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CASE REPORT

New insights in diagnosing *Schistosoma* myelopathy

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Summary At present non-invasive tests for diagnosing *Schistosoma* myelopathy are sub-optimal. We present a novel serological method, using paired liquor and serum samples, resulting in the diagnosis of *Schistosoma* myelopathy in a male patient with proximal muscle weakness. The patient recovered after praziquantel treatment.

Case description

A 35 year-old male presented to the emergency department with progressive pain and muscle weakness in the upper legs. His past medical history was unremarkable except from a Human Papilloma Virus infection for which he had been treated. The patient was originally from Brazil, but he had lived in the Netherlands for seven years. In his youth, he frequently sailed at a lake near São Paulo. Two months prior to presentation, he suffered from diarrhea during a visit to Brazil. The pain in his legs started four days prior to presentation and was accompanied by dysuria and a feeling of incomplete voiding.

On physical examination, hypoesthesia of both lower limbs and the saddle area was found. Muscle strength of both upper legs was decreased. Knee and ankle deep tendon reflexes were symmetrically low, plantar reflexes were normal. Urine retention of 500 mL was found. An MRI scan showed swelling and edema of the low-thoracic and lumbar spinal cord and no abnormalities in the brain were described. Laboratory examination showed no signs of inflammation and normal liver enzymes. Cerebrospinal fluid (CSF) analysis demonstrated a lymphocytic pleocytosis

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(leucocytes 254×10^6/L, monocytes 237×10^6/L), a high protein concentration (1.12 g/L), a normal total IgG over albumin ratio (Total IgG index of 0.52, Table 1) and no monoclonal banding. In addition, serology was performed to exclude bacterial, viral and parasitic infections as well as auto-immune disorders.

During the next few days, muscle weakness, sensory disturbances and bladder dysfunction increased. Because of the rapid disease progression, acyclovir was started to treat a possible HSV infection (30 mg/kg/day in 3 doses for 10 days). After a few days, the results for *Schistosoma* serology turned out positive. Analysis of a second CSF-sample showed an elevated total IgG over albumin ratio (1.24, Table 1), suggesting intrathecal antibody production. Furthermore, increasing amounts of antibodies against *Schistosoma* egg- and worm-antigens were found in the second serum and CSF samples (Table 1). Schistosomal eggs could not be detected in faecal samples, but rectal biopsy showed one dead *Schistosoma mansoni* egg embedded in a granuloma. Based on these results the diagnosis schistosoma myelopathy (SM) was made. Treatment was initiated with praziquantel (50 mg/kg/day in 2 doses for 3 days) and high dose methylprednisolone (1 g/day for 5 days) followed by oral prednisone (1 mg/kg/day) tapered gradually over the next several months. Within a week the patient's condition dramatically improved and he was discharged. During the next months, muscle strength and sensibility improved, and bladder function normalized.

Discussion

Schistosomiasis is a tropical disease caused by parasitic flatworms of the genus *Schistosoma*. Infection occurs by skin penetration during contact with contaminated freshwater, after which adult worms develop in the blood vessels surrounding the gut or bladder (see[1] for details). Female worms produce hundreds of eggs per day, most of which are excreted in the faeces or urine but some get trapped in host tissues. *Schistosoma* myelopathy (SM) refers to neurological symptoms caused by an inflammatory response induced by ectopic *Schistosoma* worms or eggs in the spinal-venous plexus.[1] It is thought that eggs of schistosomes can incidentally reach the spinal cord probably via retrograde venous flow into the Batson vertebral epidural plexus, which has anastomoses with the deep iliac veins and inferior caval vein. However, when an egg-laying worm-pair reaches the veins surrounding the spinal cord, many eggs will be deposited in the spinal cord.[2,3] The cellular immune-reaction around the eggs leads to inflammation and granuloma formation at spinal T12 to L1 levels, resulting in significant neurological symptoms.[2,3]

SM can occur in man and women of all ages, although young males (age 15–35) are most frequently affected. Muscle weakness of the lower extremities, pain in the lower back or legs, hypoesthesia and bladder dysfunction, occur in over 90% of SM patients.[2,3] MRI is a sensitive test for myelopathy and shows swelling and oedema of the spinal cord (enlargement, hyperintensity on T2 weighted images and contrast enhancement) or thickened spinal roots. CSF analysis reveals pleocytosis or an elevated protein concentration in 80% of cases.[2,3] The clinical pattern of motor, sensory and autonomic dysfunction, together with signs of inflammation of the spinal cord is known as transverse myelitis (TM).[4] TM can be due to a variety of infectious and non-infectious diseases. Guidelines advise to selectively perform additional tests, depending on (travel) history, clinical signs and symptoms.[4]

Table 1 Serological data of paired serum-liquor samples.

Sample No. & type		Albumin (g/l)	Total IgG (mg/l)	IHA worm (titer)	ELISA-SEA	
					Optical Density (OD)	Dilution
A) Serological results						
1	Serum	43.3	12.4	1:2560	574	400
	CSF	0.86	0.13	1:16	395	10
2	Serum	41.2	9.8	1:5120	717	400
	CSF	0.77	0.23	1:32	773	10
B) Calculated indexes						
Sample No.	Albumin	Total IgG	Egg/worm-CSF/serum			
1	0.020	0.52	2.7			
2	0.019	1.24	4.5			

Section A shows the results of serological analysis of the two paired serum and CSF samples collected at hospital admission (no. 1) and after 12 days (no. 2). Total albumin and total IgG were determined by routine clinical chemistry methods. Antibody titers to *Schistosoma* worm-antigens were determined by a commercial indirect hemagglutination assay (IHA) and antibody levels of *Schistosoma* egg-specific antibodies were determined by ELISA and expressed as Optical Density at a given dilution, as described before.[11] Section B shows the 3 calculated indexes for the two paired samples. The albumin index [albumin CSF (g/l)) / albumin blood (g/l)] is a measure for the integrity of the blood-brain barrier and values over 0.007 are suggestive for an intermediate impaired function.[10] The total IgG index [(total IgG CSF (mg/l) / total IgG serum (mg/l))/(albumin CSF (g/l)/albumin serum (g/l))] is a measure for increased concentrations of total IgG in CSF and values >0.69 are suggestive for intrathecal antibody production.[10] The egg/worm-CSF/serum index [(anti-egg IgG in CSF (OD*dilution)/anti-worm IgG in CSF (titer))/(anti-egg IgG in serum (OD*dilution)/anti-worm IgG in serum (titer))] is a measure for the relative enrichment of anti-egg IgG over anti-worm IgG in CSF when compared to serum. Values >2 indicate intrathecal production[10] of IgG specific for schistosomal eggs, confirming SM.