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Case report

Cerebral venous sinus thrombosis accompanied by cerebral venous infarction and multiorgan dysfunction after wasp stings, A case report

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ABSTRACT

Introduction: The high incidence of wasp stings have been causing a variety of injuries in China, but systemic complications are rarely reported.

Case presentation: A 59-year-old man was severely attacked by wasps. He developed an acute onset of right hemiplegia and chest distress and was admitted to our emergency department 13 hours after being attacked. Various abnormal signals were found by biochemical tests. Magnetic resonance venography of head demonstrated that the superior sagittal sinus was not visible, indicating cerebral venous sinus thrombosis. Magnetic resonance imaging showed abnormal signals in the left frontal lobe, parietal lobe, and thalamus, indicating venous cerebral infarction and hemorrhage, coupled with subarachnoid hemorrhage. The patient was diagnosed with a rare combination of cerebral venous sinus thrombosis, cerebral venous infarction, and multi-organ dysfunction following hornet stings. After undergoing systematic treatment including blood perfusion, blood dialysis, anti-inflammatory hormone therapy, antiallergic medication, antibiotic use, and anticoagulation treatment, the patient showed significant improvement in limb muscle strength and dizziness symptoms. However, the patient developed irreversible kidney damage and is currently dependent on renal replacement therapy.

Conclusions: This case highlights the serious systemic consequences that can occur following multiple wasp stings, including rare complications such as venous sinus thrombosis leading to cerebral infarction and renal failure. Early intervention with blood perfusion, hemodialysis, and plasmapheresis, in addition to general treatment, may help prevent permanent organ damage in patients with a large number of wasp stings.

1. Introduction

Hymenoptera is one of the largest orders of insects and its representatives include wasps, ants, and bees [1]. Wasp stings often occur

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in rural areas and cause mild allergic reactions without any major problems, while fatal systemic reactions including multiple organ dysfunction are rare [2]. Serious wasp stings are frequently reported in various countries, including China, India, Vietnam, Thailand, and Malaysia [1,2]. It usually manifests as local reactions such as edema, urticaria and erythema with localized pain. However, systemic reactions are rare which usually caused by IgE-mediated type 1 anaphylaxis. Additionally, the simultaneous occurrences of these complications is rarely reported, which can result in devastating consequences. In this report, we present the case of a 59-year-old male who experienced cerebral venous sinus thrombosis (CVST) resulting in cerebral venous infarction (CVI), as well as multi-organ dysfunction after a hornet sting.

2. Case presentation

A 59-year-old man arrived at our emergency department 13 hours after being severely attacked by wasps. He was initially admitted to the nearest hospital after suffering multiple hornet stings, complaining of redness, swelling, and pain all over the body including his head, face, and neck (Fig. 1). The patient was treated with initial medications such as chlorpheneramine and hydrocortisone injection at the local hospital, he remained stable for the next 8–10 hours. Afterwards, the patient developed an acute onset of right hemiplegia and chest distress, and was then transferred to our hospital. The patient reported no history of fever, cough, breathlessness, trauma, abnormal body movement, drug intake, or hypertension.

