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CASE REPORT

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Myalgia-induced discovery of rhabdomyolysis complicating generalized varicella in an immunocompetent patient: Case report and review of the literature

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Key clinical message

In a rare occurrence, primary varicella infection led to rhabdomyolysis in a 24-year-old with no medical history. Presenting with rash, fever, and weakness, he developed diffuse myalgia at 72 h. Elevated muscle enzymes confirmed rhabdomyolysis secondary to varicella zoster virus (VZV) infection. Treatment with acyclovir and hydration resulted in significant improvement within a month.

Abstract

Primary varicella infection is rarely complicated by rhabdomyolysis. In this study, we describe a case of rhabdomyolysis complicating a VZV infection in a black subject. The patient was a 24-year-old black African with no particular medical history and was immunocompetent. He presented with an acute onset of generalized rash, fever, and generalized weakness. Physical examination revealed vesicular lesions typical of chickenpox. Antipyretic treatment combined with acyclovir was instituted in hospital. At the 72nd hour, diffuse myalgia developed. Muscle enzyme tests revealed CPK elevated to 40 times the upper limit of normal, LDH elevated to 2 times the upper limit of normal, ASAT and ALAT elevated to 7 times the upper limit of normal, and 2.5 times the upper limit of normal, respectively. We accepted the diagnosis of rhabdomyolysis secondary to VZV infection. The patient was given saline hydration and showed clinical and biological improvement 1 month later. A patient presenting with muscular symptoms during a VZV infection should be considered for rhabdomyolysis.

KEYWORDS

case report, creatinine phosphokinase, myalgia, rhabdomyolysis, varicella zoster virus

1 | INTRODUCTION

The occurrence of primary varicella rarely leads to complications in children, whereas these complications are the preserve of adults.[1] The most common complications are septic shock, encephalitis, pneumonia, toxic shock syndrome, purpura fulminans and, rarely, rhabdomyolysis.[2] Rhabdomyolysis is breakdown wall of skeletal muscle encountered in a wide variety of clinical situations, including viral diseases.[3] However, the viruses most commonly involved are influenza, coxsackie and herpes viruses, and rarely varicella zoster virus (VZV) infection.[4] We report a case of rhabdomyolysis in an immunocompetent adult hospitalized for primary varicella.

2 | CASE REPORT

2.1 | Case history

The patient was a 24-year-old male student, immunocompetent, and with no particular medical history. He was admitted to the department with a pruritic generalized cutaneous rash that had been evolving for 4 days in a fever and influenza-like symptoms with no history of myoglobinuria or arthromyalgia. He had not been involved in any intense physical activity prior to the onset of the symptoms. The lesions began on the back and pelvic limbs before spreading rapidly to the trunk, thoracic limbs, and face.

2.2 | Examination

On examination, the patient's general condition was preserved and hemodynamic were normal. Examination of the skin and skin appendages revealed polymorphous eruptions consisting of clear vesicles of varying ages, with umbilicated vesicles in places, all resting on an erythematous background affecting the anterior and posterior surfaces (Figure 1) of the trunk, pelvic and thoracic limbs, and perineum. These lesions spared the palms of the hands, the feet, and the scalp. The oral mucosa was also affected, with ruptured vesicular lesions of the enanthema type (Figure 2), and the appearance of the skin was normal. Cardiorespiratory and neurological examinations were normal. The laboratory work-up was unremarkable. This clinical picture led to the diagnosis of varicella. On admission, the patient was treated with acyclovir 500 mg daily, oral antipyretics and a daily infusion of 500 mL of saline. He also received daily cleansing with antiseptic soap, mouthwash with Saint Louis solution and application of aqueous eosin to the lesions. The evolution was marked 3 days later by the appearance of diffuse myalgia involving the proximal and distal muscles with a VAS

