First Outbreak of Human Trichinellosis Caused by *Trichinella pseudospiralis*

Somchai Jongwutiwes, Nutaros Chantachum, Phisai Kraivichian, Padet Siriyasatien, Chaturong Putaporntip, A. Tamburrini, Giuseppe La Rosa, Comkrit Sreesunpasirikul, Phisai Yingyoud, and Edoardo Pozio

This is the first report of an epidemic of human infection with *Trichinella pseudospiralis*. An outbreak of trichinellosis affecting 59 individuals, of whom one died, occurred in southern Thailand during 1994–1995. The source of this epidemic was raw pork from a wild pig that was distributed to villagers by a local hunter. The most striking clinical features among 50 individuals who could be followed were muscular swelling, myalgia, and asthenia persisting for >4 months. These were associated with significant elevations of creatine phosphokinase and lactate dehydrogenase levels. All patients had *Trichinella*-specific IgG antibodies in an enzyme-linked immunosorbent assay. Muscle biopsies, performed in six cases, showed nonencapsulated, actively migrating *Trichinella* larvae. Experimental infection of mice with larvae from human biopsies revealed nonencapsulated muscle larvae consistent with *T. pseudospiralis*. The identification of muscle larvae from a human specimen by random amplified polymorphic DNA analysis confirmed the causative agent to be *T. pseudospiralis*. Patients seemed to respond best to treatment with albendazole.

Trichinellosis, a zoonotic disease caused by nematodes of the genus *Trichinella*, is prevalent worldwide among carnivores and omnivores. Human infections can be acquired from ingestion of meat containing infective late first-stage larvae from wild or domestic animals. In Thailand, trichinellosis is still a serious public health problem among people who prefer raw or undercooked meat. At least 3,000 persons have reportedly been infected (including 85 who died), mostly in the northern part of the country, since 1962 [1]. Pigs raised by the hill-tribe people are frequently the sources of these outbreaks. Species of *Trichinella* differ in their epidemiology, biology, and clinical features.

Although *Trichinella spiralis* has been reported to be the most common cause of human trichinellosis, other species can also infect humans [2–6]. In contrast to trichinellosis due to other species of *Trichinella*, infection caused by *Trichinella pseudospiralis* is unique because the muscle larvae do not induce a modification of the infected muscle cell into a nurse cell. Therefore, the nonencapsulated larvae traversing the muscle tissues can cause prolonged clinical symptoms.

*T. pseudospiralis* has a cosmopolitan distribution in North America, Asia, and Australia. This parasite has been detected in raptorial birds, marsupials, wild canids, and rodents [7–9]. However, domestic pigs and monkeys can be experimentally infected with *T. pseudospiralis*, suggesting that other kinds of mammals could serve as its hosts [7, 8, 10]. To date, there has been only one case report on human trichinellosis caused by *T. pseudospiralis*, from New Zealand. The presenting symptoms in that patient included prolonged myalgia and persistently elevated transaminase and creatine phosphokinase levels [6, 7]. The diagnosis was based on a histopathologic study showing that the *Trichinella* muscle larvae were nonencapsulated, and it was subsequently confirmed by random amplified polymorphic DNA (RAPD) analysis [11].

We report here the first outbreak of human trichinellosis caused by *T. pseudospiralis*, occurring in southern Thailand following consumption of raw pork from a wild pig.

**Patients and Methods**

**Background**

An outbreak of human trichinellosis occurred in a village, Panwal No. 5, near the Thai-Myanmar border in the Ta Sae district of Chumphorn Province, located 465 km from Bangkok, in southern Thailand. Most of the villagers earn their living by working on coffee plantations. The village is surrounded by a hilly forest area where wild animals are occasionally hunted for food by local people. On 13 November 1994, a local hunter killed a wild pig and distributed its meat to other people in the village.

The outbreak of trichinellosis was reported in December 1994 by the regional medical health service. Infection control measures were undertaken and included administration of mebendazole (400 mg/d) to 59 symptomatic individuals for 4...
weeks, followed by thiabendazole (2 g/d) for 2 weeks. However, from 25 February to 8 March 1995, six cases from this outbreak were seen by one of us (S. J.) at Chulalongkorn Hospital in Bangkok. Since the history of illness and clinical symptoms were consistent with trichinellosis but with a somewhat unusually prolonged clinical course, gastrocnemius muscle biopsies were performed.

