

# Sodium Valproate Induced Leucocytoclastic Vasculitis: A Case Report

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## ÖZET:

Sodyum valproat'ın indüklediği lökositoklastik vaskülit: Olgu sunumu

Sodyum valproat bipolar bozukluk, şizoaffektif bozukluk, şizofreni ve diğer psikiyatrik bozukluklarla ilişkili davranış problemlerini kontrol etmek için psikiyatri hastalarında yaygın olarak kullanılmaktadır. Sodyum valproat'a bağlı ilaç yan etkisi olarak, lökositoklastik vaskülit (LCV) nadir olarak bildirilmiştir. LCV'nin patojenik mekanizması bilinmemekte olup hücre aracılı ve humoral immünite birlikte önemli rol oynuyor gibi görünmektedir. İlaça bağlı vaskülit, vaskülitin idyopatik formu ile benzer klinik ve serolojik/patolojik özellikler göstermektedir, kesin tanı için şüpheyle yaklaşım gereklidir.

Bu olguda psikiyatrik bozuklukların uzun dönem tedavisinde önemli bir yeri olan duygudurum dengeleyicilerden sodyum valproat'ın LCV'e yol açabileceği gösterilmiştir. Bizim düşüncemize göre, vaskülit neden olabilen ilaçlar listesine sodyum valproat da eklenmelidir.

**Anahtar sözcükler:** Sodyum valproat, lökositoklastik vaskülit, ilacın indüklediği vaskülit

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## ABSTRACT:

Sodium valproate induced leucocytoclastic vasculitis: a case report

Sodium valproate is commonly used in psychiatric patients to control behavioral disturbances associated with schizophrenia, bipolar disorder, schizoaffective disorder, and other psychiatric disorders. Leukocytoclastic vasculitis is an infrequently reported adverse drug reaction associated with sodium valproate. Its exact pathogenic mechanism is unknown, but both cell-mediated and humoral immunity appear to play important roles. Drug-induced vasculitis has an identical clinical presentation and identical serologic/pathologic parameters to idiopathic forms of vasculitis, hence a high index of suspicion is necessary to ascertain its accurate diagnosis.

The present case has demonstrated that sodium valproate, which is one of the most important mood stabilizers for long-term treatment of psychiatric disorders, may lead to leukocytoclastic vasculitis. In our opinion, sodium valproate should be added to the list of drugs that can induce vasculitis.

**Key words:** Sodium valproate, leukocytoclastic vasculitis, drug induced vasculitis

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## INTRODUCTION

Leukocytoclastic vasculitis (LCV) is primarily a chronic cutaneous small vessel vasculitis, though systemic involvement may be encountered. LCV is a process believed to be related to the presence of circulating immune complexes (1). The main clinical lesions of LCV are purpuric papules, although other clinical findings secondary to ischemia, including ulceration, may occur (2). An estimated 20-30% of all vasculitis cases are attributed to drug administration (2-4). Skin reactions associated with sodium valproate (SV) are an uncommon occurrence (5,6). In patients with biopsy proven LCV, 24% had drug exposure within a week of presentation (7). Hypersensitivity

vasculitis due to drugs can be identified on the basis of five defining characteristics: (1) age>16 years, (2) use of a possible offending drug in temporal relation to the symptoms, (3) palpable purpura, (4) maculo-papular rash, and (5) biopsy of the skin showing neutrophils around an arteriole or venule (8). We present a patient, who developed LCV associated with the administration of SV.

## CASE REPORT

A case of LCV associated with sodium valproate administration in a woman is reported here. A 39-year-old married Turkish woman, accompanied by her husband, presented to our psychiatry outpatient department. She had

been in treatment intermittently since 1991 for schizophrenia, undifferentiated type. She had taken risperidone (4 mg/day) for the last five years. Socially she reported smoking two packs of cigarettes per day, but she had no history of alcohol or any other illicit substance abuse. Also, she had no history of allergic reaction or vasculitis.