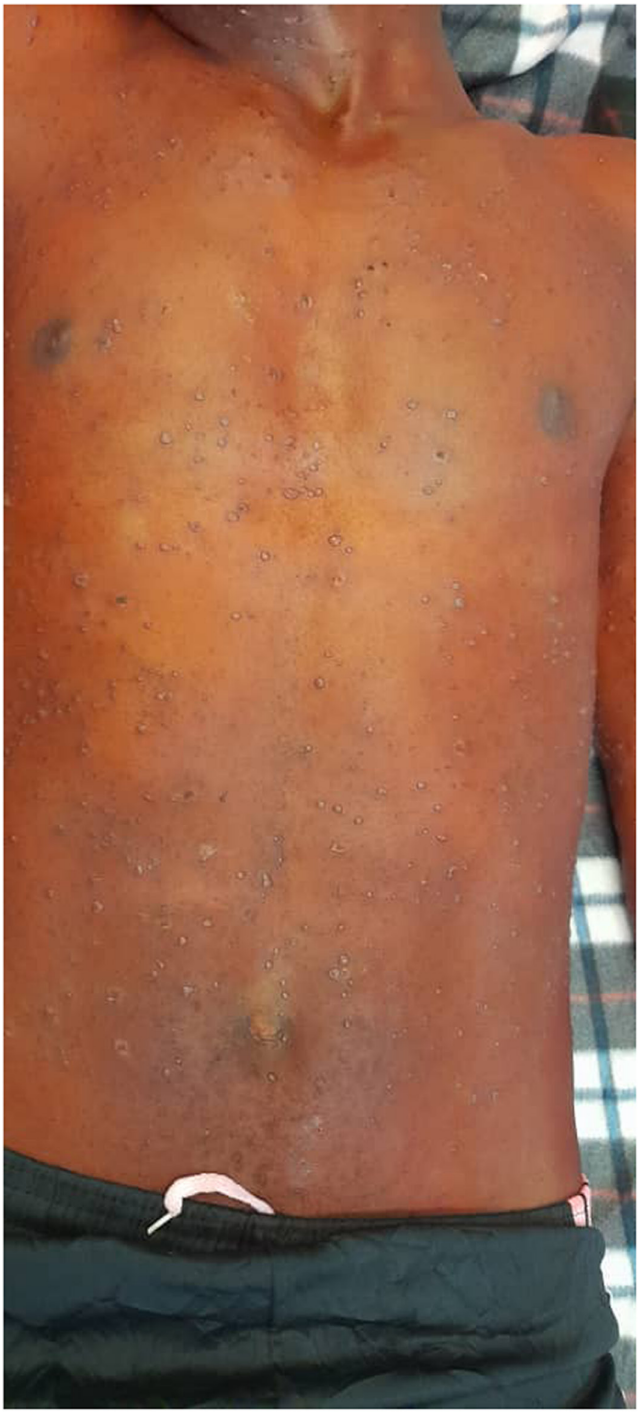

FIGURE 1 Vesicular lesions on the trunk.

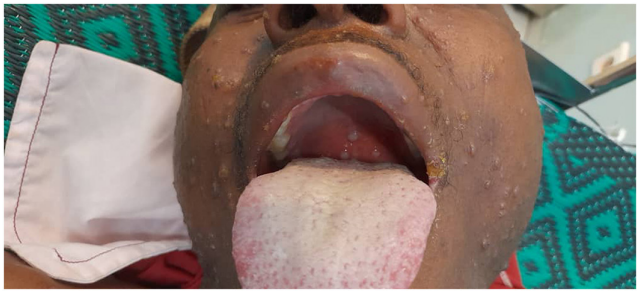

FIGURE 2 Enanthema on the buccal mucosa.

(Visual Analogue Scale.) of 7 out of 10 without any notion of myoglobinuria.

2.3 | Investigation

A laboratory work-up revealed rhabdomyolysis, with total creatinine phosphokinase (CPK) elevated to 7850 U/L (40 times the upper limit of normal) and lactodehydrogenase (LDH) elevated to 803 IU/L (2 times the upper limit of normal), creatinine normal at 62 µmol/L ($N = 88–105$ µmol/L), aspartate aminotransferase (ASAT) at 202 IU/L (7 times the upper limit of normal), and alanine aminotransferase (ALAT) at 81 IU/L (2.5 times the upper limit of normal). The rest of the laboratory work-up was unremarkable.

