Crimean-Congo haemorrhagic fever presenting with undiagnosed chronic myeloid leukaemia†

Marius J Coetzee*, Lucille H Blumberg†, Janusz T Paweska¶, Pat Leman⁴, Robert Swanepoel⁴ and André de Kock†

†Department of Haematology and Cell Biology, University of the Free State and National Health Laboratory Service, Bloemfontein, South Africa
§Centre for Emerging and Zoonotic Diseases, National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg, South Africa
¶Special Pathogens Unit, National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg, South Africa
⁴Department of Veterinary Tropical Diseases, University of Pretoria, Pretoria, South Africa
*Corresponding author, email: coetzemj@ufs.ac.za
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A patient with Crimean-Congo haemorrhagic fever (CCHF) presented with a high white cell count and splenomegaly. Underlying chronic myeloid leukaemia was diagnosed. The management of this complex case was difficult, and the patient demised. This case illustrates that in patients with an acute febrile illness with haemorrhage, a thorough history and examination, as well as a high index of suspicion for concurrent conditions, is important.

Keywords: chronic myeloid leukaemia, Crimean-Congo haemorrhagic fever virus, leucocytosis, South Africa, tick-borne diseases

Introduction

Since Crimean-Congo haemorrhagic fever (CCHF) was first described in South Africa in 1981, there have been at least 203 laboratory-confirmed cases. Even though it is a viral disease, the haematology laboratory is involved in the diagnosis and management because haematological coagulation parameters are of prognostic significance, and guide supportive treatment. Patients with underlying CCHF are not frequently worked up for a bleeding diathesis or haematological pathology initially, such as immune thrombocytopenia. CCHF can present with a myriad of clinical findings. Here we report a case of CCHF presenting with previously undiagnosed chronic myeloid leukaemia. The case report was approved by the Health Sciences Research Ethics Committee of the University of the Free State (approval number 177/08).

Case report

A significant number of CCHF cases have been reported from the Northern Cape province. A 35-year-old male farm worker from the town of Prieska presented with fever, headache and myalgia after being bitten by a Hyalomma tick two days previously. He was admitted to the isolation unit of Kimberley Hospital, with clinical and laboratory features of CCHF. These included a thrombocytopenia of 43 x 10⁹/l, a haemoglobin of 11.4 g/dl and raised transaminases. The splenomegaly and a white cell count of 75 x 10⁹/l were considered unusual for CCHF. However, based on the history of exposure to ticks, in an area well-known for CCHF, the clinical picture was compatible with CCHF. Taken together with concerns about health worker risks of infection, it was deemed essential to test for CCHF and to continue isolation procedures in the interim. CCHF was confirmed by reverse transcriptase polymerase chain reaction and serology at the National Institute for Communicable Diseases of the National Health Laboratory Service (NICD/NHLS).

The white cell differential showed 1.29 x 10⁹/l blasts, 0.43 x 10⁹/l promyelocytes, 5.16 x 10⁹/l myelocytes, 0.43 x 10⁹/l metamyelocytes, 0.86 x 10⁹/l band cells, 3.01 x 10⁹/l eosinophils and 3.44 x 10⁹/l basophils. This is typical of chronic myeloid leukaemia (CML) in the chronic phase. The morphological diagnosis was confirmed in the referral haematology laboratory in Bloemfontein (Figures 1 and 2). Since the white cell count was raised due to the CML, the finding by Swanepoel et al. that a white cell count > 10 x 10⁹/l in the first five days is a predictor of poor prognosis could probably not be applied strictly.

Fluorescent in situ hybridisation (Vysis LSI BCR/ABL Dual Color Single Fusions Translocation Probe Set, Abbott Molecular, Des Plaines, IL, United States) done on a blood smear demonstrated the t(9;21)(q34.1;q11.21) translocation pathognomonic of CML. The translocation between the BCR and ABL genes results in constitutively active tyrosine kinase that leads to the growth of CML clones. In an otherwise healthy patient, tyrosine kinase inhibitors are the treatment of choice. The leucocytosis alerted the laboratory to do a white cell differential count, leading to the confirmation of CML. The clinical picture and history of tick exposure in an endemic region suggested CCHF and prompted laboratory testing for CCHF, despite an initial high index of suspicion for an alternative diagnosis of a haematological condition. Appropriate infection control measures for a suspected viral haemorrhagic fever were immediately instituted to prevent nosocomial transmission.

