

A rapid favorable outcome after sofosbuvir induced leucocytoclastic vasculitis.

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Abstract

Background: Sofosbuvir, a very effective new direct-acting antiviral agent (DAA), has revolutionized the therapeutic management of people infected with hepatitis C virus. It has a low reported rate of side effects. Leucocytoclastic vasculitis can be associated with hepatitis C but can also be induced by many drugs. We describe a case of leucocytoclastic vasculitis induced by Sofosbuvir that resolved 3 days after drug withdrawal. We observed a temporal relationship between the treatment and the onset of vasculitis. We emphasize the multidisciplinary approach to patients with hepatitis C to make the difference between drug-induced skin damage and damage caused by the virus itself. Case presentation: A 61-year-old woman, with a history of hepatitis C virus infection started treatment with the combination ledipasvir sofosbuvir in June 2020, 400 mg per day. Five weeks later, she developed a slightly itchy erythematous and symmetrical rash on lower members. The patient initially suspected the treatment and she stopped it. Histological finding revealed a diffuse neutrophile infiltration of vessel walls confirming leukocytoclastic vasculitis. These lesions disappeared completely three days after drug withdrawal without any symptomatic treatment. Conclusions: Sofosbuvir is one of the several recent drugs that should be prone to further attention.

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Abstract:

Background: Sofosbuvir, a very effective new direct-acting antiviral agent (DAA), has revolutionized the therapeutic management of people infected with hepatitis C virus. It has a low reported rate of side effects. Leucocytoclastic vasculitis can be associated with hepatitis C but can also be induced by many drugs. We describe a case of leucocytoclastic vasculitis induced by Sofosbuvir that resolved 3 days after drug withdrawal. We observed a temporal relationship between the treatment and the onset of vasculitis. We emphasize the multidisciplinary approach to patients with hepatitis C to make the difference between drug-induced skin damage and damage caused by the virus itself.

Case presentation: A 61-year-old woman, with a history of hepatitis C virus infection started treatment with the combination ledipasvir sofosbuvir in June 2020. Five weeks later, she developed a slightly itchy erythematous and symmetrical rash on lower members. The patient initially suspected the treatment and she stopped it. Histological finding revealed a leucocytoclastic vasculitis. These lesions disappeared completely three days after drug withdrawal without any symptomatic treatment.

Conclusions: Sofosbuvir is one of the several recent drugs that should be prone to further attention.

Keywords: Sofosbuvir, Hepatitis C, Leucocytoclastic vasculitis

Introduction:

Sofosbuvir is a non-structural protein 5B RNA-dependent RNA polymerase inhibitor engineered for the treatment of chronic hepatitis C virus (HCV) whose efficacy was established in subjects with HCV genotype 1, 2, 3 or 4 infections, including those with hepatocellular insufficiency and with human immunodeficiency virus-1 co-infection (1). It is generally well tolerated. Reported adverse events in sofosbuvir's monograph are usually not serious such as headache, nausea, insomnia, itching, weakness, decreased appetite, chills, flu-like illness, joint pain, and irritability. Vasculitis was rarely associated with sofosbuvir(2).

We report an exceptional case of a minor leucocytoclastic vasculitis with a rapid favorable outcome after the drug withdrawal.

Case report

A 61-year-old woman, with no medical history, was diagnosed with viral hepatitis C and started treatment with the combination ledipasvir sofosbuvir in June 2020, 400 mg per day.

Five weeks after starting the treatment, she developed a slightly itchy erythematous rash on lower members. The patient initially suspected the treatment and she stopped it.

Physical examination revealed purpuric lesions with confluent erythematous macules at the lower third of the thighs reaching the knees. Lesions were symmetrical. Skin biopsy was performed. Histological finding revealed a diffuse neutrophile infiltration of vessel walls confirming leucocytoclastic vasculitis.

Lesions disappeared completely three days after drug withdrawal without any symptomatic treatment.

Discussion:

The assessment of causality was evaluated with the Naranjo adverse drug reaction probability scale(3). In this case the adverse event has a score of 5 and was classified as possible in front of the evocative delay, the favorable outcome after sofosbuvir withdrawal and the data of skin biopsy.

Leucocytoclastic vasculitis is a cutaneous small-vessel necrotizing vasculitis. The main symptom is a vascular purpura. It can be infiltrated, non-pruritic, petechial or papular and rarely necrotic. More rarely, the skin involvement may correspond to supra malleolar ulcers, Raynaud's syndrome or urticarial vasculitis (4). Skin biopsy shows lesions of leucocytoclastic vasculitis involving small-calibre vessels with a mixed inflammatory infiltrate.

This condition can be idiopathic or associated with infections, neoplasms, autoimmune disorders, and drugs. Cutaneous manifestations generally resolve when the causal agent is eliminated.

Drug induced vasculitis was reported with penicillins, macrolides, nonsteroidal anti-inflammatory drugs, gabapentin and tumor necrosis factor inhibitors(5–8)

Sofosbuvir induced vasculitis was reported for the first time in 2015 in association with dalatasavir (9). A prospective cohort study of 3,000 patients taking sofosbuvir and ribavirin, showed that this drug association induced 85 cases of ANCA-associated vasculitis (10). In a French study of drug-associated ANCA vasculitis including 483 patients, sofosbuvir was the responsible drug in 46 cases (2).

One case of non-ANCA associated sofosbuvir-induced vasculitis was published in 2019. In this case, symptoms appeared one month after the beginning of the treatment. Skin lesions disappeared one month after the drug withdrawal (11). In our case, the patient recovered rapidly in only 2 days after stopping sofosbuvir without any symptomatic treatment. This was the main evidence that the condition was drug induced.

The responsibility of ledipasvir was evaluated as less likely in front of the lack of bibliographic data describing this side effect.

Although the efficacy and safety of sofosbuvir in patients with HCV has been amply proven in clinical trials, a specific prescriber attention to this drug is needed.

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