CRIMEAN CONGO HEMORRHAGIC FEVER

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INTRODUCTION

Crimean Congo Hemorrhagic Fever (CCHF) is a severe acute hemorrhagic fever caused by Crimean Congo hemorrhagic fever virus. It was first described in 1944 in Crimea and identified in 1956 in Congo and thus developed the current name for the disease and its causative virus [1]. The geographical distribution is wide spread. Evidence of CCHF virus has been found in Asia, Africa, Middle East and Eastern Europe [2,3]. CCHF was first reported in Pakistan in 1976 [1]. Fourteen outbreaks have occurred so far. Baluchistan and NWFP have been most affected [1]. We are reporting a case of CCHF who presented to Rawalpindi General Hospital in Sept 2004.

CASE REPORT

A 45 years old man was admitted to Rawalpindi General Hospital, on Sept 20, 2004. He was brought from a town of Hazro in District Attock, approximately 75 km west of Islamabad. He was having high-grade remittent fever for 8 days and haemetemesis and malena for one day. There was no history of abdominal pain or intake of drugs. Past history was insignificant. He was non smoker and non alcoholic. By profession he was a livestock trader. On physical examination he was found to be drowsy, pale and mildly jaundiced. His pulse rate was 120/min, temperature 37 C, blood pressure 120/90 mm of Hg and respiratory rate 28/min. There was a purpuric rash on his body and he was bleeding from gums. Liver was not enlarged. Spleen was mildly enlarged and there was no free fluid in the abdomen. Chest was clear and heart sounds were normal. Signs of meningial irritation were absent and there was no focal neurological deficit. A provisional diagnosis of septicemia with disseminated intravascular coagulation was made. The patient was shifted to medical intensive care unit and was given antibiotics, red cell concentrate and fresh frozen plasma. His lab reports received on evening of Sept 21 revealed

Hb 4.5gm/dl, MCV 93 fl, MCH 31.6 pg, WBC 4300/cumm. Neutrophils 52%, Lymphocytes 45%, Platelet count 8000/cumm, Total bilirubin 2.1 mg/dl, ALT 1260 U/L, Alkaline phosphatase 454 U/L, Serum Albumin 1.8 gm/dl. Blood urea 142 mg/dl, Creatinine 1.6mg/dl, Prothrombin time 50 sec (control 13 sec), APTT > I20 sec (control 30 sec), Fibrinogen 117 mg/dl, Fibrinogen degradation products 210 µgm/dl. Urine analysis showed Albumin (+++), Blood (+++), Pus cells 8-10/HPF.

The patient did not respond to treatment and continued to bleed from multiple sites. At this time, the case was reviewed and Crimean Congo hemorrhagic fever was considered a strong possibility. A blood sample was taken for confirmation of the disease .On the morning of Sept 22; he had generalized tonic clonic fits and died approximately 48 hours after admission on day 10 of illness. Subsequently, the result of blood sample came out to be positive for IgM antibodies and RNA for CCHF virus by PCR.

DISCUSSION

Crimean Congo hemorrhagic fever virus belongs to genus Nairovirus and family Bunyaviridea. Bunya viruses are single stranded RNA viruses, are primarily zoonotic and maintained in nature in a complex life cycle involving an arthropod vector and a vertebrate host. In case of CCHF the arthropod vector is a tick belonging to genus hyalomma. The vertebrate host includes goat, sheep, cattle and camel. Humans are

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accidental hosts. They get infected either through bite of an infected tick or through direct contact with infectious blood or tissues from an infected animal. Human to human transmission occurs through body fluids particularly blood. Often the medical team and family members are infected with fatal outcome [2]. Viral replication takes place in lymphoid cells [3]. It also causes endothelial dysfunction with development of leaky capillary syndrome [4]. Anemia, leucopenia, thrombocytopenia and raised alanine aminotranferase (ALT) and aspartate aminotranferase (AST) has been reported [2-4]. Disseminated intravascular coagulation (DIC) occurs in severe disease [2,3].

The incubation period is 3-12 days after tick bite and 3-6 days after contact with contaminated blood or tissue [2]. The virus initially causes influenza like illness followed by a variety of hemorrhagic manifestations. Mortality rate is high and varies from 15 – 70% [4]. Deaths have been reported to occur on days 6-14 of illness [3].

Our patient was a live stock trader and had slaughtered a cow 3 days prior to becoming sick. There was no history of tick bite. At the time of admission, he had fever of 8 days duration and was bleeding from multiple sites for 1 day. He had a purpuric rash and splenomegaly on physical examination. His laboratory reports showed normocytic normochromic anemia, normal white cell count, thrombocytopenia, prolonged prothrombin (PT) and activated partial thromboplastin times (APTT), raised fibrinogen degradation products (FDPs), decreased fibrinogen and raised ALT. He died of DIC related complications on day 10 of illness.

Diagnosis of the disease is made by detecting the viral RNA early in the disease by RT-PCR, by detection of IgM antibodies by indirect immunoflorescence and capture ELISA and IgG antibodies by rNP based ELISA [5-7]. Virus or nucleic acid is easily detected during the first 8 days of illness. Specific IgM and IgG antibodies are present by days 7 to 9 of illness [3]. Diagnosis is performed in specially equipped biosafety level 4 laboratories [5-7]. A Blood sample of the patient was sent to National institute of Virology, South Africa for confirmation of CCHFV infection in the present case. Result was obtained after three weeks. Viral nucleic acid was detected by PCR and IgM antibodies were positive whereas IgG antibodies were negative.

Ribavirin, a purine nucleoside analogue has been used to treat cases of CCHF with favourable outcome [6-8]. Prominent side effects are anemia, hemolysis and CNS and GI symptoms. It is also teratogenic [9]. We could not give ribavirin to our patient because the patient reached the hospital at a very late stage of illness and also due to delay in reaching to the provisional diagnosis of CCHF virus infection.

Virus is notorious for nosocomial outbreaks which typically follow admission of an index case to a health care facility where it was not suspected. Clinically apparent attack rate was estimated to be 5 infections per case of hemorrhagic fever in the former Soviet Union [2]. In Pakistan eight nosocomial outbreaks have occurred since 1976. Sixteen health care workers were affected and nine lost their lives [1]. Secondary cases were not detected in the present study.

Biosafety is the key to avoid nosocomial spread [10]. Health care workers who are exposed to the patient should be monitored for fever, headache and myalgia for 14 days from the day of last contact with the patient. If the temperature rises to 38.5 C, and they develop severe headache and myalgia, oral ribavirin should be started after doing baseline blood tests. Health care workers who develop accidental needle stick injury or other accident where blood or secretions were in direct contact with open wound or mucus membrane should have base line blood tests directly after the accident and then be placed on prophylactic oral ribavirin. Contacts should be tested for CCHF only if they develop fever, head ache and myalgia during

the monitoring period. People exposed to the same animal as the patient and members of the patient's family or others exposed to the patient should be managed in the same manner [10].

In our view, people involved with livestock should be educated about protection from tick bites and handling and butchering of animals. More importantly, awareness about this dreadful disease needs to be increased among health care workers especially front line medical staff and Crimean Congo hemorrhagic fever should be included in the differential diagnosis of any unexplained fever with hemorrhagic manifestations.

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