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Clinical case

Early and repeated use of plasma for the management of Ebola patients: Reflection around a case

Utilisation précoce et répétée de perfusions de plasma dans le traitement des patients Ebola : réflexion autour d'un cas

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Abstract

In December 2013, the most widespread epidemic of Ebola virus disease began in Guinea and continued for over 2 years. At the request of the Guinean state, France deployed a military field hospital to treat Ebola infected healthcare workers. From January to July 2015, our center supported 26 healthcare workers suffering from Ebola virus disease. Despite an individualized care and optimal treatment, the fatality rate remained high at 30.7%. Improved therapies are required to reduce mortality risk in Ebola virus disease. We report the case of a patient admitted to the hospital on the 4th day after onset, who survived despite several clinical and biological predictors of fatal outcome. We transfused plasma at a high dose and spread over time. This innovative therapeutic approach was based on our clinical experience of Ebola patients' management, literature review and knowledge of plasma ability to restore coagulation disorders and endotheliopathy. Even without any bleeding sign, coagulopathy and endothelial permeability disorders participate in hypovolemia and fatal multi-system organ failure. Early intake of therapeutic plasma at repeated doses seems to reduce the endothelial permeability and coagulation disorders related to Ebola virus disease.

Keywords: Ebola; Endothelial permeability; Coagulation disorders; aPPT

Résumé

En décembre 2013, la plus importante épidémie de maladie à virus Ebola éclatait en Guinée. À la demande de l'état guinéen, la France a déployé un centre de traitement pour les personnels soignants touchés par la maladie. De janvier à juillet 2015, notre centre a pris en charge 26 patients atteints de maladie à virus Ebola. Malgré une prise en charge individuelle optimale, le taux de létalité est resté supérieur à 30,7 %. Il est nécessaire de développer de nouvelles thérapies qui puissent faire baisser ce taux de létalité particulièrement élevé. Nous rapportons le cas d'un patient admis dans notre centre au 4e jour de la maladie. Ce patient a survécu malgré plusieurs signes cliniques et biologiques prédictifs de décès. Il a bénéficié au cours de sa prise en charge de perfusions précoces et répétées de plasma. Cette initiative thérapeutique était basée sur notre expérience clinique associée à une revue de la littérature en faveur d'une action du plasma sur la restauration des troubles de coagulation et d'endothéliopathie présents dans la maladie à virus Ebola. En effet, même en l'absence de signes hémorragiques, les troubles de la coagulation et l'endothéliopathie présents dans la maladie à virus Ebola participent à l'hypovolémie et à la défaillance multiviscérale fatales aux patients. La perfusion précoce et répétée de plasma semble agir sur ces deux mécanismes physiopathologiques.

Mots clés : Ebola ; Endothélipathy ; Coagulopathie ; TCA

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1. Case report

In June 2015, a 22-year-old man was admitted in our French military field hospital. He was on the 4th day of an Ebola virus disease. He suffered from fever associated with headache, abdominal pain, diarrhea, vomiting and arthralgia. The clinical examination revealed bilateral conjunctival hemorrhage. Biologically, on day 5 of illness, the patient had several adverse criteria [1]:

- a viral cycle threshold (CT) at 19.6 in relation with a high viral load;
- severe hepatic dysfunction (SGOT = 1028 UI/L, SGPT = 322 UI/L);
- severe renal impairment (creatinine = 699 µmol/L, urea = 31.9 mmol/L);
- coagulation disorders suggesting an incipient coagulopathy (INR = 1.2; aPTT = 66.2 seconds, D-dimers > 5000 UI/L).

No patient managed in our center from January to July 2015 and combining these four biological signs of severity had previously survived despite optimal treatment. This treatment included:

- an intravenous over-hydration (4–6 L/day);
- favipiravir according to JIKI trial [2], including for patients like ours who were supported late after the onset of symptoms;
- intravenous broad spectrum antibiotics (metronidazole 1,5 g/J + ceftriaxon 1 g/J);
- treatments against digestive disorders (antiemetic, antispasmodic and antidiarrheal).

Given the gravity of the patient, we decided to associate with the usual treatment lyophilized plasma transfusions at a dose of 20 mL/kg. Units of 210 mL were transfused two by two every 8 h, from day 5 of illness. On day 7, the patient presented significant clinical improvement. We also noted a normalization of laboratory parameters from day 10, with the exception of kidney function which normalized later, on day 13. Viral load, assessed by CT, decreased to 30 at day 9 (Fig. 1).

