CASE REPORT

A Case Report of Unusual Vasculitic Reaction after Methocarbamol Injection

Maryam Sahebari[1], Amir Hossein Jafarian[2], and Bita Abbasi[3]

[1] *Department of Rheumatology, Rheumatic Diseases Research Center (RDRC); School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

[2] *Department of Pathology, Ghaem Hospital, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

[3] *Medical Student, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran*

Received: 24 May 2009; Received in revised form: 29 Aug. 2009; Accepted: 4 Nov. 2009

Abstract: Descriptive case report of a 42-year old woman with coetaneous vasculitis, and severe abdominal pain, which was led to diagnostic laparotomy. These presentations are probably as a side effect of Methocarbamol injection. This is the first report according to our literature search (PubMed, google scholar, ISI web of knowledge, ProQuest, MD consult, Science Direct, SCOPUS) about Methocarbamol related vasculitis from 1966 since now. Vasculitis is not a known side effect of Methocarbamol. This case indicates, likely the potential for development of vasculitis with this medication.

Acta Medica Iranica 2011; 49(3): 192-194.

Keywords: Drug toxicity; Methocarbamol; Vasculitis

Introduction

One of the accepted classifications for adverse drug reactions is: "Immune mediated and non immune mediated" mechanisms. Drug induced vasculitis; most of the time is due to type III hypersensitivity (1). We report here a patient with biopsy-verified leukocytoclastic vasculitis, and GI involvement after Methocarbamol injection with a history of using oral Methocarbamol for a period of time, in the past. In addition to the case presented, a literature search (PubMed, google scholar, MD consult, Science Direct, SCOPUS, ISI web of knowledge, ProQuest) for articles published from 1966 to present has been performed using the Medline subheading keywords "Methocarbamol" and "leukocytoclastic vasculitis", "Methocarbamol" and "vasculitis", "Methocarbamol" and "side effects", "Methocarbamol" and "Drug reactions", "Robaxin" and "side effects". We have found no case report or related article. The relevant references of side effects were retrieved but nothing was found.

Case Presentation

A 42 –year old woman was referred to emergency ward because of severe abdominal pain, rectal bleeding, and widespread palpable purpuric lesions on her hands, buttocks, legs, and abdomen. The patient suffered from spastic pain of calf muscles after a vigorous physical activity. Therefore, she had received an intramuscular Methocarbamol (Relaxin, 1gr/10ml, Caspian, Tamin, Pharmaceutical Co; Rasht Iran) injection. Seven hours later, she noticed widespread palpable purpuric lesions, progressive edema, and severe abdominal pain. Positive findings in her admission were axillary temperature of 38.5^{0C}, pulse rate of 120 b/min and blood pressure of 100/90 mmHg, respiratory rate of 25/min, and foamy strawberry like stool in rectal examination.

In addition of normal CBC, without eosinophilia, Hemoglobin 11.5 mg/dl, reticulocyte count 0.1%, and platelet count 240000, normal PT, PTT and INR other biochemical markers are summarized in table 1. She had a past medical history of, seasonal atopy, a history of receiving oral Methocarbamol for three weeks, four month earlier because of myofascial pain. She had no history of flue like symptoms, or other viral and bacterial infections and medications before Methocarbamol injection. The echocardiography was normal. Further work up revealed free fluid in abdominal sonography. Rectosigmoidoscopy was not performed due to risk of perforation. Therefore, she was been candidate for diagnostic laparotomy to rule out the peritonitis and bowel perforation or infarction.

