Group A *Escherichia coli*-related purpura fulminans: an unusual manifestation due to an unusual strain?

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Intended category: Case report
We report an exceptional case of life-threatening group A *Escherichia coli*-induced purpura fulminans. Genotyping of common polymorphisms in genes involved in innate immunity or coagulation did not reveal known susceptibility to such manifestation. Genetic analysis of the strain revealed an unusual Conserved Virulence Plasmidic region, pointing out its potential virulence.
Case report

A 53-year-old woman had a medical history of penicillin allergy and morbid obesity (Body Mass Index, BMI: 46 kg/m²) treated by a Banding Gastroplasty in 2007. In 2009, she suffered from a gastric necrosis complicated by a peritonitis associated with a first episode of *E. coli* bacteraemia. At that time, she presented a septic shock without disseminated intravascular coagulation (DIC). She underwent a total gastrectomy with oeso-jejunal anastomosis. Following gastrectomy, her BMI decreased dramatically to 16 kg/m².

In May 2013, she presented at the emergency department with weakness. Her central body temperature was 38.6°C, heart rate: 144 beats/min and blood pressure 85/52 mmHg. Physical exam did not point to a particular site of infection. Thoraco-abdominal CT scan did not show an infectious process. Laboratory results showed evidence of severe sepsis: C-reactive protein 113 mg/L, leukocyte count 1.8x10⁶ /L, arterial lactate level 7.3 mmol/L. The other results were subnormal: creatininemia 80 µmol/L, platelet count 201x10⁶/L, prothrombine ratio 59%, factor V 81 %, CPK 111 IU/ L (N <200). Vancomycin, aztreonam and gentamicin were initiated along with a fluid loading of 3L crystalloids and continuous noradrenaline infusion up to 2,4 µg/kg/min.

The patient was referred to the intensive care unit (ICU) and, 6 hours after admission, she suddenly developed diffuse map-like purple skin lesions particularly prominent in the lower limbs (Figure 1, A and B). The legs became cold and mottled. Simultaneously, she developed multiorgan failure and severe DIC (platelet count 36x10⁶/L, prothrombin rate 32%, factor V 31 %, D-dimers 1830 ng/mL). Arterial Doppler examination of the legs ruled out arterial thrombosis.

The diagnosis of *purpura fulminans* was made. Fresh frozen plasma and platelet concentrate were transfused. The patient’s status slowly improved, the coagulation tests normalized at day 3, norepinephrine was weaned off at day 7. By day 20, the patient underwent surgical debridement.
of cutaneous and subcutaneous tissues. After 12 weeks in the ICU, she was discharged in hospital ward for renutrition. A skin graft was performed after 5 months. The two blood cultures drawn at ICU admission as well as cutaneous biopsy of a necrotic lesion grew with a Penicillinase-producing *E. coli* strain identified using a MALDI-TOF mass spectrometer Microflex (Brucker, Germany). Histopathological exam of the skin was in accordance with the diagnosis of purpura fulminans (Figure 1, C). The cytobacteriological examination of urine was negative. Following written consent, 32 well-characterized human genetic polymorphisms associated with severe sepsis susceptibility were searched for (1). The patient’s genotyping did not reveal any variant of the genes associated with Gram-negative detection (TLR2, TLR4 and CD14) (2) severity of sepsis (TNF-α, IL-6, IL-10) (3) and coagulation disorders (coagulation factor V, Tissue Factor, Protein C Receptor Endothelial, Thrombin and PAI-1) (4). The 2009 and 2013 *E. coli* strains were further characterized by MLST sequence typing. Both of the 2009 and 2013 strains belonged to the phylogenetic group A and harbored the sequence type ST398 and ST 10 respectively. The search for 14 virulence factors (VFs) was performed by PCR as previously described (5,6). The 2013 strain did not carry any of the adhesin/invasin (Pap, Sfa, and IbeA) nor any of the toxin (Hly, Cnf-1, Sat, Vat and colibactin) genes sought. Interestingly, it harbored two iron acquisition systems, yersiniabactin and salmochelin, as well as the sit system; plasmidic OmpT (OmpTp) encoding a putative outer membrane protease (omptin) and eva encoding colicinV, hlyF encoding α-haemolysin, a poreforming toxin, ets operon encoding a type I secretion system and iss, the increased serum survival gene. This combination of genes, together with the aerobactin gene, lacking in this observation, is considered to be the signature of the Conserved Virulence Plasmidic (CVP), which contains eight operons or genes amplified by multiplex PCR as previously described (7). Complete or almost complete CVP region was
identified in sequenced plasmids, from human, avian and environmental origin (7–11). The 2009 strain did carry neither the CVP region genes nor any of the VFs sought.

Purpura fulminans is a life-threatening condition caused by a sudden and severe DIC, typically caused by meningococcemia and sometimes pneumococcemia, but *Escherichia coli*-related purpura fulminans remains exceptional (12,13). Extraintestinal pathogenic *Escherichia coli* (ExPECs) infections represent a growing public health concern (14,15). Strains commonly belong to phylogenic groups B2 and D (16) and lead to various clinical features, such as urinary tract infections, meningitis and occasionally severe skin infections (17), (18). Phylogenic group A is, with the B1 group, the group to whom belong almost all commensal strains (19). However, some of these strains may be responsible for severe invasive infections and we recently showed that CVP region contributes to the extra intestinal virulence of *E. coli* isolates belonging to these phylogroups (7).

We report herein an unusual case of commensal group A *E. coli*-related purpura fulminans in a patient that had previously exhibited an episode of *E. coli* bacteraemia without such presentation. At the time of the second bacteraemia, the patient had experienced a total gastrectomy and a severe weight loss. The alteration of the gastrointestinal tract anatomy may predispose to bacterial translocation and malnutrition could increase the severity of the infection, however none of these two factors are involved in DIC. The absence of DIC during the first episode of bacteraemia, together with the fact that known genetic markers for increased susceptibility to DIC were lacking in the host suggest that the unusual presentation was related to the pathogen’s genotype and possibly to the presence of CVP region, since the strain does not carry other particular VFs.
In conclusion, this observation points out the potential virulence associated with the CVP region, which could be involved in the emergence of “unconventional” ExPECs belonging to human commensal phylogroups A/B1 (7) and should be explored in further studies. The role of bacterial genetic determinants such as the CVP region in this life threatening syndrome remains to be elucidated.

Acknowledgments: We thank Mr Christophe Rousseau for his technical help for the genotyping and Dr Maher Anous for his help in the redaction of this manuscript.
References:


Figure caption:

FIG. 1 Bilateral necrotic legs lesions of *Purpura fulminans* (A and B). Histopathological exam of the skin revealed a sparse infiltrate of often altered neutrophils around the vessels, extravasated erythrocytes and edema of the dermis (C).