Chagas Disease: Clear and Present Danger

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Chagas disease is a zoonotic disease caused by the parasitic protist Trypanosoma cruzi. T. cruzi is transmitted by blood-sucking triatomine insects. Other routes of infection include transfusion, vertical transmission, and contaminated food or drink, such as fresh fruit juice. Chagas disease is only endemic in the Americas, due exclusively to the limited distribution of the insect vectors, whereas a number of patients have been found outside the Americas, particularly among Latin American immigrants. In August 14, 2013, the Japanese Red Cross Society and the Ministry of Health, Labour and Welfare of Japan announced that one blood donor from Latin America had been found to be seropositive for T. cruzi and that blood products prepared from the donated blood had already been delivered to medical institutions. Although later reports denied the occurrence of secondary infection through those blood products, Chagas disease has now become a reality in Japan. Thus, further monitoring and preparedness for Chagas disease are necessary.

Key words: Chagas disease, Trypanosoma cruzi, reduviid bugs, transfusion, zoonosis

Overview

Chagas disease, or American trypanosomiasis, is endemic in Central and Latin American countries and affects 10 million people with more than 10,000 annual deaths1). The parasitic protist, Trypanosoma cruzi, is a pathogen of Chagas disease and infects not only human but also many mammalian species, representing typical zoonosis.

Transmission

T. cruzi is transmitted by the insect vector, blood-sucking triatomine bugs (Figure-1). The bugs feed blood during our sleep and defecate on site; feces of infected bugs contain an infective form of T. cruzi, metacyclic trypomastigote, and the excreted parasites invade via wound skin, conjunctivae, and mucosal membranes. Metacyclic trypomastigote infects the host cell and transforms to a replicative form, amastigote. Amastigote multiples in the host-cell cytoplasm and transforms back to infective, non-dividing trypomastigotes after suc-
cessive multiplications. Trypomastigote appears in the circulation accompanied with destruction of the host cells, followed by the next infection-proliferation cycle. Therefore, the disease manifestation is associated with irreversible damages of the vital organs, such as heart, caused by the infection.

Infection also occurs through the direct transfer of blood-circulating trypomastigotes or parasitized cells; transfusion and transplantation are at risk of infection. Congenital (placental) infection is often seen in a newborn baby from an infected mother.2) Another serious concern is the oral infection via contaminated foods and beverages.3) Fresh juice prepared from fruits, such as guava and açai palm, appears an important source. The outbreaks of oral infection have been reported in Brazil, Argentina, Bolivia, Colombia, Ecuador, and Venezuela.2)

Clinical course

Manifestation and progress of Chagas disease are complex. In the acute phase, erythema and swelling, called Chagoma, may appear at the site of infection. Infection via conjunctiva may cause unilateral painless edema surrounding eye, called Romaña’s sign. Systemic expansion of the parasite (weeks after infection) may lead to malaise, fever, and anorexia. The acute phase is often obscure and confused with common infectious diseases. Myocarditis rarely occurs in the acute phase, but becomes a main cause of death.

Almost all patients enter the indeterminate (asymptomatic) phase and only 10–30% of the patients develop chronic symptoms years to decades after infection. Manifestation of the chronic phase includes heart failure, such as arrhythmia, cardiomyopathy, and thromboembolism, and mega-colon/megaesophagus (called megadisease) caused by the severe impairment of gastrointestinal peristalsis. Importantly, the clinical course of Chagas disease varies extensively patient by patient; some may develop severe acute syndromes leading to death within months, whereas others can live out their natural life. Thus, prognosis of Chagas disease is unpredictable.

Diagnosis and treatment

Acute Chagas disease should be diagnosed by the detection of trypomastigotes circulating in the blood. Trypomastigotes can be detected in the Giemsa-stained blood smears oruffy coat concentrated in the micro haematocrit tube. Alternatively, detection of the parasite DNA in the blood samples using PCR is useful. Serodiagnosis by the detection of specific antibodies to the parasite antigens is helpful, however, false-positive reactions may occur and the seronegative does not necessarily mean the absence of the parasites in the very acute phase. On the other hand, chronic Chagas disease is diagnosed by the detection of the parasite-specific antibodies, because trypomastigotes may be undetectable. Because the organic insult to the parasitized tissues has already progressed in the chronic phase, the palliative therapy rather than the parasiticidal treatment is needed.

Unfortunately, chemotherapy is unsatisfactory. Two drugs, benznidazole and nifurtimox, are currently available but not a silver bullet. Both drugs are effective in the acute infection, however, their efficacy is rather limited particularly in the chronic infection. Furthermore, severe side effects including rash, peripheral neuropathy for benznidazole and anorexia, nausea, vomiting, weight loss, and abdominal pain for nifurtimox may appear, which often results in discontinuation of chemotherapy. Chemotherapeutic treatment of asymptomatic or chronic Chagas disease is still a matter of debate, because the cure rates in these phases are considerably inferior to the acute phase. In Bolivia, chemotherapy is only conducted in the chronic patients who possess the parasites in the blood (personal communication).

