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Short communication

# Purpura fulminans associated with acute West Nile virus encephalitis

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ABSTRACT

Purpura fulminans is a progressive thrombotic disorder that presents with widespread purpura due to deficiency or dysfunction of protein C or protein S. Lesions present as well-demarcated erythematous macules that progress to irregular areas of hemorrhagic necrosis.West Nile virus is a member of the Flaviviridae family transmitted to humans through the bite of various mosquito species. It manifests as West Nile fever in 25% of those infected and less commonly as neuroinvasive disease. An African American man in his fortiespresented with altered mental status and was noted to have evidence of disseminated intravascular coagulation according to his lab data. He then developed dusky skin discoloration and systemic flaccid bullae with desquamation. Biopsy was consistent with purpura fulminans and the patient eventually developed symmetric peripheral gangrene, requiring amputations of all four extremities. Infectious work up revealed positive testing for IgM and IgG antibodies in serum and cerebrospinal fluid leading to the diagnosis of acute West Nile Virus encephalitis. We present this case to describe the rarely reported association of purpura fulminans with West Nile Virus infection.



## 1. Why this case is important

Purpura fulminans (PF) is a medical emergency presenting with widespread purpura due to deficiency or dysfunction of protein C or protein S [1]. It is a rapidly progressive thrombotic disorder with a high initial mortality and long-term morbidity in survivors. PF lesions initially present as well-demarcated erythematous macules that progress to irregular areas of centralized blue–black hemorrhagic necrosis [2]. West Nile virus (WNV) is a member of the *Flaviviridae* family and is transmitted to humans through mosquito bites. It is considered endemic in all 48 contiguous United States [3]. WNV manifests as WNV fever in approximately 25% of those infected and less commonly, but more dangerously, as neuroinvasive disease [3]. An association with hemorrhagic fever and WNV is known to rarely occur in Africa, likely due to complications of underlying conditions and not due to a predominant WNV lineage [4]. We present this case to report the rare association of purpura fulminans with WNV infection so that it may be included in the differential diagnosis of patient presenting with these findings. Additionally, we raise awareness that its initial presentation may clinically mimic Stevens-Johnson syndrome (SJS).

## 2. Case description

A 42-year-old African–American male with past medical history significant for hypertension and diet-controlled diabetes mellitus presented with a two-day history of bloody diarrhea, anorexia, chills, and altered mental status. Family members contacted local emergency medical services due to the patient's deteriorating mental status; specifically the patient was found lying on his sofa unresponsive. The patient was intubated in the field for airway protection and transferred to a medical intensive care unit. Initial laboratory data revealed evidence of thrombocytopenia (platelet count = 59 × 10e9/L), high anion gap metabolic acidosis (sodium = 139 mEq/L, chloride = 107 mEq/L, bicarbonate = 10 mEq/L, lactic acid = 9.2 mmol/L), acute kidney injury (creatinine = 5.25 mg/dL) and acute liver failure (AST = 2706 units/L and ALT = 1103 units/L).

On further evaluation, he was found to have suffered a non-ST segment elevation myocardial infarction with severe cardiomyopathy and ejection fraction of 10%. Further laboratory data was consistent with disseminated intravascular coagulation (DIC) likely due to sepsis and he was started on broad-spectrum antibiotics. His overall picture was consistent with septic shock, multi-organ failure, and DIC. He was hypotensive and febrile with temperatures up to 104° Fahrenheit. Serial blood cultures, as well as urine and sputum cultures, all remained negative for any bacterial or fungal

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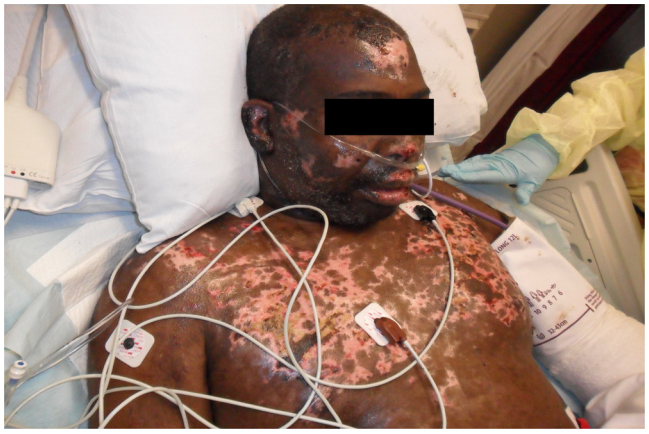

**Fig. 1.** Significant involvement of face and trunk with eroded plaques.

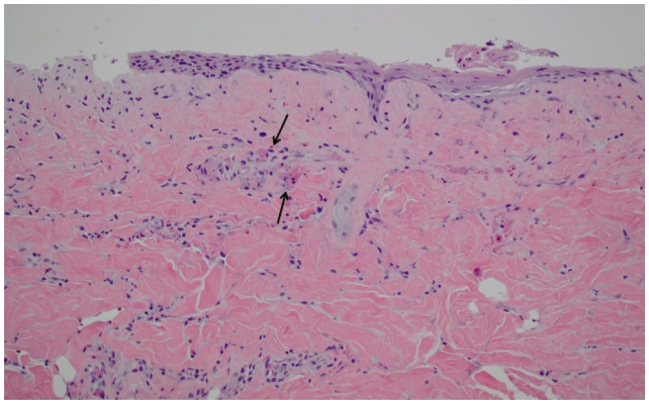

**Fig. 2.** 10× view depicting epidermal necrosis with ulceration and fibrin thrombi (arrows) in blood vessels.

pathogens. Per the family members present, the patient had had no recent travel.

