Trichinella pseudospiralis in humans: description of a case and its treatment*

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Abstract
The first known human case of *Trichinella pseudospiralis* myositis is described. A 33 years old woman reported 5 years of relatively mild symptoms of tiredness, muscle fatigue and muscle pain after exercise. She had minimal proximal weakness. Creatinine kinase was significantly elevated, and muscle biopsy showed polymyositis and *Trichinella* larvae. Steroid treatment dramatically worsened the weakness. Treatment with albendazole led to complete resolution of symptoms and laboratory abnormalities. Diagnosis and identification of the parasite were based on the distinctive appearance of the unencapsulated larvae and their movement in fresh muscle, plus clinical and laboratory findings.

Introduction
*Trichinella pseudospiralis* was described by Garkavi (1972) from the raccoon (*Procyon lotor*), and is characterized principally by the lack of encapsulation of its larval stage, allowing freedom of larval movement in and between the muscle cell. Recent opinion very strongly favours the separation of *Trichinella* into 5 species (Pozzo et al., 1992), of which *T. pseudospiralis* is the only one that has not previously been recorded from humans. Successful experimental infections in monkeys have supported the likelihood that *T. pseudospiralis* infection might be as dangerous to humans as the classical *T. spiralis* infection (Pawlowski & Rüttenberg, 1978; Teppema et al., 1981).

Case report
The patient was a 33 years old physically fit English woman. She carried out botanical fieldwork in many European countries, Indonesia, and Kenya up to 1979. During 1980–1985 she worked in Australia, mainly Tasmania, but briefly visited other Australian states. Following a visit to the United Kingdom in mid July 1985 she moved to Dunedin, New Zealand, in September. A year later she first sought medical attention because of episodic of racing heart and palpitations, which lasted several weeks and interfered with her sleep. Examination showed no tachycardia. Routine blood tests (28 October 1986) showed a mild disturbance of transaminases and mild eosinophilia (Table). During 1987–1988 she worked in the Northern Territory of Australia, where, in the tropical heat, she began to have fluctuating abnormal physical tiredness, and debilitating mental fatigue with periods 2 or 3 times per year lasting several days.

She next sought medical advice in Wellington, New Zealand (11 August 1989), again complaining of a racing heart and tiredness. The transaminases were elevated, and a glandular fever-like illness was suspected. The transaminases were still elevated in 1990, but other indices of liver function (albumin and prothrombin time) were normal. The eosinophil count was also normal.

Liver biopsy in 1990 showed mild perportal inflammation. Low-dose prednisone for presumed chronic hepatitis was begun. While visiting the United Kingdom she consulted a gastroenterologist. Her creatinine kinase (CK) level was found to be significantly elevated (3253

Table. Selected haematological data for a patient infected with *Trichinella pseudospiralis*, 1986 to 1992

<table>
<thead>
<tr>
<th>Date</th>
<th>Aspartate Alkaline Creatinine Alkaline Bilirubin Eosinophils</th>
<th>Aspartate Alkaline (15–30 IU/L) (20–200 IU/L) (5–50 IU/L) (2–5 my/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.10.86</td>
<td>82 99</td>
<td>34 13</td>
</tr>
<tr>
<td>11.8.89</td>
<td>138 136</td>
<td>9 9 0 2 × 10⁹</td>
</tr>
<tr>
<td>4.4.89</td>
<td>92 92</td>
<td>31 11 0</td>
</tr>
<tr>
<td>19.6.90</td>
<td>186 191</td>
<td>1148 48 0</td>
</tr>
<tr>
<td>8.5.90</td>
<td>225 269</td>
<td>3253 7 0</td>
</tr>
<tr>
<td>17.6.91</td>
<td>228 324</td>
<td>5436 7 0 0 47 × 10⁹</td>
</tr>
<tr>
<td>17.7.91</td>
<td>228 324</td>
<td>5436 7 0 47 × 10⁹</td>
</tr>
<tr>
<td>30.10.91</td>
<td>298 3054</td>
<td>7 0 47 × 10⁹</td>
</tr>
<tr>
<td>24.1.92</td>
<td>3532</td>
<td>7 0 47 × 10⁹</td>
</tr>
<tr>
<td>2.11.92</td>
<td>134</td>
<td>12 0 47 × 10⁹</td>
</tr>
<tr>
<td>4.11.92</td>
<td>1450</td>
<td>12 0 47 × 10⁹</td>
</tr>
<tr>
<td>16.11.92</td>
<td>385</td>
<td>0 0</td>
</tr>
<tr>
<td>23.11.92</td>
<td>142</td>
<td>0 0</td>
</tr>
<tr>
<td>4.12.92</td>
<td>141</td>
<td>0 0</td>
</tr>
</tbody>
</table>

(Decrease in eosinophils) (Normal range and units in parentheses.)

