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Identifying Chagas disease in Australia: an emerging challenge for general practitioners

Background

Chagas disease, a parasitic infection by *Trypanosoma cruzi*, is endemic in Latin America and affects 8–10 million people. It is a major emerging infection in Europe and the USA. The routes of transmission include congenital, vectorial means and through unscreened blood or organ donation. Potentially fatal complications include cardiomyopathy with conduction abnormality, arrhythmia, thromboembolic cerebrovascular events and digestive tract involvement (mega-syndrome).

Objective

We describe a case, the second reported in Australia, and provide readers with updated guidelines on the clinical management of Chagas disease.

Discussion

Treatment affords optimal results when applied early in the course of the disease. General practitioners are best placed to play a central part in the early identification and referral of infected individuals. Indeed, the decades-long asymptomatic latent period between infection and overt clinical manifestation provides an ideal context for screening and implementation of early effective interventions.

Keywords

tropical medicine; communicable /infectious diseases

Question 2

How is it transmitted?

Question 3

What are the clinical features and complications?

Question 4

As her GP, what would you do next?

Answer 1

Chagas disease, an infection by the protozoan parasite *Trypanosoma cruzi*, is endemic in Central and South America, affecting 8–10 million people.¹ Endemic countries include Argentina, Belize, Bolivia, Brazil, Chile, Columbia, Costa Rica, Ecuador, El Salvador, French Guiana, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay and Venezuela. In Europe and the USA there are 80–120,000 and 300–500,000 cases, respectively. This infection incurs high costs, given its chronicity and the need for complex interventions. In Australia there were 116,430 persons born in endemic regions in 2011, a 46% increase since 1997, not including adoptees, visitors or second-generation immigrants.^{2,3} Epidemiological models suggest that 2000–3000 persons could be infected but 95% of cases remain undiagnosed.^{3–5} Reflecting this underdiagnosis and lack of awareness, only two cases have been reported in Australia, illustrating the wide spectrum of disease, which ranges from a long asymptomatic period to end-stage cardiac complications.⁶

Answer 2

In endemic rural regions, transmission is vectorial via the triatomine bug, whereas in Australia, potential modes include congenital, blood transfusion or organ transplantation. Congenital transmission occurs in 5% of pregnancies and is

Case

A nulliparous Chilean-born woman aged 43 years recently returned from a 7-week trip to Chile, Peru and Uruguay to visit family and friends. During her visit she had a 1-day diarrhoeal illness. She presented to her general practitioner (GP) with intermittent constipation, band-like abdominal pain and vomiting for several months. She also described intermittent unilateral eye swelling associated with mild conjunctivitis and a transient erythematous skin rash. She mentioned that Chagas disease had affected four siblings.

Question 1

What is Chagas disease and where does it occur?

the main source of transmission in non-endemic regions.⁷ Cases in travellers are rare.

Answer 3

After exposure, symptoms of the acute phase can appear within 1–2 weeks for vectorial transmission or months later for blood transfusion transmissions. Commonly asymptomatic, it may include fever, hepatosplenomegaly, lymphadenopathy or mucosal oedema at the portal of entry.⁸ In severe cases, symptoms can include myocarditis or meningoencephalitis, entailing high fatality rates. Patients treated at the acute stage can be cured.⁹ Without treatment, progress to the chronic indeterminate form is characterised by positive serology, no end-organ manifestations and a normal ECG.⁸ This decades-long asymptomatic phase is ideal for screening and early therapeutic intervention. Subsequently, 30–40% cases will develop complications.

Chronic cardiomyopathy is the most severe and frequent complication. It consists of a fibrosing myocarditis leading to a dilated form of conduction abnormalities, arrhythmia and ventricular failure.⁸ Aneurysmal dilatation of the apex may lead to cerebrovascular

thromboembolic events. Symptoms include effort intolerance, palpitations, dizziness or syncope. Early ECG abnormalities include right bundle-branch block, left anterior fascicular block, ST changes, premature ventricular beats and bradycardia.¹⁰

The digestive form is characterised by progressive dysmotility and organ dilatation (megaesophagus, megacolon). Patients report dysphagia and constipation. Atypical presentations can occur in immunosuppressed patients.^{8,9,11} Congenital infection manifests as prematurity, low birthweight, hypotonicity, fever, hepatosplenomegaly or anaemia.

Answer 4

The mainstay in the diagnosis of chronic Chagas disease is serology, which should be confirmed by a second method in a reference laboratory because of cross-reactivity.¹² In Australia, serology and microscopy are offered by the Institute for Clinical Pathology and Medical Research, Pathology West.