Data Collection

Epidemiological data and clinical information were collected from 15 to 17 March 1995 at the outbreak area. Stool samples were collected to search for intestinal parasites.

Biochemical Parameters

Blood samples were taken from 50 individuals twice, at 4 months and 5 months after infection (before and after albendazole treatment). Complete blood cell counts and the levels of creatine phosphokinase (CPK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen, creatinine, and plasma glucose were determined.

Isolation and Identification of the Parasites

Six specific-pathogen-free mice were orally inoculated with 20–50 muscle larvae from biopsy specimens collected from two patients. The mice were killed on day 80 after inoculation and were searched for muscle larvae under a dissection microscope. The second passage of the muscle larvae, into six other mice, was done immediately after isolation. A single \textit{Trichinella} larva was isolated from a muscle biopsy specimen from an infected individual under a dissection microscope, and it was identified at species level by RAPD analysis as described previously [12]. Muscle larvae from five reference strains, i.e., \textit{T. spiralis}, \textit{Trichinella britovi}, \textit{Trichinella nativa}, \textit{Trichinella nelsoni}, and \textit{T. pseudospiralis} (one of each species), were used for the comparison [13].

Serodiagnosis

Serum samples from 50 individuals with clinical symptoms and signs of trichinellosis, collected 4 months after the ingestion of the infected pork, were examined for \textit{Trichinella}-specific IgG antibodies by an ELISA according to the standard protocol [4].

Treatment

Albendazole (800 mg/d in 4 divided doses) was also given, for the 4 weeks from 17 March to 13 April 1995. Subjective symptoms and physical examination findings for each patient were followed after the last dosage and 1 year later.

Results

Epidemiological and Clinical Features

Since the patients who sought medical treatment at Chulalongkorn Hospital reported that other persons with similar symptoms remained in the village, we went to the outbreak area to search for other cases of trichinellosis. A total of 59 individuals had clinical symptomatology of trichinellosis, i.e., fever, diarrhea, muscular pain, and muscular swelling, after they had eaten pork from the same wild pig. Some with severe symptoms sought medical care in a district hospital, where they received symptomatic treatment for myalgia. All infected individuals had migrated from the northeastern provinces of Thailand some years previously. Their traditional hot, spicy dishes usually consist of raw or undercooked meat.

One patient died during the outbreak. From the information provided by this patient’s relatives, we knew he was 24 years old and had been healthy before consuming a large portion of an uncooked pork dish. His symptoms included watery diarrhea, fever, and asthenia. A few days before he died, he complained of severe headache, generalized myalgia, confusion, and respiratory difficulty. He was unconscious when a relative took him to a local hospital, where he died shortly afterward. Unfortunately, it was not possible to do an autopsy.

Nine patients went back to their hometowns during the survey period, and only 50 patients could be followed. Of these, 30 were males and 20 females. The mean (±SD) age was 37.6 ± 12.6 years (range, 17–70 years). All examined serum samples were positive by ELISA for specific IgG antibodies to \textit{Trichinella} antigens. After these villagers ate “lahb” (a sour, spicy undercooked pork dish) and “nahm” (a raw, fermented sausage-like dish), they had watery and sometimes mucous, nonbloody diarrhea, lasting for 2–7 days (mean, 4.3 ± 2.8 days). The gastrointestinal symptoms occurred 3–10 days (mean, 6.9 ± 2.5 days) following ingestion of the infected pork.

Twenty-nine patients (58%) complained of having fever during the first week of illness, lasting for 3–7 days (mean, 5.8 ± 3.3 days). Subsequently, symptoms and signs resulting from the larval migration and muscle invasion of larvae appeared. These included persistent asthenia, headache, facial and periorbital edema, myalgia, muscle weakness, a tingling sensation, and muscle swelling in the shoulders, masseters, deltoids, back, and calves (table 1).