Together with supportive care, ribavirin was given orally at a dosage of 30 mg/kg initially, followed by 15 mg/kg every six hours, and then 7.5 mg/kg every eight hours, as intravenous ribavirin is not available in South Africa. He received platelet transfusions as his platelet count continued dropping. By day five, his white cell count had risen to 120 x 10⁹/l, his haemoglobin dropped to 5.4 g/dl and his platelet count dropped to 38 x 10⁹/l. Hydroxyurea at 2 g daily was started to reduce the leucocytosis. Allopurinol at 300 mg daily was given to address tumour lysis. The patient unfortunately died on day six after admission from the complications of a combination of the diseases and treatment. A post-mortem was not performed.
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†
d Department of Veterinary Tropical Diseases, University of Pretoria, Pretoria, South Africa
c Special Pathogens Unit, National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg, South Africa
a Department of Haematology and Cell Biology, University of the Free State and National Health Laboratory Service, Bloemfontein, South Africa
Marius J Coetzeea*
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Since Crimean-Congo haemorrhagic fever (CCHF) was first
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dropped to 5.4 g/dl and his platelet count dropped to 38 x 10^9/l.
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Hydroxyurea at 2 g daily was started to reduce the leucocytosis.
CML might have caused urate nephropathy. The lysis of CML cells might have
The patient would probably have presented with clinical CML a
few months later, had he not contracted CCHF. The CML might
complicated the CCHF in a number of ways. The anaemia
probably worse and the high white cell count may have
caued sluggish circulation. The lysis of CML cells might have
Karti et al.16 excluded any haematological malignancies in their
series of 19 cases with suspected haemorrhagic fever by
performing bone marrow aspirates. They reported
haemophagocytosis, a condition distinct from CML. In the present
case, we speculate that a combination of the direct effects of CML
and CCHF, and the treatment displayed adverse interactions.
CCHF virus infects the endothelium,11 leading to cytokine release,
diffuse intravascular coagulopathy and thrombocytopenia. The
myeloid precursors in the CML secrete inflammatory cytokines as
aden dorsal molecules,12 thus compounding the vascular
damage. It is unlikely that the patient had classical leukostasis as
the white cell count was less than 100 x 10^9/L.12
Hydroxyurea and ribavirin are both metabolised in the liver. The
damage caused by CCHF virus may have contributed to
higher plasma concentrations of these drugs, with potentiation of
adverse events of especially ribavirin.

The outcome of CCHF was compounded by the concurrent CML.
CCHF has been diagnosed in the presence of a number of other
conditions. Tezer et al.13 reported a case of a 14-year-old female
who had concurrent visceral leishmaniasis. A bone marrow
aspirate was done on her because of persistent splenomegaly
raised liver enzymes after clinical recovery from CCHF. Celikbas et al.14
reported a case of CCHF simulating acute appendicitis. Ergonul et al.15
point out that CCHF might be confused with the HELLP (haemolytic anaemia elevated liver
enzymes, low platelet count) syndrome in pregnancy. Doganci et al.16
mention that CCHF should be excluded in patients
presenting with diffuse alveolar haemorrhage. Accurate and
thorough epidemiological histories are important in all patients
presenting with haemorrhage, especially in areas where viral
haemorrhagic fevers are known to occur. Testing for CCHF must
be carried out and infection control practices adhered to in
all patients where the epidemiology and clinical course of illness
are compatible with CCHF, even while there is strong
consideration for other diseases.

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ORCID
Marius J Coetzee http://orcid.org/0000-0003-2762-0966
Lucille H Blumberg http://orcid.org/0000-0002-2828-7678
Janusz T Paweska http://orcid.org/0000-0001-8776-7519
Robert Swanepoel http://orcid.org/0000-0003-2538-3290
André de Kock http://orcid.org/0000-0002-2910-1273

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