Although *T. pseudospiralis* has a sylvatic life cycle favouring small wild predators, rodents, and raptorial birds as its hosts, domestic pigs have been successfully infected experimentally, thus suggesting a more accessible route by which humans could become infected (Garkavi, 1972; Pawlowski & Rüttenberg, 1978; Obendorf et al., 1990).

Thus it seemed that eventually a human case would be discovered, and notice of the first such case was given recently (Andrews et al., 1993). The present paper describes more fully the characteristics of this infection and its treatment.

All 5 known species of *Trichinella* have now been found in humans, with each species presenting a different clinical picture (Pozzo et al., 1992). This, together with the identification of species-distinctive geographical distributions and life cycles (Campbell, 1988), makes it necessary to distinguish the various disease types at present embraced by the generic term 'trichinosis'. Therefore, in the interests of clarity, we have adopted the terms 'spiralis-trichinosis' and 'pseudospiralis-trichinosis' in this paper.

iu/L), and the steroids were stopped. Once attention was directed to a possible muscle problem she recollected easy tiring of leg muscles on exertion and intermittent aches in the quadriceps and calves lasting several days. Similar symptoms had occurred in her biceps and forearms. By the time of her return to New Zealand she had developed some slight swelling problems and, for the first time, fatigue walking on the flat.

Further investigations (17 June 1991), performed in Dunedin, New Zealand, included an electromyogram, which showed fibrillations and small polyphasic units suggestive of myasthenia. A deltoid muscle biopsy showed polyclonal activation of CK levels increased (5436 iu/L).

On return to Wellington she was referred to one of the authors (D.A.) for treatment. Clinical examination showed minimal weakness of shoulder abduction, but was otherwise normal. Prednisone, 40 mg/d, was begun for the myositis (27 June 1991). After an initial improvement, weakness increased, reaching a peak when she was unable to squat or perform a sit-up, and she had increasing difficulty swallowing. Myasthenia gravis was considered and prednisone was reduced to 20 mg/d.

However, a Tensilon test and repetitive stimulation on 2 October 1991 were negative. The prednisone was increased to 80 mg/d (8 October 1991), with little change. Azathioprine was begun (30 October 1991), but one month later it was clear that immunosuppressive therapy had unaccountably worsened her condition. All treatment was stopped and a few days later she developed a hot, red, raised, itchy rash over her face, neck, and upper body, which lasted 10 d. Two months after stopping treatment she had no significant weakness.

Further review showed probable Trichinella spiralis larvae, in addition to myositis. The worsening after steroids suggested an infectious process, and the biopsy was referred to 2 of the authors of this paper (J.R.H.A. and D.A.), who noted the elongated form of the larvae and their lack of encapsulation. Larval migration through the muscle cytoplasm at the time of fixation was inferred. These features led the authors, in consultation with Dr D. A. Denham (personal communication), to suspect pseudospiralis-trichinosis. A further muscle biopsy, examined fresh, revealed unencapsulated mobile larvae, and confirmed the diagnosis.

On the basis of this diagnosis the patient was admitted to hospital (2 November 1992) and given albendazole, 400 mg q.d. and prednisone, 40 mg/d. Prednisone was discontinued. On 5 November 1992 the albendazole was increased to 800 mg/d, taken in 2 doses. This treatment continued for 4 weeks, followed by a gap of one week, then recommenced for a further month. The patient remained well and the CK levels declined sharply to normal (Table). Although she reported a return to a feeling of well-being, she experienced some ache in her leg muscles for at least 4 months following treatment. No side effect of albendazole was noticed or reported.