On day 2 of hospital admission (4 days post symptom onset), the patient began to develop diffuse dusky skin discoloration and flaccid bullae formation with desquamation involving the anterior thighs, abdomen, upper extremities, scalp, and face (Fig. 1). He also had involvement of the oral mucosa with hemorrhagic desquamation. The ocular conjunctiva was uninvolved. Given that the patient had been initiated on broad-spectrum antibiotics on admission, the clinical picture was concerning for evolving SJS/toxic epidermal necrolysis. Histopathologic examination of skin revealed epidermal necrosis and fibrin thrombi in blood vessels consistent with a diagnosis of purpura fulminans (Figs. 2 and 3 ). Further infectious work-up revealed positive testing for IgM and IgG antibodies against WNV in the serum and cerebrospinal fluid (CSF) leading to a diagnosis of acute WNV encephalitis.

As part of his clinical presentation of PF, this patient had symmetric peripheral gangrene (Fig. 4). He eventually required amputations of all four extremities. Unfortunately, the patient developed multiple secondary infections in association with his gangrenous extremities. Six weeks after his initial presentation, blood cultures were positive for multiple species, including: *Enterococcus faecalis, Trichosporon* spp., *Candida albicans,* and *Bacteroides fragilis*. After four months of intensive hospital care, the patient's family opted to discontinue aggressive medical therapy and he expired shortly after being placed on hospice care.

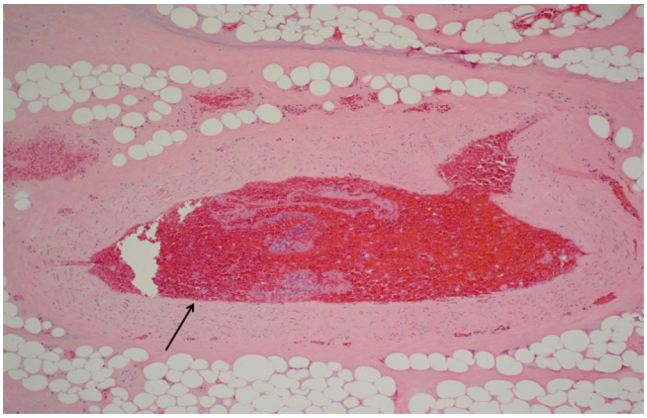

**Fig. 3.** 20× view of fibrin thrombus (arrow) in blood vessel in subcutis.

## 3. Other similar and contrasting cases in the literature

Thrombotic complications have rarely been reported in conjunction with WNV infection in African countries. While WNV lineage 2 is predominant in Africa, lineage 1 is more common in North America [5]. Recently, a case of hemorrhagic fever associated with WNV was documented in the Western hemisphere [4]. This case was diagnosed in the state of Florida whereas our case was in central Texas. Similar to the histopathological findings in PF, multiple occlusive fibrin thrombi in small vessels were found in this case of hemorrhagic fever [4].

## 4. Discussion

WNV fever is suspected to occur in 25% of people who are infected with WNV. Of these, less than 1% will develop neuroinvasive disease [1]. West Nile neuroencephalitis is diagnosed by the presence of anti-WNV IgM antibodies in the CSF as IgM antibodies do not cross the blood–brain barrier. This antibody will be present in the CSF within 8 days of symptom onset [3]. Other CSF findings include normal glucose, elevated protein, and pleocytosis. In acute settings, testing for IgG is not recommended, as it has no utility. In some cases, even WNV-specific IgM antibodies are not positive. In situations such as these, nucleic acid amplification testing (NAAT) can be used as an adjunct to serologic testing [3]. NAAT can also be used to aid in the diagnosis of immunocompromised patients [3].

Certain genetic factors are likely involved which predispose an individual for severe WNV disease. The *OAS1* gene modulates an individual's response to exogenous viral RNA. Genetic defects in the *OAS1* gene have been shown to increase susceptibility for severe WNV disease [3,4]. Defective chemokine receptor CCR5, present on monocytes and T lymphocytes, has also been shown to be a risk factor for symptomatic WNV infection. Individuals homozygous for this defective allele have been postulated to be at greater risk of death when compared with the general population [4].

Cutaneous findings in WNV fever are characteristically a morbilliform or maculopapular rash which is often seen at the time of fever resolution. This rash is non-pruritic and localized to the trunk and extremities with sparing of the palms and soles [3]. Skin manifestations are less commonly seen with the neuro-invasive disease [3].

Purpura fulminans clinically presents as extensive purpura most characteristically of the extremities but may involve any part of the body [1]. In our case, the initial clinical features were concerning for SJS given skin desquamation and mucosal involvement. A recent report reviewed a case of PF secondary to meningococcemia, which mimicked Stevens–Johnson syndrome. While PF typically presents with purpura, SJS presents with bullae and skin sloughing.