



Clinical case

Drug-induced cutaneous-systemic vasculitis: about a Malagasy case

Vascularite cutané-systémique d'origine médicamenteuse : à propos d'un cas malgache

H Ramanandafy*¹, RH Raharinoro¹, SL Ramily², FA Sendrasoa², T Ratovonjanahary², MI Rahantamalala¹,
LS Ramarozatovo², HMD Vololontiana¹, FR Rapelanoro²

Abstract

Drug-induced cutaneous vasculitis is a relatively rare condition. A 34-year-old man presented a purpuric lesion, petechial, infiltrated, and extensive with superficial necrosis, localized in the trunk and lower limbs developing in a febrile context. In his history, we noted taking amoxicillin four days before the onset of signs; he is a carrier of trigeminal neuralgia on carbamazepine since December 2020. The biological examination showed a normal platelet count, an increase in transaminases and the presence of proteinuria three crosses on the urine test strip. The diagnosis of drug-induced cutaneous-systemic vasculitis was made according to the criteria of the American College of Rheumatology, by the absence of thrombocytopenia supported by remission without sequelae of the lesions within ten days after stopping the causative drug.

Keywords: amoxicillin, purpura, drug, remission.

Résumé

La vascularite cutanée médicamenteuse est une affection relativement rare. Un homme de 34 ans présentait une lésion purpurique, pétéchielle, infiltrée et étendue avec nécrose superficielle, localisée

au niveau du tronc et des membres inférieurs évoluant dans un contexte fébrile. On notait dans ses antécédents, la prise d'amoxicilline quatre jours avant l'apparition des signes ; il est porteur d'une névralgie du trijumeau sous carbamazépine depuis décembre 2020. L'examen biologique montrait un taux de plaquettes normales, une augmentation des transaminases et la présence de protéinurie trois croix à la bandelette urinaire. Le diagnostic de vascularite cutanée-systémique médicamenteuse a été posé selon les critères de l'American College of Rheumatology et par l'absence d'une thrombocytopénie appuyée par une rémission sans séquelle des lésions dans les dix jours suivant l'arrêt du médicament en cause.

Mots-clés : amoxicilline, médicament, purpura, rémission.

Introduction

Cutaneous vasculitis is an inflammatory disease of small-caliber vessels in the dermis resulting in purpura, infiltrated, predominantly on the declining parts. It is a relatively rare entity and difficult to diagnose due to the absence of pathognomonic clinical signs.

Their incidence is estimated between 15.4 and 29.7 cases per million inhabitants [1]. The drug etiology accounts for 10 to 24% of cutaneous vasculitis [2]. The diagnosis of Drug-induced cutaneous-systemic vasculitis aided by the histological data is essentially clinical. We report a specific case of drug-induced cutaneous vasculitis which differs in its rarity and in its ocular and oral damage.

Clinical case

A 34-year-old man was hospitalized in the department of dermatology for treatment of trunk purpura. The history of his disease began five days before his admission with eye redness followed by the appearance of red macules beginning in the lower limbs then extension to the trunk, slightly itchy evolving in an unquantified febrile context, without notion of arthralgia or abdominal pain. In his history, we noted the intake of amoxicillin four days before the onset of skin signs; he had been on carbamazepine since December 2020 for trigeminal neuralgia. He is neither ethyl nor tobacco. On admission, he was feverish at 38 C °, with Glasgow 15/15 and blood pressure 110 / 80mmHg. On dermatological examination, we objected a purpuric skin lesion of the vascular type, petechial, infiltrated, extensive, and non-confluent, with superficial necrosis, of the same age, localized in the trunk (Figure 1) and lower limbs. He also presented a dried bilateral conjunctivitis and ulceration of the lips (Figure 2). The other physical exams were unremarkable. The Biology showed mild neutropenia at 1200 / mm³, platelets at 158G / L and hemoglobins at 11.7g / dl on the blood count. The C-reactive protein was elevated to 90mg / L. The renal assessment was normal with a serum creatinine of 92 μmol / L. The liver function tests were disturbed with an aspartate aminotransferase elevated to 140U / L and an alanine aminotransferase elevated to 153U / L. The hemostasis assessment was normal (prothrombin time = 15.5 s, prothrombin level = 97%). The SARS-Cov 2 RT-PCR was negative. The urine dipstick showed three crosses proteinuria, without hematuria

