Case report

Fatal human babesiosis caused by *Babesia divergens* in an asplenic host

Irina V. Kukina, Tatiana M. Guzeeva, Olga P. Zelya*, Ludmila A. Ganushkina

**Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation**

**A R T I C L E   I N F O**

Article history:
Received 22 March 2018
Received in revised form 21 May 2018
Accepted 26 June 2018
Available online xxx

**Keywords:**
Protozoan parasites
Tick born disease
Human babesiosis
*Babesia divergens*
Diagnosis

**A B S T R A C T**

We report a fatal case of human babesiosis caused by bovine pathogen *Babesia divergens* in Russia. *Falciparum* malaria was falsely diagnosed due to the presence of small ring forms in the blood smear. Laboratory diagnosis can distinguish between babesiosis and malaria according to the examination of stained blood smears.

© 2018 I M Sechenov First Moscow University (Sechenov University), Moscow, Russian Federation. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

**Introduction**

Human babesiosis caused by the bovine pathogen *Babesia divergens* is a sporadic, zoonotic, tickborne disease. To date, about 50 cases of human babesiosis have been reported in Europe [1,2]. The significance of this disease can be a severe course in immunocompromised patients resembling complicated falciparum malaria, which can be end up with a fatal outcome. *B. divergens*, a protozoan blood parasite (*Apicomplexa: Babesiidae*) is primarily specific to cattle and are widespread throughout the world within the vector - *Ixodes ricinus*. They have two different types of hosts, vertebrate and invertebrate. The invertebrate host's sexual cycle (gamogony, formation and fusion of gametes) occurs in the tick gut. Sporogony (the asexual reproduction of sporozoites) occurs within the salivary glands of a tick. There is transtadial and transovarial transmission of the parasites in the tick host [3,4]. Merogony (asexual reproduction) occurs in the vertebrate host inside the erythrocytes.

Parasites are transmitted to the vertebrate host when the infected tick takes a blood meal. The incubation period from the time of tick transmission of the organisms to the appearance of symptoms usually takes 1–3 weeks. As the tick feeds on a vertebrate host, sporozoites are inoculated into the host. These sporozoites invade the host's erythrocytes directly. The process of asexual reproduction (merogony) begins. Inside the host erythrocytes, sporozoites become trophozoites and divide asynchronously by binary fission. This process produces more merozoites, which lyse the host cells and continue to infect additional erythrocytes.

The disease manifestation of a vertebrate host is caused by the asexual stage of the organism proliferating in the erythrocytes. Rapid reproduction of the parasites can destroy a great number of the host cells and lead to severe hemolysis, massive hemoglobinuria and renal failure in the host particularly in the asplenic individual [5,6].

**Case report**

The patient, a 58-year old man, who lived in the Krasnodar Krai area of the North Caucasus region in south Russia and was a huntsman. Posttraumatic splenectomy had been performed 12 years ago. His illness was fulminant and took an acute course with severe fever (as high as 40 °C), hemoglobinuria, hemolytic anemia, jaundice, uremia, renal insufficiency, anuria. This patient was brought to the hospital extremely ill. The laboratory manifestations were: hemoglobinuria, high-level free hemoglobin (3 g/dl) and urea (49 mmol/l) in the serum, TBI (69.1 μmol/l), DBi (18.3 μmol/l), WBC (12.64 × 10⁹/μl), and Hb 72.3 g/dl. The diagnosis at admission was a renal failure of obscure etiology. Peritoneal dialysis was started and the patient was treated with prednisolone. On the fifth day of illness, the blood film was examined and the numerous intra-erythrocytic parasites were found. *Falciparum* malaria was falsely diagnosed due to the presence of small ring forms. Antimalarial therapy with quinine and doxycycline was started, but it was ineffective. The patient remained quite ill.
This patient was living in a temperate region where falciparum malaria is absent. He did not travel to an endemic area. The smear was re-examined in the reference laboratory. The numerous intraerythrocytic inclusions were single or multiple, some rod-like, pear-shaped, often circular and vacuolated. The level of parasitemia was about 23%. Pigment depositions were absent inside cytoplasm of the parasites. The paired forms were diverged at a wide-angle (up to 180°) and were situated on the periphery of the erythrocyte (Fig. 1). Complex morphological characteristics (great variation in the forms seen, pear-shaped trophozoites, paired and tetrad forms, absence of hemozoin) was sufficient to speciated parasites as Babesia divergens.

Babesiosis was diagnosed on the seventh day of illness and therapy with clindamycin was started. Pathogenetic and symptomatic therapy was continued. The multisystem failure increased progressively and the patient died on day 10 of illness.

Discussion

Delayed diagnosis and confusion between human babesiosis and malaria have been reported [7,8]. The clinical manifestations and nonspecific laboratory signs are common to both diseases. The previous case of human babesiosis in the USSR has been falsely diagnosed as malaria as well. Babesiosis has been diagnosed post mortum only [9]. The differential diagnosis is essential to determine whether the causative agent of disease is Babesia or Plasmodium. This is important as the specific therapy is different for these two diseases.