Corresponding Author: Maryam Sahebari
Assistant Professor of Rheumatology; Rheumatic Diseases Research Center (RDRC); School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
Tel: +98 511 8012753, Fax: +98 511 8410136, E-mail: sahebarim@mums.ac.ir

Table 1. Biochemical laboratory findings in the first admission of the patient

Laboratory Data	Results	Unit/Normal value
Blood Sugar	151	Up to 200 mg/dl
Urea	27	25-50 mg/dl
Creatinine	0.7	Up to 1.5 mg/dl
ionogram	normal	
SGOT(AST)	28	5-40 U/L
SGPT(ALT)	21	5-40 U/L
ALP	91	Up to 125
LDH	425	100-500 U/L
Amylase	45	Up to 90 IU/L
Lipase	400	Up to 490 U/L
Total Bilirubin	0.6	Adult≥ 1.1
Direct Bilirubin	0.1	0.25≥Adult

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, ALP: Alkaline phosphatase, LDH: Lactate dehydrogenase

After taking a punch skin biopsy and before surgery she treated with 1 gr Methylprednisolone IV as a pulse therapy. In the laparotomy procedure, one liter of serosanguineous fluid was sucked from abdominal cavity. It was reported that, all the small and large intestinal walls were edematous and were covered with patchy telangiectatic erythema, no other findings were reported. The abdominal fluid was sterile. Corticosteroid therapy was continued; she had another attack of abdominal pain before subsiding the symptoms. All the tests for vasculitis including p and c ANCA, ANA, anti dsDNA, antiphospholipid antibodies and complement levels were in the normal range, and the infectious diseases such as HTLV1 and 2, HIV, HBV and HCV, HSV and EBV serologies were negative. ASO, throat, blood and urine cultures, PPD test and Wright and 2ME were negative, too. The peripheral blood smear and clotting times were normal. Cryoglobuline test which was performed repeatedly was negative. Henoch-Schönlein purpura was suspected; therefore, we measured serum IgA immunoglobulin. It was 68 mg/dl and in the normal range (68-320 mg/dl). The light microscopic exam of the skin biopsy showed leukocytoclastic vasculitis (Figure 1). immunofluorescent microscopic examination for IgA band was negative and mostly C3 and IgG precipitation were reported.ESR^{1h} was 40 mm/h and CRP was 20 mg/dl. All investigations for probable malignancies were negative. Thyroid function tests were normal. After three weeks she got better; so it was scheduled to taper the oral prednisolone steadily.

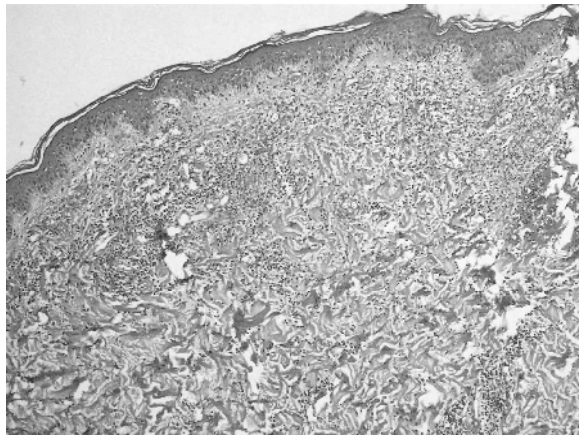

Figure 1. X100 the skin biopsy of anterior leg showed leukocytoclastic vasculitis

