltmak ve işlemi kolaylaştırmak için PAIR ile birlikte medikal tedavi verilebilir. Medikal tedavide en sık tercih edilen ajan albendazoldür. Albendazol kullanımına bağlı en sık görülen yan etki karaciğer fonksiyon testi yüksekliğidir. Kemik iliği supresyonuna nadiren neden olur. Bu makalede albendazol kullanımına bağlı lökopeni ve trombositopeni gelişen bir vakayı literatürde daha önce görülmemesi nedeniyle sunduk.

Anahtar kelimeler: Albendazol, kist hidatik, lökopeni, trombositopeni

INTRODUCTION

Echinococcosis, also known as hydatid disease, is a potentially parasitic disease that can affect animals and humans. Echinococcosis is known to be endemic in the Middle East as well as other parts of the world, including India, Africa, South America, New Zealand, Australia, Turkey and Southern Europe [1-3]. Cyst hydatid is widely found in the liver (55-70%) and lungs (18-85%). In 5-13% of the patients, cyst hydatid simultaneously develops in the liver and lungs [4,5]. It is rarely found in muscles, bone, kidneys, brain, spleen, heart, prostate and pancreas [6]. Clinical findings are highly varied and the symptoms depend on the organs where the cyst develops, the size of the cyst and its location in organs, relation between the expanding cyst and adjacent organs, complications due to rupture of the cyst, bacterial infections, and immunological reactions such as asthma, anaphylaxis, and membranous nephropathy. There may be some clinical symptoms due to medication. Albendazole-induced development of bone marrow suppression is a critical side effect since it may cause mortality and morbidity.

CASE REPORT

The patient was a 58-year-old man who presented with a cyst hydatid in the liver and applied to our clinic for pre-operative evaluation. It was reported that the patient had experienced fatigue and right upper quadrant abdominal pain for four months, and he applied to the surgery clinic with these complaints. PAIR (Puncture Aspiration Injection Reaspiration) was applied to the patient with diagnosis of liver cyst hydatid recurrence and albendazole was initiated.

Patient history: The patient was operated in 1974 and 2001 with liver cyst hydatid diagnosis. His brother died because of cyst hydatid rupture, and his two cousins were operated with liver cyst hydatid. In physical examination of the patient, pulse was 76/minute, temperature 36.8°C, and arterial blood pressure 110/70 mmHg. During abdominal examination, there was no abnormal physical finding apart from right upper quadrant abdominal tenderness. In laboratory examinations, hemoglobin (Hb) was 14.1 g/dl, hematocrit (Htc) 39.3%, white blood cell count 2,000 mm³, platelets 47,000 mm³, sedimentation 18/hour, aspartate aminotransferase (AST) 32 U/L, alanine

aminotransferase (ALT) 24 U/L, gamma-glutamyl transpeptidase (GGT) 161 U/L, alkaline phosphatase (ALP) 146 IU/L, total bilirubin 1.1 mg/dl, and direct bilirubin 0.2 mg/dl; hemagglutination test was 1/60 positive. Peripheral blood smear of the patient showed normochromic normocytic anemia and low platelet counts. Differential of leukocytes was 70% neutrophils, 20% lymphocytes, 8% monocytes, and 2% eosinophils. Bone marrow aspiration and biopsy were hypocellular. No meaningful atypical cell or blast increase was observed in bone marrow aspiration and biopsy. A cystic lesion (82 x 75 mm) was observed in the right lobe of the liver during abdominal ultrasonography (USG) (cyst hydatid type 2). Other findings were normal. There was no abnormal finding in thorax computerized tomography (CT). In previous laboratory tests of the patient, one week prior to albendazole treatment, Hb was 14.3 g/dl, Htc 42.5%, white blood cells 4,100 mm³, and platelets 173,000 mm³. Treatment with albendazole was stopped on admission to our clinic. One month following admission to our clinic, Hb was 14 gr/dl Htc to 42%, white blood cells to 4,600 mm³, and platelets to 196,000 mm³. Bicytopenia in the patient was thought to be albendazole-induced.

DISCUSSION

Medical treatment in cyst hydatid is applied with PAIR in patients with multiple cysts in two or more organs in order to decrease the risk of post-surgery recurrence. A benzimidazole compound, albendazole, is an agent which has been used in human cyst hydatid cases since 1980. Albendazole shows its activity by deteriorating microtubular formation of the parasite [7]. Suggested dose of albendazole is 10-15 mg/kg/day. The drug is applied in monthly treatments and with 14-day intervals. Although the rate of patients who respond with a long treatment period has slightly increased, additional benefits of the treatment for longer than six months have not been reported in many patients. As it is known that there is not any significant decrease in cystic activity, three cure treatments are suggested as routine [8].

The most common side effect of chemotherapy with benzimidazole compounds is elevated levels of liver enzymes, found in 10-20% of the patients in a part of the treatment. Elevations are self-mini-

mizing and usually recover after the treatment is stopped. In one study, 14.7% of the patients had elevated levels of liver enzymes, 5.7% abdominal pain, 2.8% alopecia, 1.3% vertigo - lethargy, 1.3% nausea, 1.2% leukopenia, 0.6% tenderness, 0.5% urticaria, 0.3% thrombocytopenia, 0.3% anaphylaxis and 0.1% cystic pain. Although rarely seen, bone marrow suppression is a significant side effect as it can lead to death. Two patients are reported in the literature who died due to albendazole-induced agranulocytosis. It has been reported that aplastic anemia developed in a case with portal hypertension due to long-term post surgery albendazole use [9,10]. Albendazole-induced amegakaryocytic thrombocytopenia purpura development was also reported. In a study on rats, large doses of albendazole (60-120 mg/kg/day) were observed to cause pancytopenia and loss of hematopoietic cells in the bone marrow [11]. The effect of albendazole on bone marrow suppression due to dose levels is not known. There are studies which show the frequency of leukopenia due to single-dose albendazole or long-term use of albendazole as similar.

Albendazole undergoes virtually 100% first-pass metabolism in the liver, and is rapidly converted to albendazole sulfoxide by both the microsomal flavin mono-oxidase and P450 CYP3A enzymes [12]. It then undergoes partial further metabolism to albendazole sulfone via a separate P450-dependent enzyme CYP2C [13,14]. Conversion to albendazole, albendazole sulfoxide and albendazole sulfone decreases in case of hepatic failure, where production of liver oxidase enzymes falls. High inhibition of high albendazole level and tubulin polymerization inhibit microtubule dependent cases. Bone marrow suppression may occur due to these effects.

A review of the literature shows that albendazole-induced neutropenia and thrombocytopenia development have not been reported previously. In our case, three cure albendazole treatment with PAIR was applied in a recurrent liver cyst hydatid case following two surgical treatments. The routine complete blood counts of the patient were normal before chemotherapy with albendazole. In the fourth month of the treatment, leukopenia and thrombocytopenia were found in the laboratory tests of the patient. We present a case with leukopenia and thrombocytopenia development following long-term albendazole use, which has not

previously been published in the literature. Individuals who use albendazole should be closely monitored for development of bone marrow suppression. Liver function tests and complete blood counts in the patients should be monitored before and during the treatment.

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