Medullary Gnathostomiasis in a White Patient: Use of Immunodiagnosis and Magnetic Resonance Imaging

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A 48-year-old French diplomat presented with a sensory-motor paraparesis of rapid onset, leading to paraplegia. Successive magnetic resonance image scans showed lesions of the thoracic spinal cord that were at different levels from one examination to the next. Specific anti-gnathostome antibodies were detected by means of enzyme-linked immunosorbent assay and Western blot test in both plasma and cerebrospinal fluid. Albendazole treatment prevented disease progression, but only partial regression of the neurologic symptoms was obtained.

Human gnathostomiasis is a well-known parasitosis in Southeast Asia and Mexico, where most cases are diagnosed [1–3]. The disease often manifests itself with swelling or migratory swelling or cutaneous signs and symptoms, accompanied by visceral symptoms related to larval or adult parasite migration to the deep tissues [4]. We report a case that occurred in a white French patient who presented with only neurologic symptoms and who had this condition diagnosed relatively late in the progression of disease. Specific immunology techniques and MRI scan led to a diagnosis.

Case report. A 48-year-old man presented to Amiens University Hospital in October 1997 with neurologic symptoms that had appeared during the previous year. He was a commercial attaché to the French Embassy and had worked in Japan during 1979–1989, in Egypt during 1989–1995, and in Hungary during 1995–1997. During his time in Japan, he traveled often to other Southeast Asian countries. He married a Japanese woman and adopted Asian eating habits, including consumption of semicooked food. He also frequented Asian restaurants in other countries he visited. His only significant medical history was an operation for lumbar disc herniation (L5–S1) in 1985.

In March 1996, a few weeks after eating in an Asian restaurant in Budapest, he presented with paroxysmal crises of bilateral lower thoracic pain that lasted a few seconds to a few minutes. Sensory symptoms in his left leg appeared during the following weeks. He was hospitalized in July 1996 in Hungary, and analysis of fluid obtained from lumbar puncture showed 0.30 g/L of protein (normal, <0.33 g/L) and 9 cells/μL (normal, <2 cells/μL). Typing was not done. Blood test results and liver function were normal. Ten days of corticosteroid therapy that was administered im and 1 month of orally administered treatment had no effect. The neurologic symptoms worsened gradually, with the appearance of sphincter problems, asymmetrical leg paresis, and extension of the sensory deficit in the same areas.

During hospitalization in France in October 1996, MRI scan revealed an enlarged dorsal spinal cord between the first and fourth thoracic vertebrae, with isointense signal on T1 weighting and intramedullary high-signal intensity on T2-weighted images (figure 1, *left panel*). On T1 weighting, after injection of gadolinium chelate, a nodular zone of contrast enhancement appeared at the level of the second thoracic vertebra (figure 1, *right panel*). Brain images were normal. The findings of tests of CSF were abnormal, with 0.76 g/L protein (with no oligoclonal band on electrophoresis) and 15 cells/μL (50% lymphocytes, 38% eosinophils, and 4% neutrophils). Blood test results were normal. There was no biologic evidence for an inflammatory, metabolic, or neoplastic cause. The results of thoracic and abdominal radiologic tests (radiographs and CT scans) were normal.

We eliminated tuberculosis, syphilis, HIV, human T cell leukemia type I, brucellosis, and Lyme disease as diagnoses. The results of immunologic tests for filariasis, hydatidosis, cysticercosis, larva migrans, trichinellosis, and bilharzia were negative for specimens of both blood and CSF. No schistosomal eggs were found by use of urinalysis, stool culture, or biopsy of rectal mucosal specimens. An initial course of praziquantel (40 mg/kg given in a single dose) was prescribed because of the CSF hypereosinophilia, but it did not improve the clinical picture. The results of a bilharzia serologic test, which was rechecked 2 weeks after stopping treatment, remained negative for specimens of both blood and CSF. Corticosteroids (methyl-