Materials and Methods

Muscle tissue from the first biopsy (18 June 1991) was sectioned by the Pathology Laboratory, Dunedin Hospital, New Zealand, and sections were stained with haematoxylin and eosin or with trichrome. We examined fresh muscle tissue from the second biopsy (8 October 1992) by teasing fibres in ResDel® mammalian saline, followed by examination under a compound microscope for Trichinella larvae. Other tissue from this second biopsy was sectioned by the Pathology Laboratory, Wellington Hospital, New Zealand, and stained with periodic acid-Schiff reagent (PAS), PAS-diastase, β-nicotinamide adenine dinucleotide (reduced form; NADH), adenosine triphosphatase, Gomori trichrome stain, or haematoxylin and eosin.

Laboratory findings and Pathology

The muscle tissue taken by biopsy (18 June 1991) showed active myositis, and contained intracuticular parasites in transverse section (18–25 μm diameter) and oblique section (50–150 × 25 μm). The parasites contained sections of immature reproductive tissue as well as gut, indicating that they were well developed larvae stages. The parasites contained well developed reproductive tissue and, in transverse section, some loosely compacted brown granular haematin-like material. None of the parasites was encapsulated.

Fresh muscle tissue taken from the second biopsy (8 October 1992) contained motile worms, 300–500 μm long, at an estimated density of 16–20 worms per gram of muscle. The movement of the worms was similar to that described by KINER & FAUBERT (1981) for T. pseudospiralis larvae.

In whole specimens the haematin-like material extended for approximately three-quarters of the worm's length. Certain aspects of the morphology, including the state of development, were thought to be typical of Trichinella larvae (Ooi & Van Knippenberg, personal communication). However, an enzyme-linked immunosorbent assay on 27 August 1992 gave a positive result for Trichinella (optical density 0.403; positivity threshold 2.0–400; CDC, Atlanta, Georgia, USA) and deoxyribonuclease analysis and Western blotting, currently being carried out, strongly support the identification as T. pseudospiralis.

Raised levels of the non-specific enzymes aspartate and alanine aminotransferases and the specific muscle enzyme CK, as found in the present case (Table), are well known in trichinosis (POZMANSKA et al., 1981). The levels of CK were very high (up to 5532 iu/L), and can be compared with an average level for spiralis-trichinosis of 232 iu/L (STUMPF et al., 1981). In spite of fluctuations in CK level over time there was no overall trend indicating any decline in larval activity, or change in activity resulting from the administration of prednisone, although clinical symptoms subsided substantially during this time. High CK levels resulting from persistent larval movement within the muscle cell may be helpful in differential diagnosis.

The muscles appear to be the only source of increased enzyme activity in trichinosis, with neither the liver nor the parasite contributing to any marked degree (POZMANSKA et al., 1981). However, a study of T. pseudospiralis in mice (GRAYET et al., 1989) found that changes occurred in the kidney and the spleen, and the presence of the liver being regarded as non-specific hepatitis—one of the apparent symptoms of the case reported here.

The serum albumin level was normal in our case, consistent with the findings of KOCHERKA et al. (1981b), who suggested that this might be useful in differential diagnosis. T. spiralis infections characteristically present a marked reduction in serum albumin.

Eosinophilia was found to develop rapidly in monkeys infected with T. pseudospiralis and to reach a peak in a little over 3 weeks, gradually declining to low levels by 100 d after infection (KOCHERKA et al., 1981b). In the present case only one raised eosinophil count was recorded, followed by a period when no record was made or the levels were normal.

The sustained presence of larvae in host muscle suggests an ineffectual immune response on the part of the patient. In the present case the inflammatory response revealed by tissue sections appeared relatively weak, a feature of pseudospiralis-trichinosis also seen in monkeys (Tsiperka et al., 1981). This contrasts with the marked inflammatory response to spiralis-trichinosis.

