

## LETTERS TO THE EDITOR

**Clinical-scientific notes****Symptomatic hypereosinophilia associated with *Necator americanus* self-inoculation**

A 2006 systematic review found that, in populations with endemic hookworm infection, there was a reduction in long-term asthma risk in those who were infected, compared with those who were not.<sup>1</sup> However, no benefit of helminthic therapy in previously uninfected patients with asthma and other allergic diseases has been demonstrated in several studies.<sup>2</sup> A 2012 Cochrane review of helminthic therapy for allergic rhinitis showed no significant reduction in overall medication use, although there was less use of rescue medication in one study using pig whipworm.<sup>3</sup> Despite this lack of evidence, the treatment is marketed online for a plethora of autoimmune, inflammatory and uncategorised conditions. As a cautionary tale, we present here the first report of organ damage due to hypereosinophilia after deliberate helminth infection used in an attempt to modulate allergic symptoms.

A man in his early 60s presented to an Emergency Department with palpitations and was found to have atrial fibrillation with a ventricular rate of 120–180 bpm. Reversion to sinus rhythm occurred after treatment with adenosine. He had a mild elevation in troponin I of 0.75 µg/L (<0.03), which remained stable on serial measures and was presumed to be secondary to the arrhythmia. A chest radiograph revealed a small left pleural effusion with ipsilateral lower zone patchy peri-bronchial infiltrates. He was stable overnight with cardiac monitoring and discharged home with beta-blocker therapy, and cephalexin for presumed mild community-acquired pneumonia. Three days later, the patient experienced new progressive retrosternal chest pain associated with malaise, and re-presented to the Emergency Department. Arrhythmia did not recur; however, electrocardiography revealed new T-wave inversion with ST segment depression in leads V3–V4. Plasma troponin I was now elevated to 1.9 µg/L (<0.03), and infiltrates remained present on chest radiography.

The patient was transferred to our tertiary referral hospital for coronary angiogram and commenced dual antiplatelet therapy for presumptive acute coronary syndrome with intravenous ceftriaxone and oral doxycycline for a concomitant provisional diagnosis of community-acquired pneumonia. However, the coronary angiogram showed normal coronary arteries and

left ventricular function. An echocardiogram performed at this time showed normal LV size and systolic function, normal RV size and systolic function, and borderline left atrial enlargement.

At this stage a persistent eosinophilia ( $\approx 10 \times 10^9/L$  (<0.7)), present since his first presentation, was noted. Further questioning revealed the patient had self-initiated inoculation with *Necator americanus* (New World hookworm) parasites, obtained online, to treat his asthma and allergic rhinitis. Inoculation was performed three times transdermally according to the supplier's advice: an initial dose of 35 parasites 9 months prior to presentation, a second dose of 50 parasites 4 months prior, and most recently 50 parasites 7 weeks prior. His pretreatment IgE was 248 kU/L (<100) and eosinophil count 0.6–1.15  $\times 10^9/L$ , last measured 9 months prior to his current presentation. Other relevant test results at presentation are shown in Table 1.

A provisional diagnosis of eosinophilic damage to the myocardium and Loeffler's syndrome affecting the lungs (rather than a community-acquired pneumonia) was made. An acute eosinophilic myocarditis was the presumed cause of the elevated troponin level and arrhythmias seen in this patient. Other differential diagnoses considered included eosinophilic granulomatosis with polyangiitis – previously known as Churg-Strauss syndrome – (due to the patient's history of asthma, sinusitis and nasal polypectomy 3 years prior), idiopathic hypereosinophilia, and an eosinophilia secondary to a haematological malignancy. As shown in Table 1, tests relevant to these diagnoses were negative. There was no other past medical history, and prior to presentation the patient was taking only medications for asthma and sinusitis. There was no recent history of travel but 30 years prior the patient had been treated for a parasitic gastrointestinal infestation while working in the Northern Territory, Australia. At that time, he had also travelled extensively around Asia and Europe.

