

Laboratory-acquired blood-borne parasites from accidental exposure

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Received 28 November 2016

Accepted 4 February 2017

Journal of The Arab Society for Medical Research

2017, 12:1–5

Background

Infection caused by blood protozoa is becoming very common, especially in developed countries because of immunosuppressed persons and travelers. Therefore, this review aimed to illustrate the dangers of blood protozoa exposure among persons working in medical laboratories, especially when dealing with samples containing blood protozoa such as *Babesia*, *Leishmania*, *Plasmodium*, and *Trypanosoma* spp.

Conclusion

As protozoa multiply rapidly in humans even with a small inoculum, they can cause illness, in contrast to helminths. Diagnoses of infection can be confirmed through dermal scraping, examination of the stained slides by light microscopy, obtaining biopsy specimens for thin, stained smear, and needle aspiration for cultures of *Leishmania* spp. In addition, protocols should be provided for handling specimens that could carry viable organisms, using protective laboratory equipment.

Keywords:

african trypanosomiasis, babesiosis, chagas disease, laboratory infections, leishmaniasis, malaria

J Arab Soc Med Res 12:1–5

© 2017 Journal of The Arab Society for Medical Research
1687-4293

Introduction

Blood-borne parasites are found worldwide, and usually spend a certain part of their life cycle in the blood of the host. Blood-borne parasites may be transmitted in two ways according to the Centers for Disease Control and Prevention: parasites may be spread through infected blood during needle prick or blood transfusion, or they may also be transmitted by a vector such as an infected insect that bites a host and injects the parasites into the blood stream. Although rare in the USA, blood-borne parasites are responsible for thousands of deaths annually in developing countries [1].

Because of the renewed interest in parasitic diseases, increasing number of persons working in medical and laboratory studies are exposed to parasites. People working in laboratories are exposed to the dangers of acquiring parasitic infections [2]. The dangers of such infections are not defined [3]. A common survey of infections reported in 1976 [4] showed that 4079 laboratory-acquired infections due to 159 agents occurred. At least 173 deaths have resulted from laboratory-acquired infections from 1965 to 1979 [5,6].

According to this review, parasitic diseases that are frequently reported are babesiosis, leishmaniasis, malaria, and trypanosomiasis. Most of the laboratory workers who acquired blood-borne protozoan diseases felt that they were accidentally exposed to these parasites through their work in the laboratory.

Babesiosis

Babesia spp. infection is caused by bite of an infected tick, *Ixodes dammini* (*I. scapularis*), or by blood transfusion [7,8]. In the USA, human infection with *Babesia* is caused by *B. microti*. Other species of *Babesia* have been detected occasionally to cause infection in humans [9,10]. *Babesia* parasite causes destruction of red blood cells, and may cause hemolytic anemia. Diagnosis of babesiosis is based on medical history, exposure to endemic areas for babesiosis or ticks which carry the pathogen, and observation of clinical signs and symptoms [9].

The disease is most commonly diagnosed by examining a blood smear under a microscope for evidence of *Babesia* organisms in red blood cells [10,11]. Diagnosis can be confirmed accurately and rapidly by PCR [11]. *Babesia* spp. may be detected indirectly by serological methods, which provide supporting evidence of exposure to organisms and immune response through production of antibodies [12]. Most of the reported cases are due to tick bites in Europe, and have been caused by *Babesia divergens*. Cases of *Babesia* infection could be acquired through contact with infected ticks or blood from infected

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persons or animals [1]. The risk of becoming infected by ticks is relatively low because they can be controlled easily than mosquitoes in the laboratory.

Humans can also be accidentally infected with *Babesia* spp. [10,13]. The Food and Drug Administration [10,14,15] has reported that blood transfusion from an infected donor with *B. microti* is common. Moreover, *Babesia* can be transmitted congenitally [16]. Infection with *B. microti* can be prevented and treated with a combination of atovaquone and azithromycin or clindamycin and quinin.

Leishmaniasis

Leishmania spp. cause leishmaniasis. These organisms are transmitted through infected female phlebotomine sand flies [17]. Transmission can occur congenitally or by blood transfusion as well [7]. In the sand fly's midgut, the parasites differentiate into promastigotes, which multiply and migrate to the proboscis, and amastigotes multiply in infected cells (macrophages) and affect different tissues, depending in part on the *Leishmania* spp. Visceral leishmaniasis affects internal organs (spleen, bone marrow, and lymph nodes). Cutaneous leishmaniasis causes skin lesions that can persist for months or years and mucocutaneous lesions that involve the nasopharyngeal mucosa and can result in morbidity. Leishmaniasis can be acquired through direct contact with infected sand flies, contact with cultured parasites, or from infected persons or animals (accidental needle-stick injuries or through skin abrasions).