2.4 | Diagnosis

We make the diagnosis of rhabdomyolysis complicating a VZV infection.

2.5 | Treatment

The same treatment was continued, with a combination of injectable tramadol and venous hydration with 2 l of isotonic saline per day for 7 days, before the patient was discharged home after 10 days in hospitalization.

2.6 | Outcomes

One-month follow-up showed a clinical and biological improvement, with disappearance of lesions and normalization of rhabdomyolysis enzymes (Table 1).

3 | DISCUSSION

The first description of rhabdomyolysis complicating a viral infection was described by Favera et al in 1967 and concerned a case of coxsackie virus.[5] Rhabdomyolysis occurring during varicella was described in 1994 by Pratt et al.[6] To date, only around 10 cases have been described in the literature.

We searched for articles on PUBMED using the keywords "Varicella" and "rhabdomyolysis" alone and in combination. This literature review enabled us to identify 12 cases from 10 referenced English-language articles (Table 2). These articles are similar in several respects to the case we are describing. No similar cases were found in the French-language literature referenced. One very similar case was found in the unreferenced French literature, as were 2 cases in the unreferenced English literature.[7-9] The reported cases, including our own, were mainly young adults with a mean age of 24.8 years. The youngest patient, aged 4.5 years, was reported by Karadag et al., and males were the most represented, with 11 out of 13 cases. These cases mainly concern Caucasian subjects and to our knowledge our case is the first described in subSaharan Africa.

Although rhabdomyolysis due to primary VZV infection is considered rare, it may be under-diagnosed because CPK levels are not routinely measured in patients with chickenpox. Mild to moderate cases of rhabdomyolysis could therefore go undetected in the absence of symptoms or suggestive signs such as abnormal urine color, muscle weakness, or myalgia.

The suspicion of rhabdomyolysis in our patient arose from the myalgias that occurred during hospitalization. Other causes of rhabdomyolysis were ruled out in view of our patient's presentation, namely inflammatory myopathy, toxic, and metabolic etiologies. An infectious cause was the most likely, with our patient's primary varicella infection diagnosed clinically.

Rhabdomyolysis with subsequent myoglobinuria is a well-known cause of ARF. It has also been associated with metabolic acidosis, dehydration, and hypotension.[9,10] In our patient, there was no evidence of myoglobinuria or impaired renal function. This could be explained by the fact that the patient was hydrated with isotonic saline from the start of hospitalization. There is also no data in the literature correlating the extent of VZV lesions with the occurrence of rhabdomyolysis.

In the literature, rhabdomyolysis has led to fatal complications in some patients. These often include

TABLE 1 Biological results of rhabdomyolysis enzymes at Day 3, Day 10, and Day 30.

Date	Day 3	Day 10	Day 30
CPK (U/L)	7850	552	202
ASAT (UI/L)	202	83	43
ALT (IU/L)	81	58	36
LDH (UI/L)	803	507	185
Blood myoglobin (g/L)	–	160	72

TABLE 2 Characteristics of patients with rhabdomyolysis due to VZV infection reported in the literature.