or leukocyturia. The immunosuppression virus (HIV) and hepatitis (HBV, HCV) serologies were also negative. The streptococcus rapid diagnostic test was negative. The purpuric lesion biopsy was not done for financial reasons. The diagnosis of drug-induced vasculitis is evoked by the presence of three out of five criteria from the American College of Rheumatology namely, age 29 years, taking amoxicillin, palpable and infiltrated vascular purpura supported by the absence of thrombocytopenia on the blood count and on the one hand by the scar-free regression of the lesions in ten days after stopping the suspected drugs according to the working group. The drug re-administration test was also not performed.



Figure 1: Infiltrated petechial purpura of similar age with slight superficial necrosis



Figure 2: Lip ulceration and bilateral dry conjunctivitis

Table I: Diagnostic criteria according to the American College of Rheumatology

• Age > 16 years old at the onset of the disease
• Triggering drug intake
• Palpable purpura
• Maculopapular rash in relief
• Presence of polynuclear neutrophils around an arteriole or a venule on biopsy

The diagnosis of drug-induced vasculitis is suggested if at least three criteria are present with a sensitivity of 71% and a specificity of 83.9%.

Table II: chronological accountability criteria according to the working group in cases suspected drug-induced vasculitis

1. Time of occurrence symptoms	<ul style="list-style-type: none"> • Very suggestive if between 7 to 21 days • Compatible if < to 7 days or > to 21 days • Reintroduction: all deadlines are compatible
2. Drug elimination half-life in the absence of symptomatic treatment.	<ul style="list-style-type: none"> • Suggestive if there is a further absence of absence in less than 3 weeks • Not suggestive if new outbreak
3. Readministration	<ul style="list-style-type: none"> • Positive if recurrence within < to 3 weeks. • Negative if no recurrence

Discussion

Drug-induced cutaneous vasculitis, formerly called hypersensitivity angiitis by Ms. Zeek in 1940, is defined as damage to small vessels in the dermis [3]. It is distinguished from other types of vasculitis by its acute course, hypersensitivity to a drug allergen and by the harmless remission within a few weeks of lesions upon discontinuation of the causal drug. In Madagascar, this clinical entity is less described. To our knowledge, no study, no case, nor series of cases have been reported. A few cases have been identified in Maghrebian Africa due to 1.3 new cases per year [4]. During this affection, the drug acts as a

haptent and binds with antibodies forming circulating immune complexes deposited on the wall of vessels which, after activation of the complement pathway, will be destroyed by polynuclear neutrophils [5]. In the absence of a skin biopsy, the diagnosis is based on the criteria of the American College of Rheumatology (Table I) [6], on the criteria of imputability of the working group (Table II) [7] and on the absence of thrombocytopenic purpura. According to this working group, compared to our case, the delay in onset of symptoms in four days is compatible and on the other hand, the absence of new outbreaks in ten days after stopping the suspicious drug is suggestive of a drug etiology (amoxicillin). The diagnosis of drug-induced vasculitis with anticytoplasmicneutrophilic antibodies was ruled out in our case by its longer time to remission [5]. Infectious causes were also ruled out. Rheumatoid purpura could be mentioned, but the chronology of drug intake, the regression of signs without sequelae on discontinuation of the drug and the absence of abdominal pain made the diagnosis of drug-induced vasculitis probable. The integration of anamnestic, clinical, and biological elements generally allows an early diagnosis of drug-induced vasculitis in order to initiate the appropriate treatment and prevent a systemic extension that could constitute an element of poor prognosis. Clinical manifestations of drug-induced vasculitis occur within two days to ten years after medication with an average of three weeks [8] in the form of a symmetrical infiltrated purpura, more or less necrotic, preferentially affecting the sloping areas of the lower limbs. It can also affect the upper limbs, neck and trunk. This sign is suggestive of cutaneous vasculitis in the absence of histological evidence. The mucous membranes are rarely affected [9] with ocular and oral involvement in our case. Multivisceral manifestations are possible and sometimes with a poor prognosis [10], such as renal (three crosses proteinuria) and hepatic impairment in our patient. Stopping the suspected drug is the first measure to take, allowing clinical recovery within a few weeks [11].

