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Case Report

Fever of Unknown Origin for Three Months in a Patient with Multiple Myeloma

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Abstract

This is a case of a 50-year-old relapse and refractory Multiple Myeloma (MM) patient with a Fever of Unknown Origin (FUO) for three months. It occurred after the transfusion 24 hours accompanied with chills, muscle pain, joint pain, and fatigue. A peripheral blood smear showed 0.01% parasitaemia with one ring body of Babesia, and Polymerase Chain Reaction (PCR) amplified the Babesia's DNA band. Treatment for Babesia was started and infection was controlled. Babesia is a zoonotic intraerythrocytic parasites. Symptoms of babesiosis can range from a mild flu-like illness to acute, severe, and fatal disease. Severe disease is common in older populations and immunocompromised patients. Recently, babesiosis has become an emerging health problem in humans all over the world. Therefore, rare infections in myeloma patients suffered the longtime of a FUO should not be neglected by hematologist.

Keywords: Multiple myeloma; Fever of unknown origin; Babesia

Introduction

Multiple myeloma is a malignant tumor of plasma cell dysplasia, which abnormally proliferates and secrete a large number of monoclonal immunoglobulins to inhibit normal immunoglobulins. Therefore, MM patients have a high risk to suffer from FUO, which at onset caused mostly by bacterial, fungal infections, and virus, and considered relatively rare tumor fever. The rare infection is easily ignored, herein, we report AMM patient with FUO for three months was eventually diagnosed with Babesia.

Case Presentation

A 50-year-old man worked as prison guard living in Dongguan province. He was diagnosed MM (DS stage IIA and ISS stage I) and received multiple chemotherapy regimens in other hospital (including Rituximab + Cyclophosphamide + Fludarabine (R-FC), Bortezomib + Dexamethasone (VD), Lenalidomide + Dexamethasone (RD), radiotherapy etc) during September 2010 to March 2014 with the best response at Partial Response (PR). On 1st April 2014, he came to our center to further treat for the serious bone pain and extra modularly involvement. We re-evaluated the patient with λ light chain type in DS stage IIIB and ISS stage III. We firstly prescribed V-TD-PACE regimen considering his high tumor burden status. The third degrees of myelosuppression occurred after chemotherapy one week. G-CSF injection and transfusion were adopted in his hometown. However, he got a fever up to 39.6°C accompanied with chills, muscle pain, joint pain, and fatigue after the transfusion 24 hours. Imago logical, serologic examinations, bone marrow, blood, urine, stool, and sputum specimens, for Bacteria, fungi, viruses, were all negative. Various combinations of antibiotics had been used, but the fever persisted from 38.5°C to 39.6°C. Small dose glucocorticoid or non-steroidal anti-inflammatory drugs are beneficial to anti-febrile. He came back after suffering the fever two weeks. We evaluated the Patient Response at (PR) that tumor fever should not be considered, while degree of anemia further deteriorated. To avoid delay treatment and no more evident of infection, the same regimen combined with antibiotics were given. Unfortunately, his fever emerged when dexamethasone was end in chemotherapy. During this period blood tests showed prominent hemolytic anemia (hemoglobin 5.4 g/dl) with an increased reticulocyte production index and except for a mild elevation of direct bilirubin (18 umol/L), serum chemistries were almost normal. We conferred the patient might be suffered from very rare etiological infection, although parasite, virus and so on, had been determined several time based on the current reached assays.

Considering the patient's all clinical features, especially low dose glucocorticoid could work; we discussed carefully and reviewed the literatures to figure out the rare etiological infection need to be screened. Subsequently, peripheral blood and peripheral blood smears were sent to Shanghai Institute of Parasitic Diseases Control and Department of Medical Microbiology and Parasitology. Ultimately, only one ring body of Babesia was found in the patient's peripheral blood smear among 10thousands red cells (Figure 1A), and Polymerase Chain Reaction (PCR) amplified the Babesia's DNA band. The sequence showed 80% homology with the Babesia worms derived from Spanish dog (Figure 1B).