Initial examination revealed a white blood cell range of 39.55 $\times$ 10^9 g/L (normal range: 3.5–9.5 $\times$ 10^9/L), a neutrophile of 92.5 % (normal range: 40–75 %), and a hemoglobin level of 169 g/L (normal range: 130–175 g/L). Routine urinalysis showed elevated levels of troponin T level at 0.433 ng/mL (normal range: 0–0.045 ng/mL) and myoglobin level >3000 ng/mL (normal range: 28–72 ng/mL). Other biochemical tests displayed abnormal results including blood urea nitrogen at 16.58 mmol/L (normal range: 2.3–7.6 mmol/L), creatinine at 304.50 μmol/L (normal range: 53–123 μmol/L), aspartate aminotransferase at 1353.60 U/L (normal range: 9–50 U/L), alanine aminotransferase at 840.9 U/L (normal range: 15–40 U/L), serum total bilirubin at 65.3 μmol/L (normal range: 5.1–19.0 μmol/L), direct bilirubin at 31.7 μmol/L (normal range: 0–6.8 μmol/L), indirect bilirubin at 33.6 μmol/L (normal range: 3.4–14.0 μmol/L), lactate dehydrogenase at 1992.0 U/L (normal range: 109–245 U/L), creative kinase MB at 1356.3 U/L (normal range: 0–24 U/L), and creatine kinase at 69552.0 U/L (normal range: 18–198 U/L). However, the electrolytes and blood lipid, as well as electrocardiograph, chest X-ray, and echocardiography were normal. Coagulation tests revealed antithrombin activity at 50 %, and prothrombin time and activated partial thromboplastin time were normal. Tests for other causes of hereditary thrombosis, such as serum homocysteine, protein C, protein S levels, factor V Leiden mutation, anti-PF4-autoantibodies, and antiphospholipid antibodies (anti-nuclear antibodies and lipid profile) were also within normal limits.

Upon admission, magnetic resonance imaging (MRI) of the head and magnetic resonance venography (MRV) were performed. MRV demonstrated that the superior sagittal sinus was not visible, indicating CVST (Fig. 2). MRI showed abnormal signals in the left frontal lobe, parietal lobe, and thalamus, indicating venous cerebral infarction and hemorrhage, coupled with subarachnoid hemorrhage (Fig. 3A–E). The patient subsequently received the following treatments, including hemoperfusion, hemodialysis, systemic antibiotics, anticoagulants and anti-inflammatory (methylprednisolone 80 mg per day intravenously for 10 days, with the dose gradually reducing after the condition improved). After fifteen days of treatment, the patient's right-sided strength improved significantly and he began to move the right upper and lower limbs, but the kidney function was not recovered.

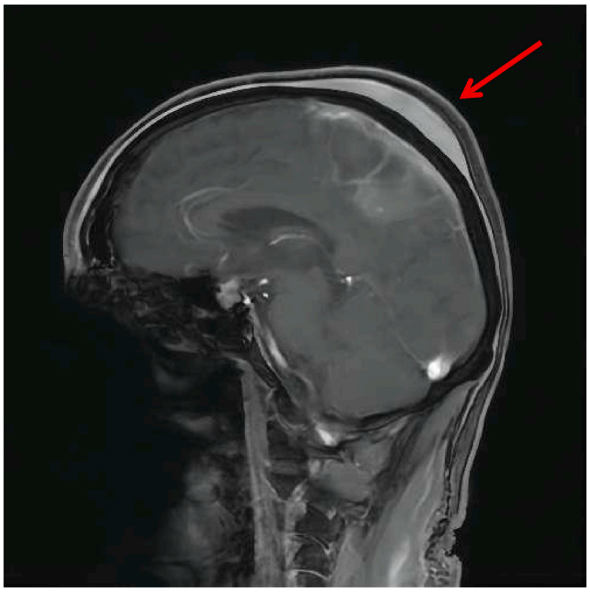

Fig. 1. Magnetic resonance imaging showed huge swelling in the head.

