International Journal of Infectious Diseases 33 (2015) 196–198

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Acute generalized livedo racemosa caused by *Capnocytophaga canimorsus* identified by MALDI-TOF MS

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ARTICLE INFO

Article history:
Received 23 September 2014
Received in revised form 3 February 2015
Accepted 4 February 2015

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Septic shock
Capnocytophaga canimorsus
Livedo racemosa

SUMMARY

Independent of the size of the dog and the type of injury, serious infections may follow a dog bite and these may result in the abrupt onset of multiorgan failure. Early recognition of the warning signs with regard to the underlying severity of the infection is of the utmost importance. Reticulate skin eruptions constitute a precursory phenomenon.

1. Introduction

A wide variety of dermatological manifestations have been reported among the different infectious diseases. Dog-bite wounds account for almost 60% of bite wounds;[1] with these wounds there may be a localized eschar and cellulitis at the site of the bite, non-specific macular or maculopapular lesions, petechiae, purpura fulminans, and symmetrical peripheral gangrene.[2] In contrast, livedo racemosa is a prodromal and very specific skin lesion, mostly reported in association with antiphospholipid syndrome (APS) and systemic lupus erythematosus (SLE) with or without APS, and has very rarely been reported in infectious diseases.[3] Livedo racemosa is characterized by a striking violaceous net-like patterning of the skin and is similar to the familiar livedo reticularis from which it differs by its location (more generalized and widespread, non-infiltrated, found not only on the limbs but also on the trunk and/or buttocks), shape (irregular, broken, circular segments), and biopsy results.[3]

Livedo racemosa induced by sepsis is a rare, life-threatening manifestation. This clinical sign should be recognized promptly, so that early antibiotic treatment can be instituted. After an extensive literature review, we found only one case report of livedo racemosa skin lesions caused by a Capnocytophaga infection, which involved an immunocompromised adult patient. We emphasize the importance of this particular skin rash for the severity of the infection.

2. Case report

In April 2014, a previously healthy 57-year-old man was admitted to the intensive care unit of our tertiary care hospital because of a 1-day history of respiratory distress with severe tachypnoea, along with abdominal pain and nausea. Although the patient was in shock with renal and respiratory failure requiring haemodiafiltration, intubation, and mechanical ventilation, he was alert and well-oriented. There was no past medical or social history. On physical examination 28 h after symptom onset, the patient was febrile (39.5 °C), with a blood pressure of 77/50 mmHg and pulse rate of 120 beats per minute. The most striking physical sign was a generalized, purple–red skin discolouration, only partially blanchable, with a net-like formation resembling livedo reticularis; this had appeared 6 h before admission. It was mostly apparent on his earlobes, his abdomen, his buttocks, and his upper and lower extremities, with involvement of the palms of the hands and soles of the feet (Figure 1, A and B). The discolouration was persistent and not reversible with rewarming. Echocardiography revealed global hypokinesia requiring the administration of dobutamine. Two days before his admission the patient had sustained a Pekingese dog puncture wound to his right little finger. Resuscitative measures were attempted with crystalloids and vasopressors. He was immediately started on tazobactam/piperacillin and linezolid.

The patient's white blood cell count was 21.030×10^9/l, with 94% neutrophils and 6.0% lymphocytes. The haematocrit was

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http://dx.doi.org/10.1016/j.ijid.2015.02.008