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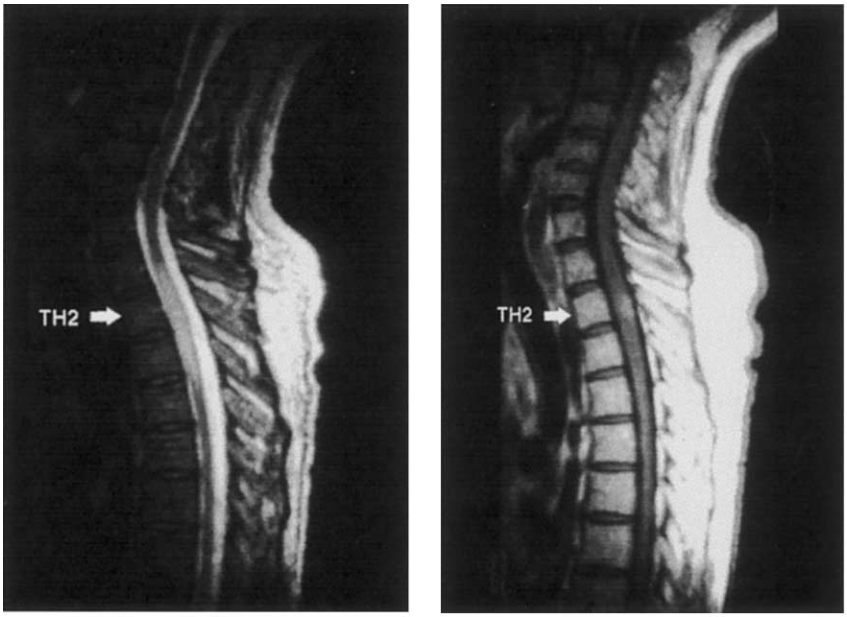

Figure 1. Spinal MRI scan, October 1996. *Left panel,* Sagittal T2-weighted fast spin echo sequence: increased cord diameter with high signal intensity from the first to fourth thoracic vertebra. *Right panel,* Sagittal T1-weighted fast spin echo sequence after gadolinium chelate injection: nodular contrast enhancement with irregular contours in the dorsal cord at the level of the second thoracic vertebra.

prednisolone at 1 g/d for 5 days, then prednisolone at 60 mg/d, decreasing over the course of 15 days) gave a slight clinical improvement. At this time, the MRI scan showed a return to normal cord caliber but persistence of high-signal intensity at the level of the second thoracic vertebra on T1-weighted images.

After the patient's return to Hungary in early 1997, the leg neurologic symptoms and sphincter problems worsened, and a pyramidal syndrome appeared. Three successive MRI scans (obtained in February, April, and June) showed no further intramedullary signal abnormalities, whatever the sequence used, and a normal caliber spinal cord. Analysis of fluid obtained via lumbar puncture in February 1997 found it to be normal (protein, 0.21 g/L, with a polyclonal aspect on electrophoresis and <1 cell/μL). However, CSF sampled in June 1997 showed 0.39 g/L protein, 13 cells/μL (with 18% eosinophils), and anti-bilharzia antibodies at 1:32 dilution on hemagglutination, the limit of positivity. A second course of praziquantel 40 mg/kg as a single dose once again was ineffective.

After the patient's arrival in Amiens in October 1997, the leg neurologic symptoms were unchanged, and urodynamic investigations showed a hyperactive bladder with sphincter relaxation difficulties associated with high intravesical pressure. He started neurologic and sphincter physiotherapy and monthly injections of 1 g of methylprednisolone. This did not prevent the progressive aggravation of his symptoms, including the reduction of his maximum walking distance to 50 m. In March 1998, MRI scan revealed increased cord diameter between the fifth and seventh thoracic vertebrae, with hyperintensity on T2 weighting (figure 2, *left panel*) and a nodular area of contrast enhancement at the level of the fifth thoracic vertebra on T1-weighted images (figure 2, *right panel*). The corticosteroid injections were stopped.

In June 1998, the patient underwent surgery to improve bladder emptying. In November 1998, the MRI scan was normal, but the patient could no longer stand without support. At this time, we looked for blood and CSF antibodies by means of ELISA and using recombinant schistosome egg antigens, the results of which were positive for *Schistosoma japonicum* (Sj26GST) antigens, but not for *S. mansoni* and *S. haematobium*. Because these results appeared to support a bilharzia cause, the patient began a third course of praziquantel. Three consecutive days of praziquantel at 75 mg/kg did not alter the neurologic symptoms. In early 1999, analyses done at the Faculty of Tropical Medicine, Mahidol University, Bangkok, gave a positive IgG ELISA result, by use of the antigen from *Gnathostoma spinigerum* third-stage larvae, and revealed a specific 24-kDa band by means of Western blot assay, by use of the same antigen in both plasma and CSF.