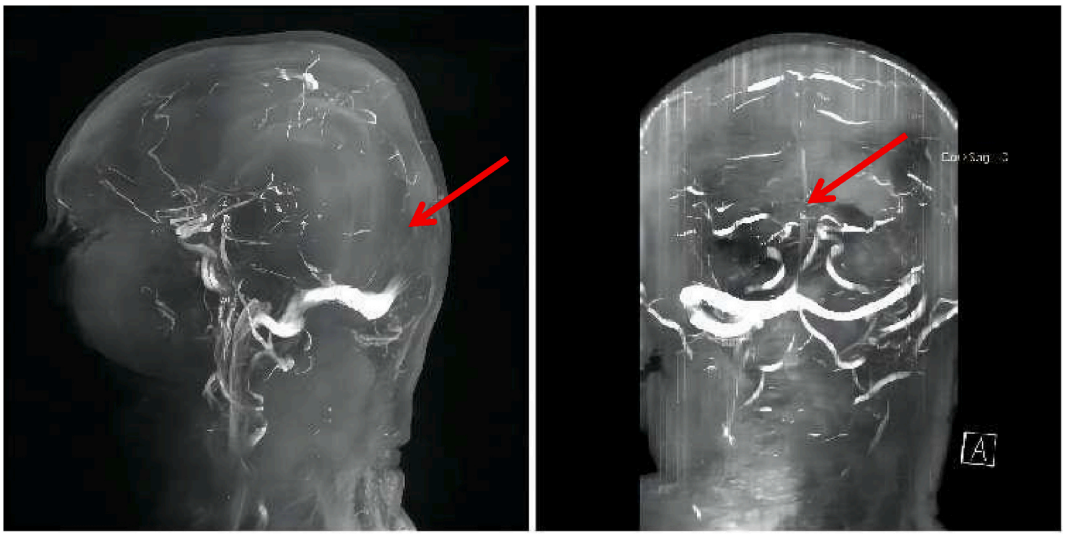

Fig. 2. Brain magnetic resonance venography scans demonstrated the loss of signal in the superior sagittal sinus, representing venous sinus thrombosis.

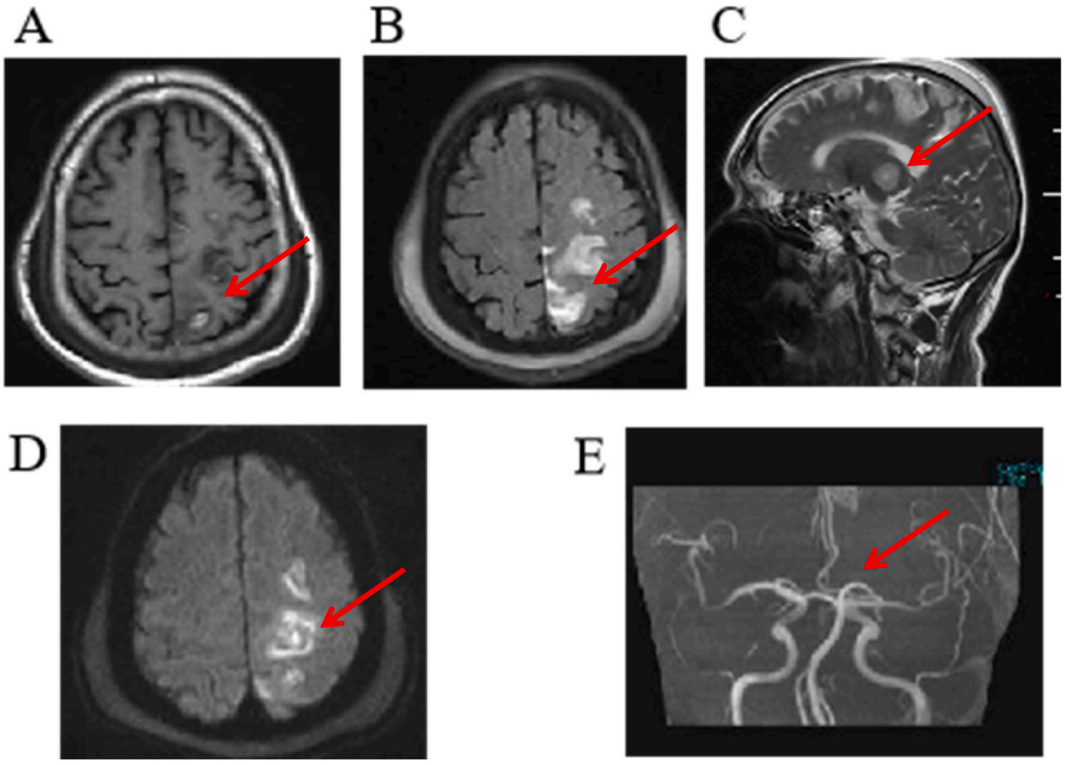

Fig. 3. Magnetic resonance imaging showed abnormal signal on the left frontal, parietal and thalamus on T1-Flair(A),T2-Flair(B), T2-Flair sagittal (C), DWI(D) and generally normal on MRA(E), which indicated venous cerebral infarction and hemorrhage, coupled with subarachnoid hemorrhage.