Definitive diagnosis of babesiosis infection generally must be established by the microscopic identification of the organism on stained blood smears [2,8,10]. The main morphological differences exist between the asexual stages Babesia and Plasmodium.

1 Polymorphism is definitive of the erythrocytic stages of Babesia. There is a great variation in the morphological forms seen: rod-like, pear-shaped, or ring. The small ring forms B.divergens seen inside the erythrocytes can be wrongly identified as Plasmodium falciparum. Babesia parasites divide asynchronously by the binary fission forming «Figure 8s» and rare tetrad «Maltese Cross», whereas malarial parasites are divided synchronously by schizogony. P. falciparum has a tendency to appear in the peripheral blood at two points only in the whole course of its development in the human host: the early trophozoite stage – ring and the gametocyte stage.

Fig. 1. Babesia divergens. Romanovsky-stained thin blood smear. Diversity forms of trophozoites: rod-like (1), pear-shaped (2), multiple invasion of the ring forms (3), paired form – figure «eight» (4), tetrad form «Maltese Cross» (5). (Original), (× 1000).

Fig. 2. Plasmodium falciparum, malignant infection. Romanovsky-stained thin blood smear. There is no pigment in the cytoplasm of the numerous ring forms (1). The deposition of pigment is seen in the cytoplasm of the late trophozoite (2). The cytoplasm of neutrophil contains the phagocytosed mass of hemozoin (3). (Original), (× 1000).

All asexual stages of Babesia do not contain hemozoin within the cytoplasm. There is no pigment in the early ring forms of P. falciparum as well. But phagocytosed masses of hemozoin may be seen inside the cytoplasm of leukocytes (neutrophils and monocytes) in the case of malarial infection (Fig. 2).

Conclusion

Animal babesiosis is widespread throughout the world. A transovarial and transstadial transmission can theoretically result in large numbers of infected ticks in the area where babesiosis is endemic. People working in the rural areas are frequently exposed to the bites of infected ticks. The immunocompromised patients (splenectomized, elderly, HIV infected) are in the vulnerable group of morbidity rate of babesiosis. Human babesiosis is probably underdiagnosed disease. The diagnosis of babesiosis is based on appropriate clinical manifestations, epidemiological and medical history, physical examination, and confirmatory laboratory detection parasites in the blood.

Competing interests

The authors declare that they have no competing interests.

Funding source

None.

Ethical approval

None.

References

[1] Hildebrandt A., Hunfeld KP. Human babesiosis – a rare but potentially dangerous zoonosis. Dtsch Med Wochenschr 2014;139(May (18)):957–62, doi: http://dx.doi.org/10.1055/s-0034-1369936 German. PubMed PMID:24760717.
[2] Rożył-Bieńicka W, Styropińska-Miśurewicz H, Goląb E. Human babesiosis. Przegl Epidemiol 2015;69(3):489–94 Polish, PubMed PMID:26519845.
[3] Vasilieva IS, Ganushkina LA. Ticks that harm human health Rostov on Don: Phoenix; Russian, 2017.
[4] Rabinoovich SA, Zelya OP. Babesiosis. In: Sergeev VP, Yushchuk ND, Vengerov YY, Zavoiski VD, editors. Tropical diseases. Guide for doctors. Moscow: BINOM; 2015. p. 432–5 Russian.
[5] Gorenflot A, Moubri K, Preciquest E, Carcy B, Schetters TP. Human babesiosis. Ann Trop Med Parasitol 1998;92(June (4))489–501 PubMed PMID:9683900.

[6] Hunfeld KP, Hildebrandt A, Gray JS. Babesiosis: recent insights into an ancient disease. Int J Parasitol 2008;38(September (11))1219–27, doi:http://dx.doi.org/10.1016/j.ijpara.2008.03.001 PubMed PMID:18440005.

[7] Garnham PC. Human babesiosis: European aspects. Trans R Soc Trop Med Hyg 1980;74(2):153–5 PubMed PMID:6770500.

[8] Homer MJ, Aguilar-Delfin I, Telford 3rd SR, Krause PJ, Persing DH. Babesiosis. Clin Microbiol Rev 2000;13(July (3))451–69 PubMed PMID:10885987; PMCID: PMC88943.

[9] Rabinovich SA, Voronina ZK, Stepanova NI, Maruashvili GM, Bakradze TL. 1st detection of human babesiosis in the USSR and a short analysis of the cases described in literature. Med Parazitol (Mosk) 1978;47(May–June (3))97–107 Russian. PubMed PMID:149906.

[10] Hildebrandt A, Gray JS, Hunfeld KP. Human babesiosis in Europe: what clinicians need to know. Infection 2013;41(December (6))1057–72, doi:http://dx.doi.org/10.1007/s15010-013-0526-8 PubMed PMID:24104943.