Over the previous three to four months, she had suffered from new complaints including impulsive behaviors, aggression, and second person auditory hallucinations. Twenty days prior to the current admission to our clinic, she was admitted to a hospital in another city. Her psychiatrist there added SV to her treatment regimen and the daily dosage was increased to 1500 mg for aggressive symptoms. After that, the patient and her husband came to visit their relatives living in Ankara.

On admission to our psychiatry clinic, her valproic acid level was in the normal range (88.0 mg/Lt). Apparently, the persisting symptoms of psychosis were causing partial restless. However, there was a significant reduction in the impulsive behaviors. Her husband stated that, the patient had been complaining of severe itching and rash on the abdominal area and bilaterally on her legs for 15-20 days before admission to our clinic. The appearance of the rash was getting worse, even days later than the onset of her symptoms. On the other hand, the patient and her husband denied any psychiatric hospitalizations. In our clinic, the risperidone dose was increased to 6 mg/day and biperiden (4 mg/day) was added for the persisting symptoms of psychosis. The patient was referred to a dermatologist on the same day. The evaluation notes, revealed violaceous purpuric patches and macules that were palpable, distributed on both legs and abdomen. The initial differential diagnosis included Rocky Mountain spotted fever, Churg-Strauss syndrome, microscopic polyarthritis, mixed cryoglobulinemia, and Henoch-Schönlein purpura. According to the notes, the laboratory studies were within normal limits. At follow-up, a skin biopsy was performed and the histopathological examination demonstrated that there was destruction of the vessel wall in multiple layers in the upper dermis what appeared to be fibrin and large collections of neutrophils. On physical examination the findings were unremarkable. Her popliteal, posterior tibial, and dorsalis pedis pulses were palpable. Based on these findings, LCV was diagnosed by the dermatologist. Subsequently, the SV was discontinued and bed rest was prescribed. The course of the disease was

favorable. In the following seven days, her cutaneous findings partially resolved. Complete recovery was noted seventeen days after discontinuation of SV. Due to continued psychotic symptoms and partially impulsive behaviors, quetiapine fumarate was administered instead of SV, with the belief that it might help to reduce her symptoms.

In the subsequent week, while on quetiapine fumarate 100 mg twice a day, some clinical improvement was observed. Repeated interviews confirmed that the patient had no further episodes of skin rash during the following four weeks.

## DISCUSSION

In addition to quetiapine fumarate's antipsychotic properties, its broad mood stabilizing potential may uniquely benefit the management of some patients who can tolerate this agent (9,10,15). Based on these data, quetiapine fumarate was administered instead of SV. After that no cutaneous findings were reported.

Risperidone, as an atypical antipsychotic drug, is widely used in the treatment of psychoses associated with schizophrenia (11,12). Our patient had taken risperidone (4 mg/day) for the last five years. However, no allergic reaction or vasculitis history were reported during this time.

As in our study, SV is suggested to be used in schizophrenic patients who have accompanying symptoms of impulsive behaviours (13,14). Co-administration with risperidone may increase the levels of SV in the blood (11,15). This could lead to increased risk of side effects from SV (11,14,15). However, in this case, the level of drug was in the normal range.

In the literature, only a few cases of LCV induced by SV have been reported (5,6,16). LCV can be treated either by the use of drugs such as anti-inflammatory medications or as in the present case, by removing the trigger agent (3,4,7,12,15). Our case developed a rash between the seventh and tenth days of SV administration. After the diagnosis, treatment with SV was discontinued and bed rest was prescribed. Following initiation of this treatment, a rapid improvement of the cutaneous lesions was achieved.

Lastly, the diagnosis of SV induced LCV was made, because our patient's age was >16 years old, she had recent medication adjustments and she showed isolated skin involvement (7,8). We suggest that clinicians should be aware of the risk of LCV in association with SV.

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