Laboratory technicians should handle blood specimens carefully, and guidelines for this have been reported in 1931 and 1950 [18–26]. Most of the infected persons develop lesions on the skin, and rarely visceral leishmaniasis. Infected cases are diagnosed by leishmanin skin test, Indirect Fluorescent Antibody Technique, Western blot analysis, and other tests.

Therapy for leishmaniasis

The concept of whether to treat primarily depends on the exposure of the technician to a species that can cause visceral leishmaniasis, and is complicated by the factor that the most effective therapy for leishmaniasis is given intravenously. Oral therapy available is miltefosine, as reported by Sundar *et al.* [27] for Indian visceral leishmaniasis. The authors reported that this drug is the most potent antileishmania agent currently in use.

Postaccidental management

Laboratorians who have been accidentally exposed to *Leishmania* spp. could be informed about the evidence

of infection. Skin lesions that develop near the site of exposure could be detected [17]. Serological examination periodically should be performed, especially when the organisms to which the person is exposed can cause visceral infection.

Malaria

Plasmodium spp. are transmitted through infected *Anopheles* mosquitoes, as well as congenitally and through blood transfusion [7]. Human infection is caused by *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium falciparum*, and *Plasmodium malariae*. Laboratorians can be infected accidentally through unexpected contact with an escaped mosquito from its colony. Laboratorians who dissect mosquitoes could be infected through subcutaneous injection of sporozoites or through contact with infected blood, from infected persons or animals, or from cultured parasites. Acquired malaria infection has been reported by Tarantala [28] following laboratory needle-stick injury. About 34 cases of *Plasmodium* spp. in laboratorian and workers in medical centers have been reported [29–42].

Most of the cases of *P. vivax* and *P. falciparum* infections occurred among healthcare and laboratory workers rather than among researchers, and resulted from needle-stick injuries that occurred when obtaining blood or preparing blood smears from patients [1].

Postaccidental management

Malaria infection should be expected in persons with unexplained febrile illness who might have been exposed to malaria parasites. A stained blood smear should be examined for the presence of parasites in the red blood cells. PCR and serological tests by Indirect Fluorescent Antibody Technique can be useful [1]. When prescribing treatment for confirmed cases, the identity of the infecting species and its drug susceptibilities should be considered. Generally, treatment is given when infection is confirmed. However, preliminary treatment may be indicated in special cases – for example, persons who cannot tolerate fever.

Treatment of malaria [43]

Artemisinin and its derivatives are prescribed for their potent antimalarial activity. They have found their way for clinical use in many cases where malaria is endemic. The in-vitro concentration at which artemisinin can inhibit 50% of the growth of *P. falciparum* ranges from 3 to 30 µg/1 ppm. The general approach for malaria

treatment is reported by Centers for Disease Control and Prevention [44].

Trypanosomiasis [45,46]

Trypanosoma cruzi [17] is the causative organism of Chagas disease. American trypanosomiasis is endemic in Latin America, and is transmitted by the *triatomine* bug belonging to the genera *Triatoma*, *Rhodnius*, and *Panstrongylus*. Infection occurs when feces of the *triatomine* bug containing infected metacyclic trypanosomes come in contact with wounds or the mucous membrane. Congenital transmission [47] and blood transfusion can also occur [7]. The parasite replicates in the mastigotes stage and differentiates into a trypomastigote, which is released when infected host cells are taken by the vector. The acute phase is asymptomatic and lasts for weeks to months. It can be associated with mild or nonspecific clinical manifestations. Laboratorians can become infected through exposure to the feces of infected *Triatomine* bug, by holding cultures or specimens from blood, infected individuals or animals, and sometimes by inhaling aerosolized organisms [48]. Although the more common stage of the parasite is in axenic cultures, the epimastigote stage is found as well. *T. cruzi* can infect persons through needle-stick injuries or pre-existing microabrasions in the skin. Clinical and epidemiological aspects of Chagas are reported in the study by Prata [49]. Laboratory-acquired infections have also been reported by Allain and colleagues [50–59].

