CASE REPORT

Babesiosis as a cause of false-positive HIV serology

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SUMMARY

This is a case of a 71-year-old homosexual man who presented with a 4-day history of fever, weakness and headaches, near syncope, nausea and poor oral intake. The patient denied recent travel or sick contacts but had significant tick bites in the last 4 weeks. A peripheral blood smear showed 0.5% parasitaemia with signet ring appearance organisms consistent with *Babesia microti*. Serology testing for HIV 1 and 2 by ELISA and western blot were positive. Treatment for *Babesia* was started and the patient improved. Repeat serology testing for HIV was negative. To the best of our knowledge, this is the first case of false-positive HIV serology that is associated with active babesiosis. In this case, the positive HIV serology turned negative after successful treatment of babesiosis.

BACKGROUND

Babesiosis is caused by *Babesia microti* and rarely by *Babesia divergens*. The *Ixodes* tick, the same vector that transmits *Borrelia burgdorferi*, the causative microbial agent of Lyme disease, transmits *B. microti*. Coinfection with Lyme disease and babesiosis has been reported.¹ Babesiosis has several clinical manifestations that include fever, progressive malaise, fatigue and weakness.² HIV infection can exacerbate the severity of Lyme disease or babesiosis. Since HIV is a risk factor for babesiosis, it is important to screen for HIV in patients presenting with babesiosis. False positive HIV serology can result from recently acquired infection with *Mycobacterium tuberculosis* or *Rickettsia* species, viral agents, influenza and hepatitis B vaccinations, autoimmune diseases and malignancy.^{3,4} A thorough understanding of other causes of false positive HIV testing is necessary for appropriate diagnostic and management decisions.

CASE PRESENTATION

We present a case of a 71-year-old homosexual man who presented with a 4-day history of fever, weakness, headaches and fatigue, near syncope, nausea and poor oral intake. The patient denied recent travel or sick contacts. Medical history was significant for tick bites as well as recent tooth infection, which was treated with amoxicillin. Physical examination was unremarkable with normal vitals. Skin examination did not reveal any skin rash or marks of tick bites.

INVESTIGATIONS

A complete blood count showed pancytopenia with bandemia. Liver function tests showed elevated aspartate transaminase.

Laboratory data: refer to [table 1](#) below for more information.

Chest radiograph and ECG were normal.

Serology testing for HIV 1 and 2 by ELISA and western blot were positive. A peripheral blood smear showed 0.5% parasitaemia with signet ring appearance organisms consistent with *B. microti*.

DIFFERENTIAL DIAGNOSIS

- ▶ anaplasmosis
- ▶ Babesiosis
- ▶ malaria
- ▶ HIV/AIDS
- ▶ Lyme disease.

TREATMENT, OUTCOME AND FOLLOW-UP

Treatment was initiated with intravenous fluids, atovaquone and azithromycin for 10 days, which resulted in complete clinical recovery. Repeat HIV serology were negative.

DISCUSSION

Babesiosis is a disease of animals, and it may infect humans.⁵ The causative agent is *B. microti*. Babesiosis may be a life-threatening infection in patients with reduced immunity including children, the elderly, transplant recipients and patients with HIV infection or cancer.⁶

False positive results of HIV testing have been widely reported and attributed to variety of causes. Some of those causes are:

- A. Human African trypanosomiasis (HAT) infection which could be related to direct cross-reacting between HAT and HIV antigens and/or the presence of high levels of polyclonal B-cell activation in early HAT infection.⁴
- B. Helminthic infections modulate and stimulate immune activation and may thereby constitute a risk for false positive reactions in diagnostic tests, including HIV tests.⁴
- C. Being infected with malaria has been reported to be associated with false positive HIV test.^{4,7}
- D. False positive HIV serology can result from recently acquired infection with *M. tuberculosis* or *Rickettsia* species, viral agents, influenza and hepatitis B vaccinations, autoimmune diseases and malignancy.^{3,4,8}

The patient is homosexual, which is considered a risk factor for HIV infection. A series of immune markers are assessed to evaluate for HIV infection. Initially, an 'eclipse phase' is observed in which HIV infection has not yet reached systemic circulation. This phase lasts about 10 days before lymphatic and systemic dissemination occurs. During early viraemia, HIV-1 RNA is measurable in the plasma. Within 7 days of initial HIV-1 RNA detection and