The microscopic examinations of all six biopsy samples showed actively migrating nonencapsulated larvae, traversing the muscle fibers. The worm burden varied from 10 to 50 larvae per gram. It was difficult to correlate the infecting doses and disease severity accurately. However, the estimated amount of pork consumed by 15 infected individuals suggested that consumption of >100 g of the infected pork resulted in more severe myalgia, muscular swelling, and asthenia than did consumption of <100 g. Therefore, the severity of symptoms seemed to be related to the amount of the infected pork con-
Table 1. Clinical features of patients infected with Trichinella pseudospiralis during the outbreak of trichinellosis in the Ta Sae district, Chumporn Province, Thailand.

<table>
<thead>
<tr>
<th>Sign or symptom</th>
<th>No. (%) of cases</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myalgia</td>
<td>50 (100)</td>
<td>&gt;4 mo</td>
</tr>
<tr>
<td>Asthenia</td>
<td>50 (100)</td>
<td>&gt;4 mo</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>50 (100)</td>
<td>2–7 d</td>
</tr>
<tr>
<td>Headache</td>
<td>39 (78)</td>
<td>10–24 d</td>
</tr>
<tr>
<td>Fever</td>
<td>29 (58)</td>
<td>3–7 d</td>
</tr>
<tr>
<td>Difficulty in chewing</td>
<td>24 (48)</td>
<td>10–30 d</td>
</tr>
<tr>
<td>Anorexia</td>
<td>24 (48)</td>
<td>4–8 d</td>
</tr>
<tr>
<td>Palpitation</td>
<td>21 (42)</td>
<td>14–30 d</td>
</tr>
<tr>
<td>Vomiting</td>
<td>14 (28)</td>
<td>3–5 d</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4 (8)</td>
<td>3–5 d</td>
</tr>
</tbody>
</table>

sumed by each infected individual. No parasite ova or protozoa were detected in stools, but one person was infected with an Echinostoma species.

Laboratory Features

All infected individuals had high levels of at least three of four enzymes tested (CPK, LDH, AST, and ALT). The mean levels of CPK and LDH were 865 ± 212 units/L and 1,010 ± 426 units/L (normal, up to 195 units/L and 230–460 units/L), respectively. Fifteen cases (30%) with severe myalgia had markedly increased levels of CPK and LDH (more than mean levels). Eosinophilia (>500/mm³) was detected in all 50 infected individuals in the 4th month after infection, but values subsequently normalized in almost all cases after albendazole treatment 1 month later (table 2). The levels of plasma glucose, albumin, globulin, urea nitrogen, and creatinine remained normal.

Table 2. Biochemical changes in patients infected with Trichinella pseudospiralis 4 months after infection and after treatment.

<table>
<thead>
<tr>
<th>Laboratory study (normal value)</th>
<th>No. of patients with elevated laboratory value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4 mo after infection</td>
</tr>
<tr>
<td>AST (&lt;38 U/L)</td>
<td>48</td>
</tr>
<tr>
<td>Creatine phosphokinase (&lt;195 U/L)</td>
<td>43</td>
</tr>
<tr>
<td>Lactate dehydrogenase (&lt;460 U/L)</td>
<td>42</td>
</tr>
<tr>
<td>Eosinophilia (&gt;500/mm³)</td>
<td>37</td>
</tr>
<tr>
<td>ALT (&lt;38 U/L)</td>
<td>33</td>
</tr>
<tr>
<td>Alkaline phosphatase (&lt;279 U/L)</td>
<td>3</td>
</tr>
</tbody>
</table>

NOTE. AST = aspartate aminotransferase; ALT = alanine aminotransferase.

Clinical Course After Treatment

Mebendazole and thiabendazole were given by the local medical officers at 1 month after the onset of disease. However, these did not alleviate the persistent, painful muscular swelling in any of the cases. After administration of albendazole at 4 months, all infected individuals showed marked improvement during the first week and gradually recovered after 2 weeks of treatment. No adverse effect of albendazole was detected.

During the first few days of treatment in three severe cases, the patients experienced difficulty in respiration and an increase in myalgia. Therefore, prednisolone was administered orally at the dosage of 30 mg/d for 5 days, and subjective abatement of the symptoms occurred. No patients complained of myalgia, a tingling sensation, or asthenia after 1 month of treatment. Two patients with severe myalgia did not have any recurrent symptoms, and their biochemical parameters remained normal after 1 year of follow-up.