A xenodiagnosis-confirmed case resulting from ocular mucosal contact with *triatomine* feces has been reported [60]. Thirteen days after exposure, the investigator reported pain and redness in the internal angle of the exposed eye. The next day, the patient developed ipsilateral palpebral edema, dacryocystitis, and increased tearing, malaise, and fever. Other manifestations included myalgia and edema of the ipsilateral cheek. A case report of accidental infection by *T. cruzi* followed-up by PCR was reported in 2009 [61].

Treatment of Chagas disease

Benznidazol and nifurtimox have been used with promising results in the acute stage of the disease; however, their side-effects limit their prolonged use in chronic cases [62]. The drugs are administered two to three times daily for 60 days.

African trypanosomiasis [63]

Sleeping sickness is a disease caused by African trypanosomes and transmitted by the vector *Glossina*.

It occurs in 36 sub-Saharan African countries where there are tsetse flies that transmit the disease. The disease is widespread in rural areas and it depends on cultivation, fishing, and hunting of animals.

Cases of laboratory-acquired infection have been reported previously [64–66]. Human African trypanosomiasis occurs in two forms depending on the parasite involved. *Trypanosoma brucei gambiense* is involved in more than 98% of reported cases. Diagnosis of the disease is complex and requires professionally trained staff.

There are three ways of transmission:

- (1) Mother to child infection: the trypanosomes can cross the placenta and infect the fetus.
- (2) Transmission mechanically through other blood-sucking insects.
- (3) Accidentally infection in laboratorians due to prick with contaminated needles.

In the first stage, the trypanosomes multiply in the subcutaneous tissues, blood, and lymph. This is called the hemolymphatic stage, which consists of bouts of fever, joint pain, headaches, and itching.

In the second stage, the parasites cross the blood–brain barrier to infect the brain. This is called the neurological stage. Clinical manifestations include changes of behavior, confusion, poor coordination, and sensory disturbances. Without treatment, sleeping sickness is considered fatal, although cases of healthy carriers have been reported.

Treatment of African trypanosomiasis [63]

Pentamidine (suramin) is used for the treatment of the first stage of *T. brucei gambiense*. Melarsopole is used for both *gambiense* and *rhodesiense* infections.

Control, prevention, and biosafety measures in relation to acquired parasitic infections

Studies on pathogenic agents, viruses, parasites, fungi, and genetically modified organisms have generated concern because of their potential biological risks not only for people but also for the environment. Because of unexpected behavior, biosafety is associated with the emergence of new diseases or re-emergence of diseases that were already under control [67]. Parasitic diseases have decreased in occurrence in recent years. They have increased again because of globalization of trade and travel [68]. Because of the increased interest in parasitic diseases, studies in both human and veterinary medicine are mainly directed

towards human health [69]. The potential exposure to parasites in the laboratory probably increases the danger for acquired parasitic infections. Parasitic laboratory-acquired infections such as malaria, leishmaniasis, trypanosomiasis, and diseases caused by other parasites have been reported [1]

Education and training of people working in laboratories are important for preventing laboratory accidents. As some parasitic diseases are characterized by a long asymptomatic period, laboratorians who work with parasites should be tested periodically [1]

Reports of accidental infections in both biotechnology and bioengineering laboratories are scarce compared with traditional microbiology and clinical laboratories [70–72].

Precautions to be taken include the following:

- (1) Cover any cuts or abrasions on the skin with impervious dressing.
- (2) Pipetting by mouth should be forbidden.
- (3) If blood spills occur, the surface should be soaked with hydrochloride solution and wiped with a cloth soaked with hydrochloride solution.
- (4) Handling of glassware should be carried out carefully.
- (5) Used microscope slides should be discarded.

Conclusion

Prevention of laboratory-acquired blood-borne infections is preferable to manage their consequences, especially when they are symptomatic and can be diagnosed by periodic serological testing or nonspecific clinical manifestations that are primarily overlooked. Congenital transmission is a potential risk factor. Laboratorians working with parasites should be aware that they may simultaneously be at risk for infections with viruses and bacteria. Although parasitic diseases are treatable generally, some infections are difficult to treat because of antimicrobial resistance and drug toxicity or advanced diseases – for example, mucosal leishmaniasis, chronic Chagas, cerebral malaria, and neurological complications of African trypanosomiasis or immunosuppression of the host. One fatal case of laboratory-acquired parasitic infections was reported in a person with myocarditis caused by acute Chagas' disease. To decrease accidental exposures, persons who are at risk for exposure to pathogenic parasites must be instructed about safe precautionary measures. Protocols

should be provided for handling specimens that could carry viable organisms, using protective laboratory equipment.

Financial support and sponsorship

Nil.

Conflicts of interest

There is no conflicts of interest.

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