Clinical symptoms

The symptoms recorded here were those of the muscular phase of the disease. The intestinal phase is of relatively short duration and is self-limiting, and may have been relatively asymptomatic. We concluded that this phase had terminated some time before the patient first sought medical advice.
Experimental infection of monkeys demonstrated expulsion of adult *T. pseudosporalis* about 24 d after infection (Kocheki et al., 1981a), but a high number of larvae in muscle was maintained for the duration of the experiment (6 months). In the present case the period of larval viability has been extended to an estimated 7-9 years, with continuing symptoms of their presence. This compares with *T. spiralis* infections in monkeys, in which there is usually a substantial reduction in larval numbers after a few months and complete elimination (Kocheki et al., 1981a; Campbell, 1983). In other hosts (e.g. polar bears) encapsulated larvae of *Trichinella* can last for many years (D. A. Denham, personal communication). The maximum number of larvae per gram of muscle found from the patient suggests that relatively low numbers are capable of causing clinical symptoms. These figures are more or less similar to those of *T. spiralis*, but are considerably less than the clinically important levels of other species (Pozio et al., 1992).

The favored location for *T. pseudosporalis* larvae in monkeys was the masseter muscle, a feature shared with *T. spiralis*, with the tongue being less favoured by the former (Kocheki et al., 1981a). Swallowing difficulties in the present case appeared to have been related to involvement of these muscles, although the patient complained of this symptom only during steroid treatment. The quadriiceps and biceps muscles, which this patient referred to as being weaker than expected and aching after exercise, were also among the more highly favoured sites in the monkey hosts.

Episodes of racing heart and palpitations during the earlier phases of the disease may relate to heart muscle involvement. *T. spiralis* is known to enter heart muscle with various consequent cardiac symptoms, including tachycardia.

Periodic and other facial oedema is a common symptom of spiralis-trichinosis and pseudosporalis-trichinosis (Kocheki et al., 1981b). Although the patient did not complain of this, several of her colleagues and friends referred to a puffy appearance around the eyes and face that disappeared after antihelmintic treatment.

In summary, pseudosporalis-trichinosis exhibits the same pathological manifestations as spiralis-trichinosis, but with a few significant differences. The delay in seeking consultation after the first recalled symptoms (1-2.5 years) suggests that symptoms in the early stages of the disease in physically fit persons are relatively mild and non-specific.

Source of the infection

Symptoms of pseudosporalis-trichinosis can be expected to arise some 3 weeks after infection (Kocheki et al., 1981b). In the case described the patient recalled the first uncontrollable bouts of tiredness occurring in Australia during 1984-1985 when, apart from a few months on the mainland, she was living in Tasmania. A short period in the United Kingdom preceded her arrival in New Zealand in September 1985, and almost a year passed before she sought the consultation referred to above, the palpitations having begun 2-3 months earlier. Field work in New Zealand in the summer of 1985-1986 gave rise to periods of unusual fatigue, but she maintained a generally high level of activity.

*T. pseudosporalis* has an erratic distribution, possibly as a result of its having avian co-hosts. Originally described from the racoon, it has since been found in capybara-fowling birds from Russia and North America, and from quolls (Dendrolinae) in New Guinea (Saimont, 1983), and a brush-tailed opossum (Trichosurus vulpecula) in Tasmania (Osendorf et al., 1990). There are also records from Spain and India (Pozio et al., 1999). There is no record of *T. pseudosporalis* from New Zealand or mainland Australia, although 4 men in mainland Australia were recently discovered to be seropositive for *Trichinella*, with no firm species identification (P. J. McDonald, personal communication). Infrequent but persistent reports of *T. spiralis* have been made in New Zealand (Cairns, 1966; Mason, 1978), with no suggestion of misidentification of larvae. In the present case, linking the onset of symptoms to geographical locality is difficult as the patient travelled widely. Although the known distribution of *T. pseudosporalis* points to Tasmania as the likely source of her infection, mainland Australia, New Zealand, and even possibly the United Kingdom cannot be entirely eliminated.

Until early 1984 the patient was a vegetarian, but then adopted a limited diet of a few amounts of; sheep meat. This involved the normal range of domestic meats, including pork, and an experiment in 1984 with Tasmanian wallaby that was apparently well cooked. Osendorf et al. (1990) speculated that some wallaby species could act as hosts, and found that pigs could be infected by means of Tasmanian devil and quoll flesh containing *T. pseudosporalis*, but they were not regarded as ideal hosts. This conclusion is consistent with other reports of a low reproductive capacity index for *T. pseudosporalis* in pigs (Pozio et al., 1992). In spite of these reservations, pork is a possible source of infection. In the course of research the patient frequently handled faecal pellets from wallabies, kangaroos and, to a lesser extent, quolls and Tasmanian devils. Larval transmission via faecal contamination has been suggested (Faust et al., 1970), but is regarded as unlikely (D. A. Denham, personal communication).