Discussion

Babesia is a zoonotic intraerythrocytic parasite, mainly transmitted by ticks and less commonly by blood transfusion and transplacentally [1]. More than 100 species of Babesia can infect animals, where as only a few can infect human [2]. It develops

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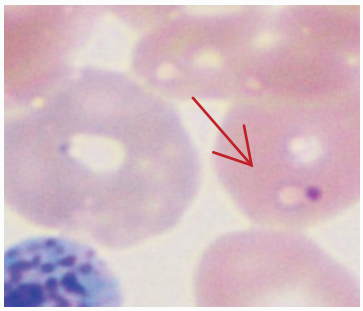

Figure 1A: Babesia determined by peripheral blood smear and electrophoresis of PCR.
A) Micro parasites in the patient's erythrocytes with Wright–Giemsa straining. The arrowheads indicate the ring forms. Magnification 1000.

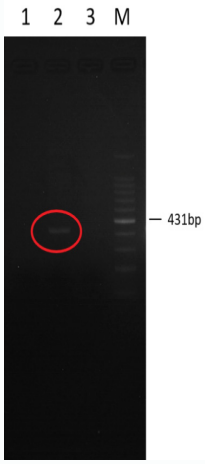

Figure 1B: Nested PCR test at the time of diagnosis.

in patients who live in or travel to an endemic area or receive a contaminated blood transfusion within the preceding 9 weeks, so this aspect of the medical history is vital [3]. Babesiosis may be suspected when a person with such an exposure history develops persistent fevers and hemolytic anemia. The clinical spectrum of babesiosis ranges from an asymptomatic infection to fulminant fatal disease. The disease severity depends on the immune status of the host and on the Babesia species involved. We retrospect the patient's history of fever progression, which showed the shorter latent period only after 24 hours blood transfusion [4]. Although he could not recall the tick bite history, it was not ruled out as a prison guarder by bit with a long latency, and it might be the risk of contracting babesiosis from a blood transfusion. Under his immunodeficiency situation, he was very susceptible for morbidity. Only specialized laboratories can adequately diagnose Babesia infection in humans, so Babesia infections are considered highly under-reported. The definitive diagnostic test is the identification of parasites on a Giemsa-stained thin-film blood smear [3,5]. So-called "Maltese cross formations" on the blood film are diagnostic (pathognomonic) of babesiosis [6]. Recently, there was a 26-fold increase in the incidence of confirmed babesiosis, in addition to geographic expansion [7]. A report showed in Nature last year, as lower-moving threat to the blood supply is spreading through the northeast and upper-Midwest regions of the United States-the tick-borne parasite Babesia microti, which infects red blood cells and causes the malaria-like disease babesiosis [8]. Therefore, careful examination of multiple smears may be necessary, since Babesia may infect less than 1% of circulating red blood cells, thus be easily over looked [9].More important, the society, regulators and blood-donation centers need to charge with ensuring the safety of the blood supply.

In this patient, Babesia infected only in 0.01% of circulating red blood cells and gel band displayed the weak visible band which also implicated the low concentration infection. He had no uncomfortable after a drop in body temperature. There are several combined drugs used in Babesia infection, including Atovaquone plus Azithromycin or Quinine plus Clindamycin or artemisinin [10]. Subsequently, the patient was transferred to the infectious department of one Shanghai's hospital to treat by atovaquone plus artemisinin, and the patient received Bird regimen to anti-MM. After one month, his Babesia infection reduced at least 50%, which confirmed by invisible gel band (Figure 1C). Three months later, he had no more fever, normal bilirubin lever, and hemoglobin raised to 110 g/L, and then to stop the drugs. Meanwhile his myeloma achieved VGPR and he subjective stopped anti-myeloma treatment as well. However, myeloma progressed after the withdrawal drugs three months and finally he died of cerebral hemorrhage after the nine months of the Babesia diagnosis.

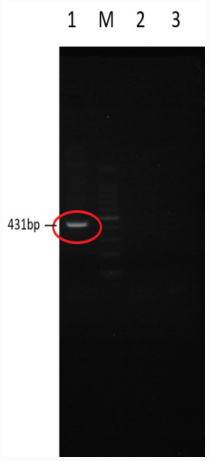

Figure 1C: Nested PCR test after one month anti-Babesia therapy.

Conclusion

To summarize, we describe a patient who presented as a FUO, and the cause was found to be a Babesia infection. Babesia infection is extremely rare, which displays the characteristics of opportunistic infections, especially for susceptible population of immunodeficiency. It is interesting to note that amongst the patients by Babesia infected many did not present with the classical clinical manifestation, normally fever occurred primarily. Thus, it serves as a teaching point to hematologist not disregard myeloma patients suffered the longtime of a FUO, which can be suggestive of rare infections.

Acknowledgement

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