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Table 1 Laboratory data

Laboratory data	Admission date	Normal
White blood cells	3.0	4.2–10.2×10 ⁹ /L
Bands	18	0%–5%
Red blood cells	3.91	4.70–6.00×10 ¹² /L
Haemoglobin	11.2	13.5–18.00 g/dL
Haematocrit	33.1	42.0%–54.0%
Red cell distribution width	15.8	11.0%–15.0%
Platelets	76	140–450×10 ¹² /L
Atypical lymphocyte	1	0%–0%
Lymphocyte absolute count	0.5	1.1–4.6×10 ³ /μL
Lymphocyte per cent	15	25%–45%
Monocyte per cent	14	2%–12%
Alanine transaminase	36	7–52 IU/L
Aspartate transaminase	45	13–39 IU/L
Glucose	103	70–100 mg/dL
Blood urea nitrogen	16	7–25 mg/dL
Creatinine	1.14	0.70–1.30 mg/dL
Sodium	135	136–145 mmol/L
Potassium	4.1	3.5–5.1 mmol/L
Chloride	103	100–108 mmol/L
Venous total CO ₂	29	21–31 mmol/L
Calcium	8.2	8.6–10.2 mg/dL
Total protein	6.5	6.4–8.3 g/dL
GFR	67	>60 mL/min
Albumin	3.2	3.5–5.7 g/dL
Alkaline phosphatase	47	34–104 IU/L
Total bilirubin	1.3	0.2–1.1 mg/dL
Troponin I	<0.03	0.00–0.03 ng/mL
BNP	33	0–100 pg/mL

BNP, B-type natriuretic peptide; GFR, glomerular filtration rate.

once HIV-1 RNA levels have reached 10 000 copies/mL, levels of p24 antigen are detected. During this time period, the affected individual's immune system mounts a significant response to the acute infection. Approximately 5 days after p24 antigen detection, or about 3 weeks after initial HIV transmission, ELISA can detect IgM antibodies against HIV-1. Ten days after positive ELISA, a total of at least 1 month after initial HIV infection, western blot becomes positive.⁹

Western blot is not consistently reliable in the diagnosis of HIV. Western blot is considered positive when there is reactivity to at least one core protein (such as p24) along with one envelope protein (gp41 and gp120/gp160). An indeterminate western blot result is associated with a number of factors, including exposure to cross-reactive antibodies that develop from infection with viruses including Human T-Lymphotropic virus 1 or vaccination against hepatitis, rabies or influenza. Additionally, patients with a history of autoimmune disorders, multiple pregnancies, blood transfusions, malignancy or leprosy can demonstrate an indeterminate Western blot result. Cross-contamination is also an important factor to consider.¹⁰

It is known that *Babesia* and *Plasmodium* are phylogenetically similar and their serologies cross-react. The distinction between *Babesia* and *Plasmodium* infections by microscopic examination is difficult and requires extensive diagnostic experience. Microscopic examination, in most cases, does not allow the identification of the *Babesia* species.

Molecular studies are ordered by an infectious disease specialist in the case of a negative microscopic result to distinguish between *Plasmodium* and *Babesia*.

Learning points

- ▶ Babesiosis may result in a false positive HIV serology, which may convert to negative with successful treatment of babesiosis.
- ▶ Malaria is a known cause of false positive HIV serology.
- ▶ *Babesia* and *Plasmodium* are both protozoan parasites, which elicit a similar pathophysiology, signs and symptoms.
- ▶ Babesiosis can be a mild to life-threatening illness, depending on the level of parasitaemia and host defence factors. HIV infection and functional or anatomical asplenia are considered risk factors for severe babesiosis.
- ▶ Peripheral blood smear is a gold standard in diagnosing *Babesia*. PCR may be used in certain cases.
- ▶ The treatment of babesiosis includes: atovaquone and azithromycin for mild illness and clindamycin and quinine for severe illness. Some cases may require exchange transfusions.^{6 14}

False positive results of indirect immunofluorescence have been reported in patients with connective and autoimmune diseases, bacterial and viral infections and parasitic invasions, including in patients with *Toxoplasma gondii* and *Plasmodium* spp.

Cross-reactivity of *Babesia* antibodies were described in case of *Plasmodium* spp.¹¹

There is further evidence that Malaria and HIV serologies cross-react.¹² Since *Plasmodium* and *Babesia* are phylogenetically linked and their serologies cross-react, and malaria and HIV serologies cross-react, it is quite possible that *Babesia* and HIV serologies also cross-react. Ours is a case report suggesting the same.

The gold standard test in the diagnosis of babesiosis is examination of peripheral blood smear (Giemsa or Wright staining). PCR testing may be applied for accurate and rapid diagnosis in certain cases.¹³

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