Leukemic ascites as an initial presentation of acute myelomonocytic leukemia with inversion of chromosome 16

To the Editor: The inversion of chromosome 16, inv(16), a cytogenetic abnormality expressed in core binding factor acute myeloid leukemias (AML), is associated with myelomonocytic differentiation and eosinophilia.[1] Even though inv(16) generally portends a good prognosis, accompanying mutations detected by molecular genetic methods, such as KIT and Ras mutations, alter their response to treatment.[2] Infiltration of leukemic cells into serous effusions is unusual. To our knowledge, there are only a few reports of AML with inv(16) presenting with leukemic ascites.[2]

We present a 33-year-old woman with jaundice and massive ascites. The laboratory tests showed the following: hemoglobin 8.3 g/dL, hematocrit 25%, total leukocyte count 135800/mm^3, and platelet count 32000/mm^3, erythrocyte sedimentation rate 45 mm/hr, AST 597 U/L, ALT 111 U/L, ALP 417 U/L, GGT 191 U/L, lactate dehydrogenase 6515 U/L, total bilirubin 9 mg/dL and direct bilirubin 8.2 mg/dL. On peripheral blood smear, myeloblasts comprised 67% of the cells and the bone marrow analysis showed 57% myeloblasts with eosinophilic differentiation. Immunophenotypic analysis of the bone marrow was positive for CD13, CD14, CD45, CD33, CD34 and HLA-DR. FISH analysis of the bone marrow revealed an inv(16) signal. The final diagnosis was acute myelomonocytic leukemia (FAB Classification M4e) with inv(16). Abdominal computed tomography revealed massive ascites and multiple lympadenopathies with a maximal diameter of 1.5 cm at the mesenteric region. A diagnostic and therapeutic paracentesis was performed. Analysis of the ascitic fluid showed an exudate with a white blood cell count 3140 cells/mL; red blood cell count 70000 cells/mL; monocyte count 1910 cells/mL. The ascitic total protein was 3.9 g/dL (serum, 7.1 g/dL), glucose 208 mg/dL (serum, 216 mg/dL), lactate dehydrogenase 1918 U/L (serum, 2813 U/L) and albumin 2.4 g/dL (serum, 3.9 g/dL). Cytocentrifuge preparation of the patient's ascitic fluid showed myeloblasts and monoblasts with irregular nuclei and prominent nucleoli (**Figure 1**). Flow cytometric analysis of the ascitic fluid showed the expression of CD13, CD14, CD33, CD34, CD45 and HLA-DR compatible with the diagnosis of acute

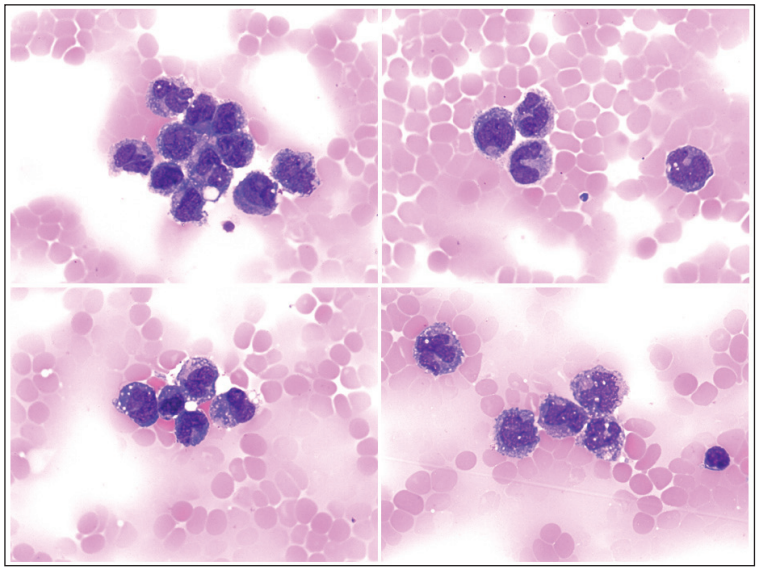

Figure 1. Ascitic fluid with monoblasts and myeloblasts.

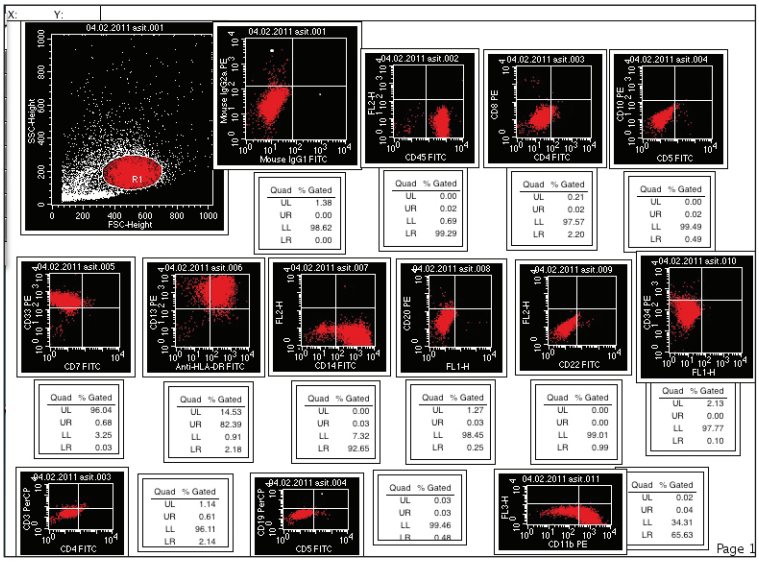

Figure 2. Flow cytometric analysis of the ascitic fluid showed the expression of CD13, CD14, CD33, CD34, CD45 and HLA-DR.

myeloid leukemia-M4 (AML-M4) (**Figure 2**). The patient was treated with cytarabine 100 mg/m^2 for 7 days and idarubucin 12mg/m^2 for 3 days. On the third day of the remission induction therapy, ascites disappeared and the liver enzymes and bilirubin levels returned to normal on completion of the first week of therapy. The patient was under follow up at our hematology department at the time of writing.