To test the specificity of the immunologic reaction, the researchers tested plasma from proven cases of gnathostomiasis with the bilharzia antigen Sj26GST that been used shortly beforehand. There was considerable reaction. Conversely, the plasma of a mouse immunized with this recombinant antigen reacted on a Western blot to the *G. spinigerum* larval antigen but without revealing the 24-kDa–specific band. The treating physicians initiated a 3-week course of albendazole 800 mg/d. At the

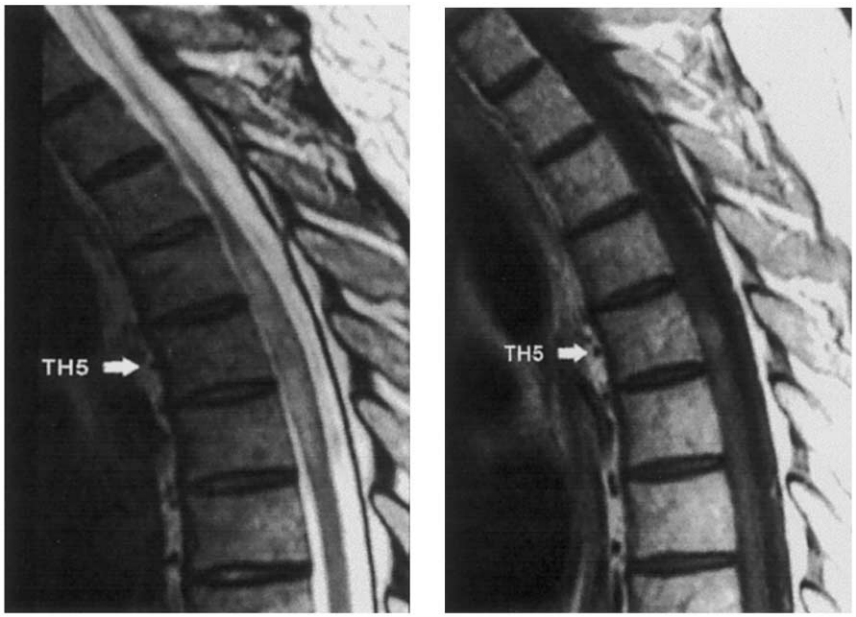

Figure 2. Spinal MRI scan, March 1998. *Left panel,* Sagittal T2-weighted fast spin echo sequence: localized (TH4–TH6) increase in cord caliber containing a heterogenous zone of high signal intensity. *Right panel,* Sagittal T1-weighted fast spin echo sequence after gadolinium chelate injection: nodular contrast enhancement in the cord at the level of the fifth thoracic vertebra.

end of the second week of treatment, left leg movement improved noticeably, the right somewhat less so; perineal sensitivity also improved. Clinical improvement slowed down thereafter; the patient still was unable to stand or to regain sphincter control. MRI scan done 1 month after the end of treatment showed total regression of the pathological images but the existence of spinal cord atrophy at the level of T5. A second course of albendazole gave no further clinical benefit. Specific antibody titer in the CSF at the end of this second treatment course had decreased on ELISA, compared with pretreatment levels. A year after the 2 courses of albendazole, the patient's condition is stable, and he is now receiving supportive therapy for his permanent disabilities.

Discussion. In all the larva migrans syndromes seen in humans, the etiological diagnosis cannot be certain until the parasite is found in the skin, the eye, or the deep tissues during autopsy. In cases where the parasite is not identified, all hypotheses remain possible, and it is difficult to confirm a precise diagnosis. However, an analysis of all the elements collected over the patient's 4-year follow-up argue in favor of gnathostomiasis, for the following reasons.

