A case of Crimean-Congo haemorrhagic fever in Greece, June 2008

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Case description
A 46-year-old woman with disseminated intravascular coagulation (DIC) died in a hospital in Alexandroupoli, in north-eastern Greece, in the end of June 2008. The woman was admitted to the hospital four days earlier, with fever, malaise, myalgia, chills and abdominal pain. One day before death, her condition deteriorated rapidly and she developed heavy hemorrhage from the genital tract, DIC and multi-organ failure.

The patient reported a tick bite four days before admission, and that she had tried to remove the tick herself. No travel abroad was reported. She was engaged in agricultural activities in a rural area near the town of Komotini, in Rhodope prefecture, south of the Greek-Bulgarian border (see Figure).

Laboratory investigations
After the patient’s death, stored serum sample taken upon admission was sent to the World Health Organization (WHO) Collaborating Centre for Reference and Research on Arboviruses and Haemorrhagic Fever viruses in the First Department of Microbiology, Aristotle University of Thessaloniki, Greece. An RT-nested PCR which amplifies a 240-bp fragment of the S RNA genome segment of Crimean-Congo haemorrhagic fever virus (CCHFV) [1] was applied and resulted positive. A quantitative real time PCR revealed high CCHF viral load, as is usually seen in fatal cases [2]. Sequence analysis of the PCR product showed that the causative CCHFV strain was similar to other strains detected or isolated in the Balkan peninsula (Albania, Bulgaria and Kosovo), Russia and Turkey, which are associated with severe, and sometimes fatal, disease in humans [2].

Control measures
Laboratory diagnosis and confirmation by sequencing was achieved in 24 hours from the time of sample receipt. The case was immediately notified to the European Centre for Disease Prevention and Control (ECDC) and WHO and information on it circulated through the Early Warning and Response System (EWRS) and ProMed. Immediately, the Hellenic Center for Disease Control and Prevention (HCDCP) sent guidelines to all hospitals in northern Greece for management of suspected hemorrhagic fever cases, infection-control measures and handling of clinical specimens. The case definition for suspected cases included patients with a clinical picture compatible with CCHF and a history of tick bite; or contact with tissues or blood from a possibly infected animal; or a health-care worker with a history of contact with a CCHF case occurring within the previous 14 days and within the prefecture of Rhodope.

In addition, residents of Rhodope and the neighbouring prefectures of Drama, Kavala, Xanthi and Evros were informed about measures for tick bite prevention and about the importance to refer as soon as possible to the closest hospital or general practitioner for tick removal. At the same time guidelines were disseminated to health-care workers for proper removal of attached ticks.

To date, no secondary or other cases have been observed in Greece. Extensive surveys have been launched recently by HCDCP to test seroprevalence in humans and to interview residents of the Thrace region (Xanthi, Rhodope and Evros prefectures) about

Figure
Map of Greece showing the area where a case of Crimean-Congo haemorrhagic fever was reported in June 2008
the history of tick bites and any associated symptoms. Surveys in animals have also started through the Hellenic Ministry of Rural Development and Food, and studies aiming at establishing what species of ticks are circulating in the Thrace region per season and estimating the rate of CCHF infection per species.

Discussion

During March and April 2008, six probable CCHF cases have been reported in a known endemic area in Bulgaria, close to the border with Greece [4]. In addition, many CCHF cases have been reported in Turkey this year, but none of them in the European part of the country [5].

The strain identified in our case was similar to those found in the Balkan peninsula, Russia and Turkey, but differed greatly from the Greek strain AP92, isolated from ticks in 1976, which has been suggested to cause inapparent infections in humans [3]. CCHF is endemic in the Balkan peninsula. However, it has never been reported in Greece before and the anti-CCHFV antibodies detected in 1% of the human population were most probably produced against the strain AP92 [3]. Further phylogenetic studies may show possible relations between CCHFV strains circulating in the region.

Whether climatic and environmental changes played any role in providing the favourable conditions for CCHF emergence in Greece has to be further investigated. It is not possible to predict the future occurrence of CCHF in Greece. However, clinicians have to include CCHF in the differential diagnosis of febrile hemorrhagic syndromes, even in non-endemic regions, as coincidence of factors benefit the emergence of new pathogens in an area, especially when neighbouring countries with similar landscape are endemic.

References