Current situation of Chagas disease in Japan

Because the occurrence of the domestic life cycle of triatomine bugs is not officially reported in Japan, Latin American immigrants and their offspring are typically the risk group. Historically, many Japanese have settled in Latin America, especially in Brazil, Peru, and Bolivia, before and after the World War II. Today, about 300,000 immigrants live in Japan, of which the majority is the Japanese diaspora (Nikkei) from Brazil. Although the epidemiological data for the Chagas disease is limited in Japan, Miura et al. reported that 15 seropositive cases were detected among 1,108
下記1～3のいずれかに該当する方は、献血の受付時にご申告をお願いいたします。

1. 中南米諸国で生まれた、又は育った。
2. 母親が、中南米諸国で生まれた、又は育った。
3. 上記1に該当しない方で、中南米諸国に通算4週間以上滞在した。

※シャガス病の安全対策のため、いただいた血液は、血漿分画製剤用の原料血漿として利用させていただきます。

【中南米地域対象国・地域】
- アルゼンチン
- パラグアイ
- ブラジル
- ベネズエラ
- ゴアテマラ
- ベルリン
- コスタリカ
- ポルトガル
- ポトゥス
- エルサルバドル
- サンルイス
- チリ
- フランス領ギアナ
- フォントランヌ諸島（英領）

※シャガス病とは、メキシコを含む中南米に流行地をもつマサゴム（激症）に類似されて、急性が続発する病気です。
日本には中南米諸国から来たあとが20～30万いると推定されており、5年、そのうちの1人にシャガス病の感染者がいることが指摘されています。
この度、国の調査において、輸入によるシャガス病に対する安全対策の方針が示されました。

Figure-2 Notification by the Japanese Red Cross Society (JRC) for blood donors at risk of Chagas disease, who were born or grown in Latin America, whose mother is Latin American, or who stayed for more than 4 weeks in Latin American countries. A corresponding person is requested to proffer and the donated blood will be only utilized for blood plasma products. This article is reproduced under the permission of JRC and appears in the following website: http://www.jrc.or.jp/vcms_if/ketsueki_20121002_sha-gasu.pdf.
immigrants (1.35%) using the commercially available detection kits. In addition, 16 of the 42 immigrants, who had circulatory disturbances and were asked for further parasitological tests by Japanese medical institutions, were diagnosed to be chronic Chagas disease by the antibody detection; among them, 5 cases were positive for the T. cruzi DNA by PCR and 3 of the 5 cases were confirmed to be parasite-positive by haemoculture.

In Latin America, screening of donated blood against Chagas disease by the detection of antibodies to T. cruzi has been conducted to minimize risks of the parasite transmission. U.S. Government approved serodiagnostic kits for Chagas disease in January 2007 and U.S. blood donors are being screened. In Japan, screening of blood donors for blood-transmitted parasitic diseases, such as Chagas disease, African trypanosomiasis (see below), and malaria, is also compulsory under the regulation of the Japanese Red Cross Society (JRC); however, it was not a reality. In August 14 2013, JRC and the Ministry of Health, Labour and Welfare of Japan announced that one blood donor originated from Latin America was found to be seropositive, suggesting the chronic patient of Chagas disease. This patient had already donated blood 9 times and these blood products had been delivered to 8 medical institutions and used for at least 10 recipients. Fortunately, there was no secondary infection investigated so far. After this accident, JRC began to ask Latin American immigrants and the person who have stayed more than four weeks (in total) in Latin American countries to fill out a questionnaire about Chagas disease (Figure-2).

Chagas disease as a “Neglected Tropical Disease”

As well as other trypanosomiasis such as African trypanosomiasis (sleeping sickness) and cutaneous/visceral leishmaniasis, Chagas disease is classified as “Neglected Tropical Diseases (NTDs)”1. In a broad sense, these parasitic diseases can be regarded as “poor man’s diseases”, because they are endemic in the developing countries. In a limited sense, more importantly, the term NTDs represents “the diseases without drugs”, because these diseases had long been neglected by the governments and pharmaceutical companies of the developed countries, especially from an economical reason. Indeed, benznidazole and nifurtimox have been used for more than 50 years. Thus, the development of new drugs under the initiative of non-profit organizations and foundations in collaboration with universities and research institutes is urgently requested against all of NTDs.

Conclusion

In Japan, Chagas disease cannot be considered a fire on the other side of the river. Although monitoring of the blood donated by Latin American immigrants has just begun, further preparedness is certainly required. For example, Chagas disease is regarded as a death disease, like AIDS, in the endemic area and therefore, not only clinical cares but also mental and financial cares for both patient and the family are absolutely necessary.

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References