# Drug induced vasculitis , Thiazide or COVID-vaccine ? : A case report and literature review

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**Abstract**

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Abstract

A middle-aged woman with history of the administration of COVID-19 vaccine and valve replacement surgery before her symptoms, was admitted with bilateral palpable purpuric lesions in the lower extremities and headache . Based on the initial diagnosis of vasculitis , corticosteroid therapy was initiated and resolved the skin lesion .

keywords : vasculitis, warfarin , COVID-19 vaccines ,thiazides

Key clinical message : Drug induced vasculitis should be considered in the setting of vasculitis after the initiation of a new medication or the administration of COVID vaccines.

Introduction

Drug induced vasculitis (DIV) can be presented with a broad spectrum of clinical signs and symptoms . As an inflammatory process in blood vessels , it may affect different organs with localized or systemic manifestations . Initial diagnosis should be made after the exclusion of infectious diseases ( especially parasitic infections

), autoimmune collagen vascular diseases and different related neoplasms (1, 2). Here ,we present a case of drug induced vasculitis with a specific initial presentation and course .

Case Presentation

A 55 year-old woman was admitted with progressive palpable purpura in both lower extremities and pruritus without systemic symptoms such as arthralgia or myalgia (Figure 1). Her symptoms had been initiated 3 days before admission and some of her lesions were hemorrhagic. Concomitantly , she had complained of a vague headache during the days prior to being hospitalized. She had a history of mitral and aortic valve replacement (mechanical valve) 1 week prior and injection of a COVID-19 vaccine (Sinopharm BIBP COVID-19 vaccine) 3 weeks prior to the onset of symptoms and hypothyroidism. She was discharged after cardiac surgery with warfarin , hydrochlorthiazide (HCTZ) ( 25 mg once daily ) , propranolol , levothyroxine and pantoprazole

On admission, she was completely alert with stable vital signs (blood pressure =120/75mmHg , pulse rate= 80 /minute , respiratory rate =14 per minute without fever .Laboratory tests revealed creatinine =1.4 mg/dl , total bilirubin=1.6mg/ dl , direct bilirubin =0.2 mg/ dl , white blood cells=7300/cm3 , International normalized ratio (INR) =3.7 ,negative serology and polymerase chain reaction (PCR) for COVID-19 infection , qualitative C-reactive protein (CRP) =2+ and thyroid stimulating hormone (TSH) = 16.4 mIU/ml . All the rheumatologic tests, including antinuclear antibody (ANA) , Antineutrophil cytoplasmic antibodies (ANCA) , Rheumatoid factor (RF), Anti RO , anti double stranded DNA (anti ds DNA) , Anti-CCPs (cyclic interlineated peptides) were negative and complement levels were normal.

Echocardiography demonstrated normal biventricular size and function with a large pericardial effusion (about 30 mm) posterior to the left ventricle without a compressive effect . A spiral brain computed tomography ( CT) scan was performed, which showed evidence of acute and subacute foci of subdural hematoma adjacent to the left temporal lobe .

As a result , we had to transiently hold the administration of the anticoagulant regimen until the next CT scans confirmed the stabilization of the hemorrhagic area without expansion (48 hours and 5 days later).

Rheumatology and dermatology consultations were requested and the initiation of corticosteroid therapy was recommended based on the diagnosis of vasculitis . The patient refused to undergo skin biopsy and methylprenosiolone 1 gr/ day was initiated based on the clinical scenario, which led to rapid improvement of the lesions (Figure 2 ) .Oral prednisolone was continued and tapered over the next 2 months and colchicin 1 mg /d was initiated and continued for 2 months . The patient did not show any complications and the next brain CT showed elimination of the hemorrhagic focus . She received a second dose of sinopharm 2 months after the first dose without complications and underwent drainage of a massive pericardial effusion 3 months later .

Discussion

Leukocytoklastic vasculitis (small vessel vasculitis with neutrophil infiltration ) due to different medications has been reported to be the cause of 1/3 of cases of cutaneous vasculitis (1, 3-5) . Drug induced vasculitis (DIV ) can involve different size vessels but is less established in large vessels, such as the aorta. Although not very prevalent , concomitant involvement of cerebral vasculature has also been reported (4). The diagnosis of DIV should be made by exclusion of other probable causes as it is mentioned before (1) .

Although warfarin has been considered to be the potential cause of vasculitis (6, 7) , we were not able to discontinue it in our patient due to the necessity of its administration following mechanical valve replacement . Absence of the recurrence of the symptoms after the discontinuation of corticosteroids made it less likely to consider warfarin as the probable cause of vasculitis because based on previous reports , and contrary to our study, clinical symptoms have relapsed in most cases after reinitiating warfarin (3) . Another potential cause for the occurrence of vasculitis is the use of thiazides, which has been known for many years (1) .Although our patient received a low dose of hydrochlorthiazide (HCTZ) (25mg once daily ), drug induced vasculitis due to HCTZ could not be ruled out . Finally, we were curious whether the administration of COVID vaccines

could result in vasculitis .Although there have recently been some reports about the use of mRNA based COVID vaccines as a cause of leukocytoclastic vasculitis (8-12) , the role of inactivated whole virus vaccines such as Sinopharm , Sinovac (CoronaVac) and COVAXIN (Bharat Biotech) should not be overlooked (13-15) .

By discontinuing thiazides and receiving an immunosuppressive regimen , the patient showed significant improvement and all the lesions disappeared early after the initiation of corticosteroids . Hemorrhagic stroke responded well to this treatment and resolved gradually .She was admitted three months later for the drainage of a massive pericardial effusion without any complications.

Conclusion :

Irrespective of low prevalence , drug induced vasculitis should be considered in the presence of vasculitis of unknown origin .Recently ,multiple cases of COVID vaccine induced vasculitis have been reported, which necessitates further evaluation for the diagnosis of the underlying cause.

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Authors contributions :

SJ , MH : Data gathering, Editing the text

ZA , S D : Editing the text

SD , ZA : Writing the text

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Written informed consent was obtained from the patient who participated in this study. This case report did not receive any funding. Authors had access to all source data for this case report.

Data availability statement :

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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