2. Discussion

For this patient, in addition to the treatment recommended by the World Health Organization [2], we decided to add early and repeated transfusions of therapeutic plasma. We used cryopreserved plasma as far as French lyophilized plasma is the only one available for French Armed Forces Health Service (FAFHS) physicians during overseas operation. It is manufactured by the French Military Blood Institute and obtained from a small plasma pool treated by Amotosalen®. This pool is provided by blood donors with blood groups A, B and AB (up to 10 donors), and free of hemolysin or irregular antibodies. This preparation method provides an universal plasma for blood types. Apart from the rare risk of allergy to amotosalen [3], the only safety precaution for lyophilized plasma is the amount administrated to patients. It is stored at room temperature and reconstituted in less than 6 minutes, just prior its use. The simplicity of lyophilized

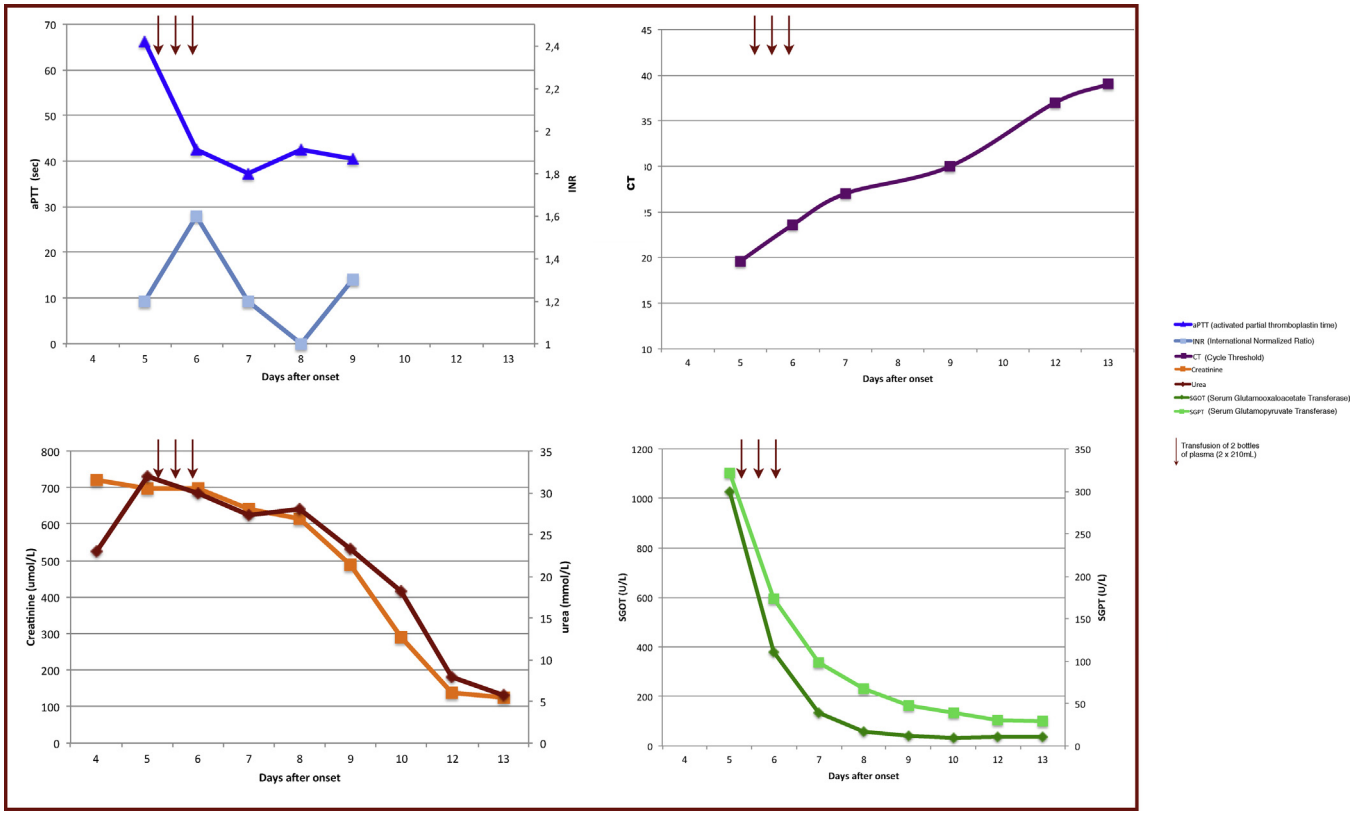

Fig. 1. Biological course of the patient during his treatment in the French military field hospital. June 2015, Guinea.