One day before discharge, the patient's blood tests showed improvements, with the white blood cell count decreasing to 12.0×10^9 g/L. The troponin T level decreased to 0.047 ng/mL and the myoglobin level decreased to >125 ng/mL. Additionally, the levels of aspartate aminotransferase, alanine aminotransferase, creatine kinase MB, creatine kinase, and creatinine all decreased (78 U/L, 56 U/L, 68 U/L, 231 U/L, and 621 μmol/L, respectively). The serum total bilirubin level remained within the normal range. The patient was subsequently transferred to a regional medical center for further treatment. This patient's headaches and dizziness improved after receiving a combination of anticoagulation and hemodialysis, but he is currently on maintenance hemodialysis due to irreversible

renal impairment. Clinical follow-up is ongoing.

3. Discussion

There is an increasing body of evidence that wasp stings occur frequently in rural areas of China, and are a serious public health problem due to the presence of lethal toxic elements in wasp venom [3,4]. Wasp venoms contain three major classes of molecules, including proteins, small peptides with different functions, and low molecular weight substances [3]. These venoms are able to trigger local immune and allergic reactions that can lead to severe morbidity and mortality. Active peptides (e.g. mastoparans, bradykinin-like peptides and chemotactic peptides) could cause the local reactions, including pain, swelling and fulminant reactions, which can last for hours and days. Additionally, venom allergens, such as phospholipase A (A1 and A2), hyaluronidase, cysteine-rich secretory proteins, antigen 5 and pathogenesis-related proteins (CAP), and serine proteases, are responsible for immunological reactions. Moreover, polysaccharides can induce allergic reactions, mainly in the form of systemic toxic reactions such as renal failure, hepatitis, aortic thrombosis, hemolysis, coagulopathy, rhabdomyolysis, and cerebral infarction [5].

In our case, the patient was a 59-year-old man who experienced multiple wasp stings. He developed not only local reactions (pain and wheal around the body), but also presented with immunological and allergic reactions that resulted in multiple organ dysfunction, including kidney, liver, and heart. More serious and rare were the emergence of CVST and CVI.

CVST is a rare complication of wasp sting, with an approximately 3–4 cases per 1 million adults per year [6]. It can cause severe but treatable neurologic impairment, accounting for about 1%–2% of all the strokes in adults [7]. The common clinical presentations of CVST are headache, papilledema, seizures, focal neurological deficits, and altered consciousness [8]. Early diagnosis and comprehensive screening of acquired or inherited risk factors are of great importance for decreasing morbidity and mortality. Risk factors for CVST include hereditary prothrombotic tendencies (including factor V Leiden mutation, protein S and C deficiency), antithrombin III deficiencies, the use of contraceptives, pregnancy, infection, dysthyroidism, malignancy and cranial trauma [9]. According a retrospective research [10], the involved cerebral venous sinus in our case was the superior sagittal sinus, followed by the transverse and sigmoid sinuses.