From an epidemiological point of view, the frequent consumption of semicooked food at home and in Asian restaurants had become an important aspect of the patient's lifestyle after his marriage to a Japanese woman. This is the principal mode of gnathostomiasis contamination [4]. Even simple physical contact with infected meat or fish has been implicated in experimental infections in rodents and cats [5].

The chronology of the patient's clinical signs and symptoms exactly mirrors the classic sequence described in neurologic manifestations of the disease [6–8], in particular in the purely medullary forms [9]. It allows us to differentiate it from other diseases, parasitic or not. The initial pains, which were of spinal root origin and which appeared a few weeks after consuming a meal potentially infested with parasites, correspond with the parasite's penetration of the nerve root and its migration to the spinal cord. The rapid onset of severe sensory and motor deficits are evidence of the damage inflicted by the parasite's migration through the nerve tissue. This situation could result in simple mechanical lesions or might involve hemorrhagic elements—possibly toxic ones [10].

The MRI scan images cannot be compared with those published earlier because, to our knowledge, neurologic gnathostomiasis lesions have never been documented in this way before. We certainly could attribute the initial images (figure 1), with high-signal intensity on T2 weighting and contrast enhancement on T1 weighting, to numerous spinal cord pathologies (inflammatory, neoplastic, vascular, or infectious causes) [11]. The further evolution of these observations and, more specifically, their variable and migratory character from one investigation to another reduces the number of diagnostic hypotheses and effectively illustrates the parasite's movements within the nervous tissue. The return to normal images between abnormal examinations would appear to indicate that, unlike the encephalic forms, the pure medullary forms, such as the present case, are only rarely complicated by hemorrhagic phenomena, which would leave a "scar" visible on MRI scan [9].

The biologic and immunologic investigations, particularly of the CSF, helped affirm the gnathostomiasis hypothesis. The absence of oligoclonal bands on CSF protein electrophoresis throughout the disease's evolution helped eliminate a diagnosis of multiple sclerosis. This occurred despite the intermittent nature of the radiological images, which appeared to be pathognomonic of the disorder, although the clinical and radiological lesions and the severe evolution affected only one area of the spinal cord with no encephalic involvement. However, the CSF eosinophilia directed us early on toward a diagnosis of parasitosis, especially taking into account the progressive elimination of differential diagnoses in which eosinophilia occurs in the CNS: allergy, infection (syphilis, tuberculosis, viruses, or fungi), or malignancy (leukemia, Hodgkin's disease, or other lymphomas) [12].

The plasma and CSF immunologic tests determined the diagnosis. Unlike the first immunoprecipitation or fluorescence tests used in this disorder [1], ELISA with a *G. spinigerum* larval antigen now has virtually 100% sensitivity and specificity [13, 14]. Demonstration on a Western blot test of antibodies in the patient's plasma and CSF reacting with the 24-kDa antigen protein is a major additional argument, considering the specificity of the antigen fraction [15, 16]. As we emphasized earlier, it is probable that the weakly positive results with schistosome antigens seen repeatedly in this patient are due to cross-reactivity between these 2 groups of parasites. Other authors already have observed this phenomenon [17].

Finally, the favorable evolution after albendazole treatment is another argument in favor of gnathostomiasis. Although anti-inflammatory therapy and praziquantel had only modest and transitory effects, this recently developed molecule [18] gave spectacular results. In stopping the apparently inexorable progression of the disease, albendazole may well have prevented the onset of cranial nerve symptoms, a common complication [4], or death, which is seen in 8%–25% of patients [7–9]. Albendazole treatment did not, however, permit full recovery of neurologic function, probably as a consequence of permanent lesions within the nerve tissue.

As far as we know, only one other case of gnathostomiasis has been reported in France. A Laotian refugee presented with skin lesions. The parasitosis, diagnosed by use of serologic tests, was treated with prednisolone and diethylcarbamazine [19].

This first case diagnosed in a French man confirms recent predictions [8]—namely, that increasing intercontinental travel and the generalization of Asian food preferences could lead to the onset of such diseases in patients whose nationality is not an obvious risk factor. In this respect, it is interesting that contamination appears to have occurred in Hungary, far from the geographical areas where this parasitic zoonosis is best known. In such cases, MRI scan and specific serologic testing can be extremely useful by reducing the time to diagnosis and thus the time to treatment.

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