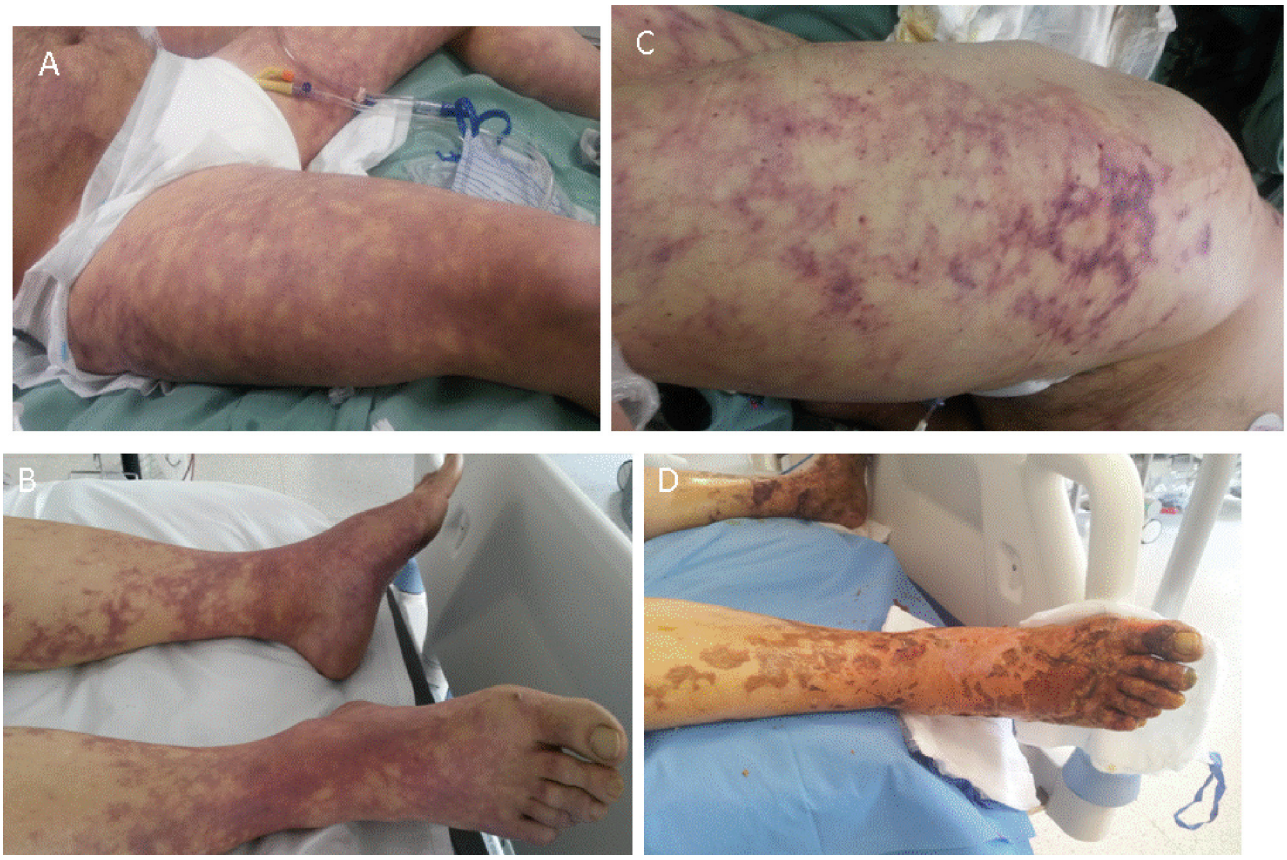

Figure 1. (A) Purple–red skin discolouration with net-like formation apparent on the patient's abdomen and buttocks, (B) his lower extremities, (C) thrombohaemorrhagic skin necrosis, and (D) desquamating of the lower leg.

34.0%. The platelet count was 18×10^9/l without schistocytes on peripheral blood smear. Liver function tests were initially normal. His creatinine level was 2.19 mg/dl and blood urea nitrogen 45 mg/dl, both of which deteriorated on a daily basis.

Soon after admission he developed disseminated intravascular coagulation (DIC), while his liver and renal function continued to worsen. Twenty-four hours after admission, his skin colour had changed to symmetrical reticulate purpura fulminans with ecchymosis (Figure 1C). Although necrotizing fasciitis with the hallmark of the preservation of the skin itself was initially considered, it was excluded because of the generalized patchy discolouration of the skin without pain, swelling, or crepitus. Based on the abrupt onset of the multiorgan failure and the generalized reticulate cutaneous lesions following a dog bite, fulminant Gram-negative sepsis due to *Capnocytophaga canimorsus* was suspected. The patient had no known risk factors associated with *C. canimorsus*,[4] and a history of hyposplenism or functional asplenia was excluded.

A blood culture on day 1 revealed a slow-growing unidentifiable Gram-negative microorganism. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) was applied to the colony specimen at another institution for definite identification. The unique molecular fingerprint of the organism identified it as *C. canimorsus*; antimicrobial susceptibility testing directly from the positive blood culture was not possible.

Fifteen days later his medical condition gradually improved. Desquamating of his skin lesions started to develop (Figure 1D), and cardiovascular, coagulation, and respiratory functions started to return to normal. Dynamic renal scanning using ^{99m}Tc-MAG-3 on day 62, demonstrated a delay in the accumulation of the radioisotope and an absence of isotope excretion into the collecting system consistent with poor renal function.

On day 28, the patient suffered acute gangrenous cholecystitis with fundus rupture and subsequently underwent a cholecystectomy; he had bilateral large-sized pleural effusions with left-sided exudative characteristics requiring chest tube placement and experienced episodes of hospital-acquired blood stream infection.

Although the patient had a complicated and long stay in the intensive care unit, he gradually became free of infection and was weaned completely from the ventilator, but continued maintenance haemodialysis. Dry gangrene developed at the site of the bite. He was eventually discharged to the floor in a perfect mental state. He has remained well during a follow-up period of 6 months.