Histology

Histologic sections of infected muscle stained with hematoxylin and eosin contained abundant eosinophils, neutrophils, plasma cells, and macrophages surrounding the muscle tissue. It was noted that all of the muscle larvae examined were nonencapsulated by a collagenous material (figure 1). Some of the muscle fibers contained several hypertrophic nuclei and some revealed edematous and necrotic changes. Trichinella larvae were found traversing the muscle fibers.

Parasite Identification

The RAPD analysis of muscle larvae obtained from an infected individual 105 days after infection showed a distinctive
A high level of muscle enzymes was detected up to 4 months after infection, and the phase of muscular invasion persisted for more than 4 months, and the persistent myositis caused by T. spiralis seemed to be prolonged [7]. In this outbreak, the symptoms of myalgia and fever were similar to those caused by T. spiralis. The disease is somewhat similar to that caused by T. pseudospiralis, but T. pseudospiralis does not induce nurse cell formation, whereas a single larva collected from frozen biopsy specimens, by using a corticosteroid treatment. Furthermore, after 1 month of treatment with albendazole, the levels of eosinophil and muscle enzymes returned to normal in almost all cases.

It was speculated that a pig could be the source of the first human T. pseudospiralis infection [7]. In the present report, the meat from a wild pig was believed to be the source of this epidemic, although inspection of the pork was not possible at the time of the study. However, it is pertinent to mention in this context that no fairs or festivals had been held where most of the village might have eaten some other meat source. It is interesting that some villagers gave parts of the same pork to a dog and two cats, and they developed muscular swelling and died a week later. The carcasses were left to decompose naturally and disappeared by the time we went to the village. Therefore, there remains the possibility that other mammals could be infected with T. pseudospiralis.

In conclusion, the present report provides the first information on a human outbreak of trichinellosis due to T. pseudospiralis. The disease is somewhat similar to that caused by T. spiralis except for prolonged myalgia. The death of one infected individual shows that T. pseudospiralis can be fatal in humans. A differential diagnosis can be made for the prolonged muscular symptoms and persistently elevated levels of muscle enzymes. Definite species identification can be performed on a single larva collected from frozen biopsy specimens, by means of electrophoretic analysis of the RAPD amplification.

On the basis of this study, it is suggested that albendazole is effective for the treatment of trichinellosis due to T. pseudospiralis.

Discussion

There have been at least 5 species of Trichinella reported to cause human infections (i.e., T. spiralis, T. nativa, T. britovi, T. nelsoni, and T. pseudospiralis); each one has different biological characteristics and can produce distinct clinical features in humans [2, 3, 6]. Unlike other species of Trichinella, T. pseudospiralis does not induce nurse cell formation, whereas it causes prolonged muscular symptoms and signs [6]. Clinical manifestations in the case report appeared similar to those caused by T. spiralis except that the phase of muscular invasion seemed to be prolonged [7]. In this outbreak, the symptomatology during the muscle invasion persisted for >4 months, and a high level of muscle enzymes was detected up to 4 months after infection.

The efficacy of treatment for trichinellosis during muscle invasion by the larvae is controversial. Generally, encapsulated larvae of T. spiralis cause little or no symptoms and signs; thus, only symptomatic treatment is required. On the contrary, the persistent myositis caused by T. pseudospiralis requires treatment with an antiparasite drug. Although the patients received mebendazole followed by thiabendazole, the clinical picture did not significantly improve. Therefore, albendazole was substituted, since successful treatments with it in a human outbreak caused by T. spiralis and in the first human case caused by T. pseudospiralis have been reported [7, 14]. Furthermore, results of experimental trials in mice infected with either T. spiralis or T. pseudospiralis showed that albendazole yielded better outcomes than did the other antiparasite drugs tested so far [15, 16].

In this study, the result of the treatment of trichinellosis with albendazole strongly supports its efficacy against T. pseudospiralis infections without apparent side effects. However, during the first few days of treatment, the release of toxic substances from damaged larvae could occur and might result in a feeling of difficulty in respiration. Such a symptom might be an allergic phenomenon that may be prevented and alleviated by a corticosteroid treatment. Furthermore, after 1 month of treatment with albendazole, the levels of eosinophil and muscle enzymes returned to normal in almost all cases.

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References