Diagnosis of acute infection relies on microscopy and delayed (4–6 weeks) serology if the initial test is negative. Congenital diagnosis

requires microscopic (and possibly PCR) cord or peripheral blood examination at birth, followed by serology at 9 months of age if the initial tests are negative.¹³ Staging requires a 12-lead ECG with a 30-second DII strip and, if abnormal, echocardiography and 24-hour Holter monitoring; prognosis is assessed by risk score.¹⁴ The presence of gastrointestinal symptoms warrants barium contrast studies. Issues to consider as part of management are other cardiovascular risk factors, co-infections and underlying immunosuppression.

Case continued

The patient's GP referred her to an infectious diseases unit for further investigations. Her serology by two methods was positive for Chagas disease and negative for HIV. She had a normal ECG and 24-hour Holter. Barium swallow, gastroscopy and colonoscopy were normal, as was ophthalmology review. This confirmed indeterminate-stage Chagas disease and after counselling about benefits, side effects and rationale for treatment, she received a 60-day course of benznidazole, which was well tolerated.

Table 1. Antiparasitic treatment recommendations

Should always be offered	Should generally be offered	Optional	Should generally not be offered	Should never be offered
<ul style="list-style-type: none"> • Acute infection • Congenital transmission to the newborn • Children up to 18 years • Reactivation in case of immunosuppression 	<ul style="list-style-type: none"> • Reproductive age women • Adults 19–50 years with indeterminate form, mild or moderate cardiomyopathy • Impending immunosuppression 	<ul style="list-style-type: none"> • Adults over 50 years without advanced cardiomyopathy • Gastrointestinal tract disease but without advanced cardiomyopathy 	<ul style="list-style-type: none"> • Advanced cardiomyopathy with congestive heart failure • Megaesophagus with swallowing impairment 	<ul style="list-style-type: none"> • Pregnancy • Severe renal or hepatic insufficiency
Treatment options (60 days) <ul style="list-style-type: none"> – benznidazole 5 mg/kg/day in 2–3 doses (maximum 300 mg/day) in adults and 5–10 mg/kg/day in 2–3 divided doses in children – nifurtimox 8–10 mg/kg/day in 3 doses in adults and up to 15 mg/kg/day in 3 divided doses in children 				
Monitoring during treatment <ul style="list-style-type: none"> – Days 7, 21, 60 or in case of adverse event – Clinical examination, full blood count, serum creatinine, aspartate aminotransferase, alanine aminotransferase 				
Post-treatment follow up <ul style="list-style-type: none"> – Serology after 1 year (children) and 2–5 years (adults) – Cardiac and digestive history, 12-lead ECG with a 30-second DII strip annually – No blood donation – Full diagnostic work-up in newborn if mother is seropositive 				

Question 5

Who should be tested for Chagas disease?

Question 6

What are the therapeutic aims and options?

Answer 5

Chagas disease serology should be performed in:

- people born or who have lived in a Chagas endemic area (including expatriates and long-term travellers (defined as ≥ 6 months) in endemic countries)
- people with a positive family history
- those who received a blood transfusion or organ/tissue donation in Latin America
- children born to mothers from an endemic country
- pregnant women with any of the above risk factors
- those of Latin American origin presenting with suggestive cardiac or digestive signs and symptoms.

Investigating the family/community of an index case is recommended given the frequently shared risk factors.¹⁵ Yearly follow up of cases to assess treatment eligibility and monitor for development of complications forms an important part of management.

Answer 6

Treatment is aimed at slowing or preventing cardiac disease progression.¹⁶ Benznidazole and nifurtimox, the drugs with proven efficacy, are not approved by the Therapeutic Goods Administration (TGA) but can be obtained via the Special Access Scheme. Treatment should be provided in a specialist setting. However, GPs should be aware of the side effects of the drugs, including cutaneous, digestive, musculoskeletal, neurological and haematological disorders;^{8,9,17} close clinical monitoring is required. The recommended treatment duration is 60 days with benznidazole as first-line treatment given its better tolerance.¹⁷ *Table 1* summarises the recommendations. Positive cases should be counselled not to donate blood and contact tracing of family members should be performed. Yearly follow up is warranted for monitoring of long-term cardiac and gastrointestinal complications. The lack of a test of cure represents a challenge for follow up.

Key points

- Chagas disease is an emerging disease in Australia.
- GPs are best placed to offer opportunistic Chagas disease screening to those at risk from endemic regions as they are likely to be the first point of contact.
- Long-term clinical consequences include potentially fatal dilated cardiomyopathy and gastrointestinal dysmotility, and vertical transmission in pregnant women.
- Treatment should be undertaken in a specialist unit with the GP as an intrinsic part of the coordinated care.

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