Acute rhabdomyolysis and delayed pericardial effusion in an Italian patient with Ebola virus disease: a case report

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Abstract

Background: During the 2013–2016 West Africa Ebola virus disease (EVD) epidemic, some EVD patients, mostly health care workers, were evacuated to Europe and the USA.

Case presentation: In May 2015, a 37-year old male nurse contracted Ebola virus disease in Sierra Leone. After Ebola virus detection in plasma, he was medically-evacuated to Italy. At admission, rhabdomyolysis was clinically and laboratory-diagnosed and was treated with aggressive hydration, oral favipiravir and intravenous investigational monoclonal antibodies against Ebola virus. The recovery clinical phase was complicated by a febrile thrombocytopenic syndrome with pericardial effusion treated with corticosteroids for 10 days and indomethacin for 2 months. No evidence of recurrence is reported.

Conclusions: A febrile thrombocytopenic syndrome with pericardial effusion during the recovery phase of EVD appears to be uncommon. Clinical improvement with corticosteroid treatment suggests that an immune-mediated mechanism contributed to the pericardial effusion.

Keywords: Ebola Virus Disease, Rhabdomyolysis, Pericardial effusion

Background

The 2013–6 West Africa Ebola virus disease (EVD) epidemic resulted in 28,616 confirmed, probable and suspected cases reported in Guinea, Liberia and Sierra Leone, with 11,310 deaths [1]. A small number of EVD cases were medically-evacuated or imported to Europe and the U.S., with limited secondary transmission in Spain and USA, in health care workers [2]. Pericardial involvement has rarely been reported in EVD patients [3–5]. Here we describe a case of acute rhabdomyolysis with delayed pericardial effusion in a nurse with EVD.

Case presentation

In May 2015, a 37-year old male nurse who had been working in Sierra Leone was admitted to the Spallanzani Hospital, Rome, Italy for EVD clinical management.

Medical, family and psychosocial history was non-contributory. Findings at admission, 3 days after symptom onset, included fever (39.0 °C), myalgia, conjunctivitis, diarrhoea, rhabdomyolysis [elevated serum creatine kinase (CK) level (785 IU/L, normal range 22–269)] with normal renal function, and Ebola virus (EBOV) load in plasma was 5 × 10⁷ copies/ml.

Oral favipiravir (Toyama Chemical Co, Japan) was administered (6-g loading dose and 1200 mg twice daily for 10 days) [6, 7]. Two doses of investigational monoclonal antibodies against EBOV (MIL77, Mabworks Beijing China) were given (50 mg/kg IV) 3 days apart. Empiric antibiotic treatment with intravenous ceftriaxone (2 g daily) and oral levofloxacin (750 mg daily), and intravenous crystalloid solution, were administered daily with progressive clinical improvement. CK level peaked on illness day 5 (4400 IU/ml) and declined to normal on illness day 10 (Fig. 1a). Renal function remained normal. The plasma EBOV load was undetectable on day 11 (Fig. 1a).

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On illness day 19, a febrile syndrome with diffuse adenopathy, confluent skin rash and marked thrombocytopenia (18,000/mm³) occurred (Fig. 1b-d). ECG showed diffuse nonspecific abnormalities in repolarisation, and an echocardiogram showed a mild circumferential pericardial effusion (largest echo-free space in tele-diastole <10 mm) (Fig. 1e-f). Chest pain and pericardial rub were absent. High-dose corticosteroid therapy was initiated with immediate clinical improvement; methylprednisolone, 1 g IV daily for 2 days, reduced to 500 mg on day 21 and 250 mg...
on day 22, and then switched to oral prednisone on day 23, with normalization of platelet count. Serum test positive for rheumatoid factor, Waaler Rose, and circulating immune complexes. At discharge on illness day 29, a minimal pericardial effusion was present. Corticosteroid treatment was stopped and oral indomethacin 25 mg twice daily was prescribed. Echocardiographic examination performed 60 days after discharge showed complete resolution of the pericardial effusion and indomethacin therapy was stopped. There was no evidence of pericardial effusion at 18 month follow-up visit.

Discussion and conclusions
A febrile thrombocytopenic syndrome with pericardial effusion during the recovery phase of EVD appears to be uncommon. Pericarditis was suggested as a cause of retrosternal pain in some patients and pericardial effusion was confirmed in one fatal EVD case during the 1995 Kikwit outbreak [3]. Pericardial effusion was reported in a critically ill EVD patient in Germany [4], and in two EVD patients in Guinea in 2014 [5].

Immune activation has been described in a small number of EVD patients [8]. In this case, EBOV infection may have triggered inflammation resulting in rhabdomyolysis, and after viremia resolved, prolonged immune activation may have caused pericardial tissue injury [9]. A serum-sickness disease induced by the monoclonal antibody against EBOV that was administered is another possible explanation [8]. Clinical improvement with corticosteroid treatment suggests that an immune-mediated mechanism likely contributed to the development of the pericardial effusion.

Abbreviations
CK: Creatine kinase; EBOV: Ebola virus; EVD: Ebola virus disease; PCR: Polymerase chain reaction

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Availability of data and materials
The datasets generated and/or analysed during the current study are not publicly available due to privacy reasons but are available from the corresponding author on reasonable request.

Authors’ contributions
EN, NP and GI designed the study. EN and GI drafted the manuscript. NP, EN, AB and TMU reviewed and helped to revise the manuscript. All the authors approved the final version of the manuscript.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

The INMIs Institutional Ethical Board assessed the criteria for access to experimental drugs and invasive procedures, approved informed consent form and analyzed ethical issues and possible solutions to minimize the physical and psychological harm for the patient. The patient signed an informed consent for any single procedure or treatment performed, after thoroughly explanation of reasonably anticipated benefits and potential hazards of intervention.

Emergency Use Authorization for investigational new drugs was issued by the Italian Drug Agency (AIFA), the authority entitled to approve medical agents to be used for therapy of disease when they are not the standard of care or supported by research that proves their safety.

Competing interests
The authors declare that they have no competing interest.

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