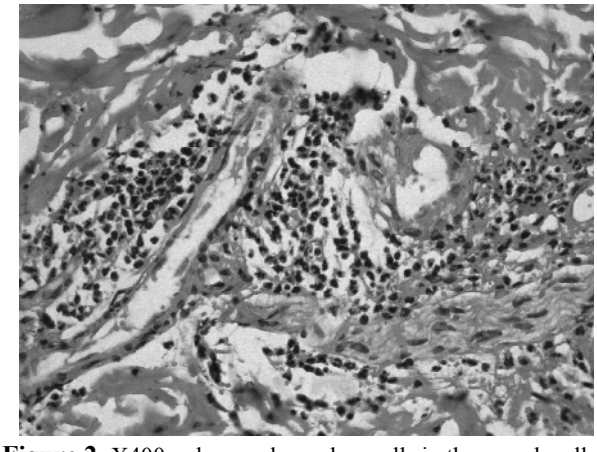

Figure 2. X400 poly morphonuclear cells in the vessel walls

Discussion

Methocarbamol belongs to skeletal muscle relaxants, a heterogeneous group of medications commonly used to treat two different types of underlying conditions: spasticity from the upper motor neuron syndrome and common musculoskeletal conditions causing tenderness and muscle spasms (2).This drug's adverse reactions frequency not defined, but some side effects have been reported with Methocarbamol prescription, like flushing, bradycardia, hypotension, syncope, drowsiness, dizziness, lightheadedness, convulsion, vertigo, headache, fever, amnesia, confusion, insomnia, sedation, coordination impaired (mild), allergic dermatitis, urticaria, pruritus, rash, angioneurotic edema, nausea, vomiting, metallic taste, dyspepsia, leukopenia, jaundice, nystagmus, blurred vision, diplopia, conjunctivitis, renal impairment , nasal congestion and local reactions such as thrombophlebitis (3). Drug eruptions may occur as a result of different immunological mechanisms: Ig-E dependent or type I

drug reaction: urticaria and anaphylaxis, in this type, dilation and increased permeability of small blood vessels results to hypotension, bronchiolar spasm, and in severe cases shock and anaphylactic reaction, it can happen during a few minutes to hours or days like penicillin shock. Antibody- mediated drug reactions are type II, these are based on binding antibodies to cell surfaces which; lead to complement mediated cytolysis, like thrombocytopenia or hemolytic anemia after some drugs. Immune complex dependent ; type III, drug reactions are in four categories, Urticaria and anaphylaxis, Serum sickness, Vasculitis and Arthus reaction. This mechanism plays a part in the pathogenesis of coetaneous necrotizing vasculitis. Deposition of immune complexes on vascular endothelium results in activation of the complement cascade, with generation of anaphylatoxins with chemotactic properties. Platelets, neutrophils, basophils and must cells all play role in this reaction, like penicillin and hydralazine induced vasculitis. It may happen after a long period of drug administration for the first time or after some hours of drug using in a patient with previous exposure to drug (1,4,5). Some authors have found that this kind of vasculitis is associated with laboratory markers like ANCA (against several neutrophil antigens simultaneously) and antiphospholipid antibodies; which can help for distinguishing the drug induced vasculitis from idiopathic types (6). The last one is cell-mediated or type IV: some fixed drug eruptions, lichenoid reactions, Stevens-Johnson syndrome and TEN, involve T-lymphocyte responses to altered self (1).

Drug-induced vasculitis is a poorly defined disorder since proving causality is frequently difficult. Some authors currently favor a classification of all suspected cases of drug-induced vasculitis by the following characteristics: The precipitating agent, the involved organs (eg, isolated to the skin, gastrointestinal tract) and the pathologic description, Also there are virtually no reliable findings that prove vasculitis results directly from a particular exposure (7). Clinical presentation varies in severity from mild to severe and even fatal illness, can be self-limiting, or follows a more chronic protracted course. There is difficult to distinguish idiopathic from drug induced vasculitis. However, it is extremely important to identify the offending drug because the discontinuation of the drug is often followed by improvement of the underlying vasculitic disorder (8). Taken together, immediate onset of symptoms and signs after receiving Methocarbamol in this case, with a history of previous drug exposure. Negative results for any other risk factor or clue to other kinds of vasculitis, despite a wide investigation. Skin biopsy, revealed leukocytoclastic vasculitis without thrombosis and IgA precipitation, makes it reasonable to attribute the symptoms to Methocarbamol. In this case symptoms didn't relive simply with conservative treatment therefore it was impossible to rechallenge Methocarbamol to prove causality. In our opinion, for this patient it is important to be aware about using this medication again. In conclusion, according to this case, it is likely appropriate to consider Methocarbamol as a potential cause of vasculitis in our further practice.

Acknowledgment

We are grateful to this patient for her kind participation.

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