The patient in our case did not have any of the aforementioned risk factors for CVST [11–13]. He was a male who had not used oral contraceptives, had no history of malignancy or dysthyroidism, and had relatively normal results in the hypercoagulable state test upon admission. Therefore, it is unlikely that these common risk factors contributed to the development of CVST in our patient. Instead, the probable mechanism of CVST in our patient can be attributed to the consequences of hornet venom resulting from multiple wasp stings. Studies have identified various toxins in wasp venom, such as factor V activator, oscutarin-C, ryncolin-3/4, veficolin, coagulation factor, thrombin-like enzyme, and venom prothrombin activator, which are known to be involved in the blood coagulation cascade [14]. Vasoconstriction and platelet aggregation also play a role in the coagulation cascade. Furthermore, wasp venom contains allergen phospholipase A (A1 and A2), and antiphospholipid antibodies has been linked to acquired thrombophilia in previous studies [15]. Based on these findings, we hypothesize that the proteases and toxins present in bee venom, along with the allergen phospholipase A, act synergistically to cause endothelial damage to blood vessels. This damage can lead to vasculitis, thrombosis, and ultimately CVST. Additionally, the observed low activity of antithrombin III in our patient may also be associated with CVST and could potentially be caused by the wasp venom. Taking all these factors into account, it is plausible that the development of CVST following multiple wasp stings in our patient can be attributed to the aforementioned mechanisms.

CVI differs from arterial infarction because of the different anatomical and physiological features of the cerebral venous system. However, the underlying molecular mechanism of CVI remains elusive. Some data showed that about 50 % of CVST could contribute to CVI [16], suggesting that the relationship between CVST and CVI is crucial. Hemodynamic and metabolic alterations following cerebral vein occlusion have been described, including increased intracranial pressure and deterioration of brain tissue edema, as well as intracerebral veins hyperaemia [17]. We hypothesized that hypertension, venom-related inflammatory, cytotoxic brain edema, and neuronal damage are critical factors in CVI, particularly venom-induced CVST.

Other sporadically reported complications of sting injuries are organ dysfunction, including kidney, liver, and heart. Explaining the pathophysiology of renal failure after wasp stings is complex. In a patient who developed multi-organ dysfunction after a massive wasp sting, autopsy reports showed renal tubular epithelial cell degeneration and necrosis [18]. Wasp venom-induced renal insufficiency may be due to toxin related hemolysis and rhabdomyolysis, allergic reaction, shock and direct renal tubular necrosis [19,20]. In this case, the extremely high levels of the creatine kinase and myoglobin revealed the existence of rhabdomyolysis, which eventually leads to tubular necrosis. Thus we postulated that venom-induced rhabdomyolysis might be the primary reason for renal failure, although there was no evidence of renal biopsy in this case. In addition, the patient presented with both acute liver failure and myocardial necrosis, but the underlying pathogenesis was remained unclear. A previous study reported the autopsy of a female who developed multiple organ dysfunction syndrome and died after multiple wasp stings [18]. That reveals the presence of diffuse fatty degeneration and necrosis of liver cells, accompanied by edema, degeneration and necrosis of myocardial fibers, as well as myocardial interstitial edema. Therefore, we speculated that the toxic effects of the venom could be implicated in hepatocyte necrosis and myocardial necrosis.

4. Conclusions

In this case report, we present a 59-year-old male who experienced CVST resulting in CVI, as well as multi-organ dysfunction after a hornet sting. This case highlights the serious systemic consequences that can occur following multiple wasp stings. Early intervention with blood perfusion, hemodialysis, and plasmapheresis, in addition to general treatment, may help prevent permanent organ damage

in patients with a large number of wasp stings.

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Statement of informed consent obtained in writing

The patient materials involved in this study (Cerebral venous sinus thrombosis accompanied by cerebral venous infarction and multiorgan dysfunction after wasp stings) have received informed written consent from the patients and can be provided at any time upon request.

Consent for publication

Not applicable.

Data availability

Not applicable.

CRediT authorship contribution statement

Jun Zhang: Writing – review & editing, Writing – original draft. **Yuming Zhou:** Data curation. **Zhenzhou Zhong:** Data curation. **Xianghong Liu:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

CVST	cerebral venous sinus thrombosis
CVI	cerebral venous infarction
MRI	magnetic resonance imaging
MRV	magnetic resonance venography

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