N°	Authors	Year	Age/gender	Pick of CPK (U/L)	Symptom on admission	ARF	Others complications
1	Pratt[6]	1994	15/M	418,240	Dark discoloration of urine and asthenia	No	Myoglobinuria
2	Pratt[6]	1994	22/M	84,000	Fever, headache, pruritus, and rash	No	No
3	Roberts[20]	1995	16/M	1,977,600	Fatigue, nausea, vomiting, and anorexia	Yes	Myoglobinuria
4	Will[18]	1996	25/M	297,000	Myalgia, arthralgia, and dark urine discoloration	–	No
5	Holleinstein[17]	1998	30/F	874	Fever and rash	–	Myoglobinuria
6	Pirounaki[16]	2007	27/M	1899	Headache, fever, skin hyperesthesia, eye pain, nausea, vomiting, and myalgia	Yes	Méningoencéphalitis
7	Ahamed[11]	2008	22/F	–	Fever, rash, and back pain	No	DIC, Varicella pneumonia, varicella hepatitis
8	Beby-Defaux[12]	2009	28/M	1079	Abdominal pain, back pain, and rashes	Yes	DIC, Varicella pneumonia, ascites, varicella encephalitis
9	Karadag	2012	4.5/M	35,981	–	–	Purpura fulminans, hepatitis
10	Kim[19]	2012	38/M	2947	Asthenia	–	Meningoencephalitis
11	Martinez-Martinez[21]	2013	29/M	11,480	Rrashing, pruritus, fever, anorexia, and asthenia	Yes	No
12	Brahim[7]	2022	42/M	50,364	Skin lesions, fever, and myalgia	Yes	No
13	Bayala	2024	24/M	7850	Rash, pruritus, asthenia, fever, and arthromyalgia	No	No

Abbreviations: ARF, acute renal failure; DIC, disseminated intravascular coagulation.

complications such as renal failure, disseminated intravascular coagulation, hyperkalemia, and even multivisceral failure.[11,12] Other complications may be linked specifically to the location of the VZV and not as a direct consequence of the rhabdomyolysis. Some patients have developed meningoencephalitis or varicella pneumonia.[11-13]

The incidence of AKI in rhabdomyolysis is not known, but it is estimated that between 33% and 40% of patients with rhabdomyolysis develop AKI.[14] Attempts to identify patients at highest risk of AKI have revealed that no single laboratory value, including serum CPK concentrations, can predict which patients are at risk of developing AKI.[15] Nor is myoglobinuria at the time of admission predictive of increased risk of AKI.[14] But also the nephrotoxicity of acyclovir, which is introduced to treat VZV infection, may precipitate renal failure.[16] Furthermore, studies have found that VZV infection can lead to ARF due to acute glomerulonephritis, in addition to that caused by rhabdomyolysis.

As a pathophysiological explanation, the suggested causes of rhabdomyolysis in viral diseases are linked to immune-mediated toxicity or direct viral invasion of the muscles.[17] The immune system can also induce harmful cytokines with efflux of myoglobin from the muscles by the mechanism of cell lysis, causing rhabdomyolysis.[18]

VZV DNA can be detected during the acute phase, and viremia usually decreases early in the acyclovir treatment phase. It becomes undetectable 14 days after the onset of chickenpox.[19] In our patient, neither the VZV antigen test nor the viral load test was performed, as the diagnosis of varicella was clinically obvious in our patient.

The principles of treatment are aimed at managing the etiology, and acyclovir was indicated in our patient as in the cases in our review hydration with isotonic saline also ensures good renal elimination in order to prevent the often fatal complications of rhabdomyolysis.

4 | CONCLUSION

This observation reminds us of the importance of carrying out a muscular assessment in patients presenting with warning signs in the context of an infection in general and chickenpox in particular. Although rare, rhabdomyolysis must be diagnosed as early as possible to avoid complications that are often fatal. The frequency of rhabdomyolysis is probably underestimated, especially in the African context.

AUTHOR CONTRIBUTIONS

Yannick Laurent Tchenadoyo Bayala: Conceptualization; resources; supervision; validation; writing – original draft; writing – review and editing. **Ismael Ayouba Tinni:** Visualization; writing – original draft; writing – review and editing. **Patricia Ouedraogo:** Data curation; formal analysis; funding acquisition; software. **Aboubakar OUEDRAOGO:** Software; supervision. **Awa Traore:** Validation. **Marcellin Bonkoungou:** Validation. **Joëlle Wendlassida Stéphanie Zabsonre/Tiendrebeogo:** Validation. **Dieu-Donné Ouedraogo:** Supervision.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONSENT

We have obtained the patient's consent for publication. Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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