Leukemic infiltration of effusions have been mostly reported in AML with monocytic differentiation, including M4 and M5 AML in the FAB classification.[3,4] Yet, development of leukemic ascites at initial presentation of AML, as in our case, is a rare entity.[5] Also, in few previous cases, leukemic ascites has been reported as the presenting feature in inv(16) AML.[2] Our case emphasizes the importance of performing paracentesis and an extensive diagnostic work-up in AML presenting with ascites to differentiate leukemic infiltration from other causes. Further studies are needed to to identify the clinical significance of inv(16) in the presence of leukemic ascites.

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DOI: 10.5144/0256-4947.2013.197

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Emergence of a highly resistant *Clostridium difficile* strain (NAP/BI/027) in a tertiary care center in Saudi Arabia

To the Editor: *Clostridium difficile* NAP/BI/027 is a hypervirulent form of the bacterium *C difficile*. NAP/BI/027 is a highly resistant strain, and infection with *C difficile* is associated with high morbidity and potential mortality. There has not been any reports of this strain in Saudi Arabia. However, its detection requires PCR techniques that are not widely available. We describe four cases of *C difficile* NAP/BI/027 infection observed in our institution over a one-year period, no relatedness found between any of the cases. All patients were >60 years of age and had a number of premorbid conditions. They received long courses of antibiotics before they developed diarrhea and tested positive for *C difficile* NAP/BI/027. All were treated with metronidazole and/or oral vancomycin. One patient developed toxic megacolon and expired, whereas the other three patients made a gradual recovery and were discharged. This report confirms that *C difficile* NAP/BI/027 exists in this region of the world and is likely underdiagnosed due to the need for specific PCR-based testing that is not widely available. This strain is highly resistant to fluoroquinolones and is associated with severe disease and high mortality rates.[1] The epidemiology of this organism has changed drastically in recent years. The incidence and severity of *C difficile* infection have increased considerably in the USA, Canada, and Europe. Several outbreaks in these countries have occurred, caused mainly by ribotype 027.[2,3] Three cases of NAP/BI/027 *C difficile* infection were reported in Asia but this strain has never been reported in Saudi Arabia.[4-6] We describe the first four unrelated cases of *C difficile* NAP/BI/027 diagnosed at our hospital.

CASE 1

A 66-year-old male diabetic and hypertensive patient was admitted to the hospital on June 14th 2011 with sternal wound infection post-coronary artery bypass graft. He was started on imipenem on June 20th for 5 weeks. Then ciprofloxacin and vancomycin were added and continued for 4 weeks. On July 29th, the patient began to have diarrhea. A stool sample tested positive for *C difficile* NAP/BI/027 via PCR. The patient was treated with metronidazole. The diarrhea stopped, and he continued to improve and was discharged from the hospital.

CASE 2

A 62-year-old hypertensive male patient known to have congestive heart failure was admitted to the hospital on December 9th 2011 complaining of abdominal distention and urinary retention. He was transferred to the ICU on

December 21st, where he was given meropenem and vancomycin (IV) for 1 week. He started to have severe abdominal distention. A CT scan of the abdomen showed features consistent with toxic megacolon. A stool sample tested positive for C *difficile* NAP/BI/027. He was treated with metronidazole and vancomycin (oral) for 2 weeks. His condition continued to deteriorate, and he died as a result of C *difficile* NAP/BI/027 infection.

CASE 3

A 68-year-old hypertensive woman was admitted to the hospital on December 16th 2011 complaining of chest pain and was diagnosed with myocardial infarction. She was admitted to the ICU. The patient underwent coronary artery bypass graft surgery and was treated postoperatively with cefazolin for 2 days. Three days later, the patient began to have diarrhea and vomiting. A stool sample tested positive for C *difficile* NAP/BI/027. The patient was given metronidazole; she made a full recovery and was discharged.

CASE 4

A 67-year-old male patient known to have large B cell lymphoma was admitted to the hospital with acute exacerbation of COPD. He was treated with ceftriaxone for 2 weeks. Because he continued to have a fever, the antibiotic was changed to a piperacillin/tazobactam regimen that was continued for 5 weeks. During his hospital stay, the patient complained of diarrhea and developed hypotension. A stool sample was positive for C *difficile* NAP/BI/027. The patient was treated with metronidazole and vancomycin (oral). He slowly improved and was discharged from the hospital.

To our knowledge, this is the first report of this serious infection in Saudi Arabia. It is likely that previous cases have been overlooked because their diagnosis requires PCR testing, which is not widely available. This report highlights the need for increased laboratory surveillance for this organism and better infection control measures. The aim of these findings is to raise health care workers' awareness of the existence and importance of this infection.

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DOI: 10.5144/0256-4947.2013.198

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