At the time of this presentation, he had no gastrointestinal symptoms and stool cultures were negative (collected within 72 h of treatment commencement). His equivocal and subsequent positive *Strongyloides* serology was attributed to cross-reactivity with hookworm with the *Strongyloides ratti* L3 larvae crude extract used in the enzyme immunoassay test (personal communication with testing laboratory). The Harada-Mori

**Table 1** Blood test results at presentation

FBC	Hb <b>122</b> g/L (135–180), WCC <b>19.8</b> × 10 <sup>9</sup> /L (4–11), Eosinophils <b>9.88</b> × 10 <sup>9</sup> /L (0–0.7), Neutrophils 7 × 10 <sup>9</sup> /L (1.8–7.5), platelets 341 × 10 <sup>9</sup> /L (150–400)
EUC	Normal
LFT	Normal
ESR	20 mm/h (<30)
CRP	<b>10.2</b> mg/L (<5.0)
B and T cell subsets	Normal
ANCA	Not detected
ANA	1:80 titre, speckled pattern
ENA	Negative
Anti-dsDNA	4 IU/mL (<40 IU/mL)
Complement levels	C3 1.14 g/L (0.82–1.85); C4 0.20 g/L (0.14–0.42)
IgE level	<b>359</b> kU/L (<100)
Other immunoglobulin levels	IgG, 14.6 g/L (7–16); IgA, 1.53 g/L (0.70–4.00); IgM, 0.8 g/L (0.4–2.3)
Tryptase	7.1 µg/L (0.0–11.4)
Strongyloides serology (UgG ratio)	At presentation: <b>1.06</b> , indeterminate (<0.80, negative), 6 months post presentation: <b>2.25</b>
Stool ova, cysts and parasite examination	Negative × 3
Harada-Mori fresh stool examination	Negative × 3
HIV	Not detected

Bold indicates values outside the normal range. ANA, anti-nuclear antibodies; ANCA, anti-neutrophil cytoplasmic antibodies; CRP, C-reactive protein; dsDNA, double-stranded DNA; ENA, extractable nuclear antigens; ESR, erythrocyte sedimentation ratio; EUC, electrolytes urea creatinine; FBC, full blood count; Hb, haemoglobin; HIV, human immunodeficiency virus; LFT, liver function tests; WCC, white cell count.

technique was used as a more sensitive examination for the presence of *Strongyloides* and was negative.<sup>4</sup>

Given the potentially fatal condition of eosinophilic myocarditis<sup>5</sup> and that an endomyocardial biopsy for definitive diagnosis of the condition was not immediately available, we decided to treat the patient presumptively with albendazole and a short course of prednisolone tapering from 25 mg to lower acutely the eosinophil count to prevent further damage. Echocardiography is typically normal during the early, necrotic stage of eosinophilic myocarditis,<sup>6</sup> and so we did not feel that the relatively normal echocardiography negated our provisional diagnosis. The pulmonary infiltrates, symptomatic chest pain and eosinophilia promptly resolved over 2 days. Twelve months after his initial presentation, the patient remains well, has a normal eosinophil count and there has been no long-lasting cardiac damage.


An inoculum of 10 *N. americanus* larvae has been shown to give the level of infection seen in epidemiological studies.<sup>7</sup> Although this level of inoculum failed to show significant benefits for asthma control, a study did demonstrate eosinophil counts of up to 8.5 × 10<sup>9</sup>/L without serious side-effects at 12 weeks of follow up, at which time the infection was eradicated.<sup>8</sup> There are no other reports in the literature of organ-damaging eosinophilia after helminthic therapy to our knowledge. This is in contrast to our patient who took a significantly larger

number of larvae and over a longer time, possibly accounting for the serious adverse events seen in this case. Our case highlights the importance of recent research to identify particular proteins secreted by helminths that may have an immune modulatory effect without requiring infection with the helminths themselves.<sup>9</sup> It also serves as a caution and highlights the potential harms of helminthic treatment when hypereosinophilia results.

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