3. Discussion

Severe sepsis caused by *C. canimorsus* is extremely rare and 60% of those who develop septic shock die within 30 days.[1] The skin appears to be an important early target organ affected by *C. canimorsus* infection, presenting reticulate skin eruptions.

Although *C. canimorsus* does not produce endotoxin, it is capable of triggering a cascade of events, such as inhibition of neutrophil motility and migration of the microorganism into the vascular space, subsequently resulting in DIC with severe multiorgan system failure.[1] It is possible that this vascular infiltration signals an underlying acute microvascular occlusive and/or inflammatory process that leads to the characteristic skin presentation – livedo racemosa – which is always a sign of an abnormal condition. Only rarely has livedo racemosa been reported in association with an infection, although it is possible

that because of its reminiscence to the appearance of livedo reticularis, livedo racemosa remains undetected.

Histological proof of the livedo racemosa was not confirmed in our patient due to the profound coagulation abnormalities during the first 7 days. Moreover skin biopsy specimens often fail to yield diagnostic arterial lesions. However, in our patient a biopsy was performed after the spontaneous rupture of the gall bladder. This biopsy revealed features of acute transmural inflammatory infiltration with extensive mucosal ulceration. This was probably a reflection of the ischemia caused by the multiple thromboses, on the basis of the livedo racemosa pathophysiology, resulting in the partial or complete narrowing of the cystic artery lumen (an end artery) that supplies the gallbladder with blood. This is the most appropriate explanation, since the ruptured gall bladder itself was a highly unexpected clinical situation for our patient, because there was no evidence of trauma, cholecystitis, or infection on admission. In the same context of endothelial injury as the initiating event, bilateral renal cortical necrosis developed.

Antiphospholipid syndrome associated with viral infections can present similar skin lesions. Catastrophic antiphospholipid syndrome was excluded in our patient. The history of recent dog bite in the context of the acute presentation of livedo racemosa prompted the diagnosis of an infectious origin as the cause.

Livedo racemosa as a very early sign of life-threatening overwhelming sepsis has only been reported recently in a patient with mild chronic obstructive pulmonary disease and alcohol abuse who finally died following bacteremia and purpura fulminans due to *C. canimorsus*.[5] Our patient had no known risk factors related to this microorganism and he was not otherwise immunosuppressed. Interestingly both cases had some common clinical and laboratory findings. The generalized violet skin lesions in our patient and in the clinical case published by Chiappa et al.[5], preceded the storm of profound renal, cardiac, liver, and hemodynamic disturbance, by about 22 h and 23 h, respectively.

Capnocytophaga can cause life-threatening overwhelming sepsis even in an immunocompetent adult patient. An indirect early clinical sign corresponding to the severity of the infection is the appearance of generalized livedo racemosa. It is an entity distinct from livedo reticularis, which is a net-like blanchable violet mottling of the skin that disappears with warming. Of note, some authors use livedo reticularis to refer to both entities. This underestimates the significance of the presentation of livedo racemosa, which usually includes a specific pathogenesis. Livedo racemosa usually precedes the purpura fulminans. Prompt initiation of antimicrobial treatment is absolutely necessary in the case of acute livedo racemosa signs associated with infection. *C. canimorsus* infection must be excluded. Apart from Capnocytophaga, other infections – meningococcal, staphylococcal, and pneumococcal – must be taken into consideration since early stage sepsis-associated livedo racemosa/purpura fulminans may be reversible with prompt therapeutic intervention.

Acknowledgements

The authors would like to thank Anna Psaroulaki (Laboratory of Public Health of Crete) for the identification of the microorganism using MALDI-TOF MS.

Conflict of interest: The author certifies no potential conflicts of interest.

References

1. Oehler RL, Velez AP, Mizrachi M, Lamarche J, Gompf S. Bite-related and septic syndromes caused by cats and dogs. *Lancet Infect Dis* 2009;**9**:439–47.
2. Kullberg BJ, Westendorp RJ, van't Wout JW, Meinders AE. Purpura fulminans and symmetrical peripheral gangrene caused by *Capnocytophaga canimorsus* (formerly DF-2) septicemia—a complication of dog bite. *Medicine (Baltimore)* 1991;**70**:287–92.
3. Kraemer M, Linden D, Berlit P. The spectrum of differential diagnosis in neurological patients with livedo reticularis and livedo racemosa. A literature review. *J Neurol* 2005;**252**:1155–66.
4. Zelger B, Sepp N, Schmid KW, Hintner H, Klein G, Fritsch PO. Life history of cutaneous vascular lesions in Sneddon's syndrome. *Hum Pathol* 1992;**23**:668–75.
5. Chiappa V, Chang CY, Sellas MI, Pierce VM, Kradin RL. Case records of the Massachusetts General Hospital. Case 10-2014. A 45-year-old man with a rash. *N Engl J Med* 2014;**370**:1238–48.