Conclusion

Drug-induced cutaneous vasculitis is rare. Its diagnosis is often complex due to the absence of pathognomonic signs. The American College of Rheumatology criteria and working group accountability in the absence of thrombocytopenia comfort the diagnosis in the absence of histological evidence. Only stopping the drug in question allows remission without sequelae.

Acknowledgements

The authors thank the patient who gave written permission for this report.

Authors Contributions

All authors have contributed to the development of this manuscript and have approved the final version.

Ethical approval

The article does not contain any personal information that could identify the patient. The authors have included only information necessary for scientific understanding.

*Correspondence

Ramanandafy Herveat

heriveat@gmail.com

Available online : Januar 4, 2022

1 : Department of Internal Medicine, University Hospital of Joseph Raseta Befelatanana, Antananarivo, Madagascar

2 : Department of Dermatology, University Hospital of Joseph Raseta Befelatanana, Antananarivo, Madagascar

© Journal of african clinical cases and reviews 2022

Conflict of interest : None

References

[1] Carlson JA, Ng BT, Chen KR. Cutaneous vasculitis

update: diagnostic criteria, classification, epidemiology, etiology, pathogenesis, evaluation and prognosis. *Am J Dermatopathol.* 2005 Dec; 27(6): 504–28.

[2] Gibson LE. Cutaneous vasculitis update. *Dermatol Clin* 2001; 19: 603–15.

[3] Zeek PM. Periarteritis Nodosa: a critical review. *Am J Clin Pathol.* 1952; 22(8): 777–90.

[4] Fathallah N et al, Vascularites médicamenteuses : à propos d'une série de 13 cas. *Therapie.* 2018 ; 8 :1-8. <https://doi.org/10.1016/j.therap.2018.07.005>

[5] Francès C, Kluger N, Doutre MS. Vasculites cutanées et cutané-systémiques. *EMC Dermatol.* 2011; 6(3): 1–19.

[6] Calabrese LH, Michel BA, Bloch DA, Arend WP, Edworthy SM, Fauci AS, et al. The American College of Rheumatology 1990 criteria for the classification of hypersensitivity vasculitis. *Arthritis Rheum.* 1990; 33(8):1108–13.

[7] Guillaume JC, Roujeau JC, Chevrant-Breton J et al. Comment imputer un accident cutané à un médicament. Application aux purpuras vasculaires. *Ann Dermatol Venerol.* 1987; 114(5): 721–4.

[8] Cuellar ML. Drug-induced vasculitis. *Curr Rheumatol Rep.* 2002; 4: 55–9.

[9] Taborda L, Amaral B, Isenberg D. Drug-induced vasculitis. *Adverse Drug React Bull.* 2013 Apr; 279(1): 1075–8.

[10] Dubost JJ, Tournadre A, Sauvezie B. Vascularites médicamenteuses. *Rev Rhum.* 2002; 69: 370–5.

[11] Ten Holder SM, Joy MS, Falk RJ. Cutaneous and systemic manifestations of drug induced vasculitis. *Ann Pharmacother.* 2002 Jan; 36(1): 130–47.

To cite this article :

H Ramanandafy, RH Raharinoro, SL Ramily, FA Sendrasoa, T Ratovonjanahary, MI Rahantamalala et al. Drug-induced cutaneous-systemic vasculitis: about a Malagasy case. *Jaccr Africa* 2022; 6(1): 8-11