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Febrile rhabdomyolysis of unknown origin in refugees coming from West Africa through the Mediterranean

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ABSTRACT

Objectives: Cases of undiagnosed severe febrile rhabdomyolysis in refugees coming from West Africa, mainly from Nigeria, has been observed since May 2014. The aim of this study was to describe this phenomenon.
Methods: This was a multicentre retrospective observational study of cases of febrile rhabdomyolysis reported from May 2014 to December 2016 in 12 Italian centres.
Results: A total of 48 cases were observed, mainly in young males. The mean time interval between the day of departure from Libya and symptom onset was 26.2 days. An average 8.3 further days elapsed before medical care was sought. All patients were hospitalized with fever and very intense muscle aches. Creatine phosphokinase, aspartate aminotransferase, and lactate dehydrogenase values were abnormal in all cases. The rhabdomyolysis was ascribed to an infective agent in 16 (33.3%) cases. In the remaining cases, the aetiology was undefined. Four out of seven patients tested had sickle cell trait. No alcohol abuse or drug intake was reported, apart from a single reported case of khat ingestion.
Conclusions: The long incubation period does not support a mechanical cause of rhabdomyolysis. Furthermore, viral infections such as those caused by coxsackievirus are rarely associated with such a severe clinical presentation. It is hypothesized that other predisposing conditions like genetic factors, unknown infections, or unreported non-conventional remedies may be involved. Targeted surveillance of rhabdomyolysis cases is warranted.

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Introduction

Rhabdomyolysis is a complex medical condition involving the rapid breakdown of damaged skeletal muscle. The severity of the illness ranges from asymptomatic elevations of serum creatine phosphokinase (CPK) to life-threatening diseases such as cardiac arrhythmia, acute renal failure, and even death. The characteristic triad of complaints, i.e. muscle pain, weakness, and pigmenturia, is seen in less than 10% of patients (Zutt et al., 2014).

According to the International Organization for Migration, 153 842 people arrived directly in Italy via the sea in 2015 and 181 436 people in 2016, mainly coming from Nigeria, Eritrea, Guinea, Ivory Coast, Gambia, Senegal, Mali, and Sudan (International Organization for Migration, 2017). An increasing number of cases of febrile rhabdomyolysis have been observed in these migrants since May 2014, and so far there has been no specific aetiological diagnosis. The aim of this study was to report and describe this phenomenon.

Materials and methods

This was a multicentre retrospective observational study of cases of febrile rhabdomyolysis reported from May 2014 to December 2016 in 12 Italian centres: nine infectious diseases and tropical medicine units, two internal medicine units, and one refugee centre (Figure 1).

Febrile rhabdomyolysis was defined as an increase in CPK levels ($\geq$1000 IU/l) associated with myalgia and fever (>38 °C). Patient demographic, clinical, and travel-related data were collected using a standardized anonymous questionnaire and were entered into a database. Data were collected retrospectively and analysed using Microsoft Office Excel 2010 (Microsoft Inc., Redmond, WA, USA). Categorical variables were expressed as the number and proportion, and continuous variables were expressed as the mean ± standard deviation (SD). The study was conducted under the provisions of the Declaration of Helsinki and in accordance with the International Conference on Harmonization Consolidated Guideline on Good Clinical Practice. Since this study was retrospective and non-pharmacological, written informed consent was not provided. In Italy, ethical authorization for these studies is not required (see Italian guidelines for the classification and conduct of observational studies, established by the Italian Drug Agency, "Agenzia Italiana del Farmaco-AIFA" on March 20, 2008).

Results

A total of 48 cases were identified; 43 were male (89.6%), and their mean age was 22.4 ± 5.8 years. They all came from West Africa, mainly from Nigeria (58.3%) (Figure 2). Libya was the departure port in all cases. After their arrival in Italy, all patients were hosted in specific shelter centres, according to Italian immigration policies. The mean time interval between the day of departure from Libya and symptom onset was 26.2 ± 39.5 days (range 2–252 days), and an average further 8.3 ± 7.85 days elapsed before medical care was sought. The mean duration of sea travel was 1.7 ± 1.26 days.

Twenty-two patients (45.8%) had travelled between September and April and 20 had travelled between May and August (this information was not available for six patients). All patients had a fever and very intense muscle aches, and were unable to stand or walk. CPK, aspartate aminotransferase, and lactate dehydrogenase values were abnormal in all cases (Table 1). Seventeen patients (35.4%) reported having a forced position during travel. No seawater ingestion was reported and no case of hypernatraemia was identified: the mean serum sodium value was 137 ± 1.26 mmol/l.

The rhabdomyolysis was ascribed by the treating physicians to an infective agent in 16 (33.3%) cases. In detail, Epstein–Barr virus (EBV) DNA was detected in eight of 32 patients tested, IgM for coxsackievirus was detected in five of 27 cases tested, and IgM for cytomegalovirus was identified in three of 29 cases tested (Table 2). The aetiology was undefined in the remaining cases. The most frequent infectious causes of rhabdomyolysis were excluded. Four out of seven patients who were tested for abnormal haemoglobin had sickle cell trait (SCT) and one patient had haemophilia A.

All patients were asked about drug and alcohol abuse, but none reported either, with the exception of one patient who declared *Catha edulis* (khat) consumption during his stay in Libya, 2–3 weeks before symptom onset.

Only one patient was treated with rifampicin, isoniazid, and pyridoxine before symptom occurrence. Following supportive treatment with hydration, almost all patients recovered completely in about a week. However, they were often symptomatic for months. Two were hospitalized in the intensive care unit and one patient had acute kidney injury.

Discussion

This study describes 48 cases of rhabdomyolysis in refugees coming from West Africa. The phenomenon caught the authors' attention because of the severity of the symptoms, the inability to obtain a definitive diagnosis, and the consistent number of cases. Cases were observed in centres distributed throughout Italy, from the north to the south. Up to 20% of individuals in the general population have an asymptomatic increase in serum CPK, and this particularly affects the black race (Gabow et al., 1982). Nevertheless, the presence of severe symptoms and fever, as well as the young age of the present study cases, prompted further investigations to determine an aetiological cause.

Many causes of rhabdomyolysis have been identified and reported in the literature, and these can be categorized into acquired and inherited causes (Gabow et al., 1982; Huerta-Alardin

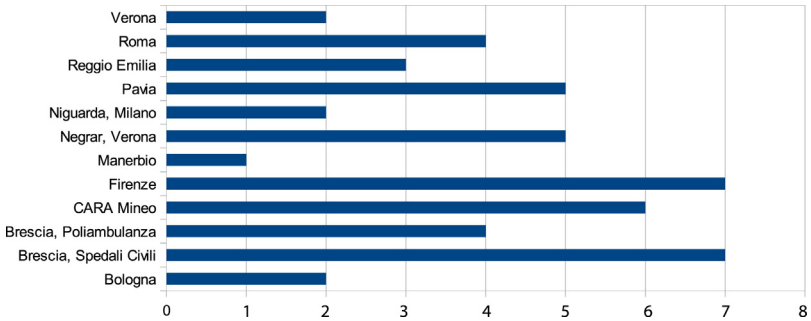

Figure 1. Number of cases reported from each Italian Centre.