The reason for an apparently recent appearance of *T. pseudosporalis* in the southern hemisphere can only be speculated upon, but migration of cattle and sheep could be responsible.

The information recorded above has led us to the following tentative conclusions: the patient was infected sometime between early 1984 and mid-1985, in Tasmania, possibly as a result of eating infected wallaby meat, pork, or pork products, with faecal contamination being, at this stage, the less likely option. A survey of 1768 Tasmanian pigs has, however, proved negative (P. B. Ryan, personal communication).

Treatment

Traditionally, trichinosis has been difficult to treat, with the choice of treatment varying according to clinical severity and the strain or species of *Trichinella* involved. In the present case it was assumed that the adult worms of the intestinal phase had long since been expelled and that treatment should be directed at the larvae of the muscular phase.

A mild or light case of spiralis-trichinosis at a late stage of the disease might call for little more than symptomatic treatment, with the self-limiting nature of the infection eventually ensuring a complete recovery. The use of larvicidal drugs is not recommended in such cases unless there are unusual circumstances (Campbell, 1983).

In the present case the persistence of larvae in the muscle and the associated symptoms called for the use of a larvicidal drug. Mebendazole has largely replaced thiabendazole as the drug of choice in view of its activity against adult worms and both encapsulated and unencapsulated larvae. However, mebendazole and its derivative flubendazole are not well absorbed through the intestine, thus limiting their efficacy on extraintestinal stages. A trial of albendazole in an outbreak of human trichinosis gave more favourable results, with respect to residual larval infection, than thiabendazole and flubendazole (Fauettie et al., 1988). Also, an earlier study had indicated that albendazole was effective (Saimton, 1985), and in this case there was no apparent side effect.

The effect of the drug was monitored through C! levels, and further biopsies were not taken. The patient continued to experience ache in the leg muscles following normal activities, but apparently this phenomenon is not
uncommon following successful treatment of spiralis-trichinosis (CAMPBELL, 1983). The possibility of anaphylactic reactions as a result of injecting living in muscle tissue was guarded against by the use of steroids during the initial stages of anthelmintic treatment.

Conclusions

*T. pseudospiralis* is capable of producing clinical symptoms in humans. Indications, gleaned from a single case, are that disease caused by this agent could be serious if the initial larval intake was high. However, the opportunities for human infection may be relatively infrequent, as the normal wild hosts of this species have limited contact with humans and are not normally consumed as meat. Also, the low reproductive capacity index for *T. pseudospiralis* in pigs may result in a low frequency and intensity of clinical symptoms acquired by consuming infected pork. On the other hand, infected meat may escape detection during routine abattoir screening, particularly when the trichinoscopy technique is used, because of the low intensity of the larvae in muscle and their free-moving nature. The possibility, however remote, of infection via faecal contamination suggests a need for further investigation to place this issue beyond doubt. The potential for pseudospiralis-trichinosis to become widespread is reasonably high, considering the presence of suitable hosts and the ability of the worm to infect rats and pigs. This is of particular public health concern for countries that are unfamiliar with any form of trichinosis, and where the disease might escape detection. The possibility of carrion-eating seabirds being carriers should be investigated.

Although many of the features of pseudospiralis-trichinosis are similar to those of the spiralis form of the disease, differential diagnosis can be made on the observation of persistent and chronic elevated CK levels and muscle symptoms, plus motile unencapsulated larvae in muscle biopsy. When the parasites are not seen on biopsy and polymyositis is diagnosed, worsening of the disease following steroid treatment should alert clinicians to the possibility of pseudospiralis-trichinosis.

Acknowledgements

We were greatly assisted by the advice of Dr D. A. Dunham, of the London School of Hygiene and Tropical Medicine, and Dr W. C. Campbell. Dr K. J. M. Dickison, Mr J. W. L. Ainsworth, and Mr R. A. Hitchin called on the manuscript, and Mr A. Vlasov assisted in obtaining reference sources.

References


Received 26 July 1993; accepted for publication 16 August 1993