Katayama fever in scuba divers

A report of 3 cases

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Summary

Katayama fever or acute schistosomiasis probably occurs more commonly than is recorded. Interviews with a 3-man scuba diving team who had had contact with a large dam in an endemic area of the eastern Transvaal Lowveld at the same time and contact area on the same day during late summer of 1986 are discussed. Two, who had not previously been exposed to infected water, presented with Katayama fever, due to *Schistosoma mansoni* infection, 21 days after contact and it took 30 - 36 months for them to recover fully after several treatments. The third patient, a keen watersportsman and resident in the endemic area for a period of 10 years, presented with a mild infection, probably due to acquired immunity initiated during previous contacts with infected water; he took about a year to recover. The pathogenesis, clinical features, diagnosis and treatment of the 3 cases are described in the light of recent observations made elsewhere on Katayama fever cases and the effects of chemotherapy on the course of illness. The necessity of obtaining basic information on the travel and water-contact activities of patients in order to make a diagnosis is emphasised.

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Katayama fever became known during the 19th century when it was reported from the Katayama River valley in Japan, an area which was then hyperendemic for *Schistosoma japonicum*. The condition was described as an illness affecting new immigrants to the area, and in view of the fact that new spouses became severely ill and died, marriages between local people and outsiders were prohibited. Similar symptoms were also reported from elsewhere in the Orient and it was variously called urticarial fever, river fever, Kiukiang wading fever, the Katayama syndrome and Yangtse River fever. The cause remained unknown until Logan[1] ascribed the fever to early infection with *Schistosoma japonicum*.

Flu[2] observed symptoms resembling Katayama fever in *S. mansoni*-infected people in the West Indies. Later, during World War I, Lawton[3] reported cases of *S. mansoni* affecting Australian servicemen in Egypt. Fairley[4] drew attention to the fact that Katayama fever occurred in individuals infected with either *S. mansoni* or *S. haematobium*.

In Africa, *S. mansoni* infection more frequently presents as Katayama fever than *S. haematobium*. Katayama fever presenting in previously non-exposed individuals, who contracted schistosome infections in different parts of Zimbabwe and South Africa have been described in several publications.[5-16]

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The majority of cases occurred in white children, mainly boys aged 5 - 14 years; but also in young adults of both sexes older than 18 years. The first cases of Katayama fever ever found in indigenous blacks were those recorded by Clarke *et al.* in Zimbabwe.[14]

Three clinical syndromes are recognised as manifestations of infection by the three human schistosome species: (*i*) an invasive stage involving cercarial dermatitis, sometimes called Swimmer's or Kabure itch, due to cercarial penetration of bare skin; (*ii*) a toxaemic stage, i.e. Katayama fever or acute schistosomiasis, that coincides with (*a*) larval migration via lymph nodes, venules, right heart and lungs to the liver, and (*b*) the onset of oviposition; and (*iii*) an established stage or chronic schistosomiasis in which lesions are related to the presence of eggs in the tissues with subsequent granuloma formation and fibrosis.

Geographical area. The entire Transvaal Lowveld with its large number of irrigation dams and network of small streams is hyperendemic for schistosomiasis. The same is true for most of the rest of the province, Swaziland and Natal at altitudes below 1 400 m,[17] where temperatures are favourable for the development of the parasite in the snail.

Case reports

We report here on interviews with 3 male scuba-diving enthusiasts, the first 2 in their early 30s and one 40 years old. They became infected while recovering a boat engine from the shallows of a 1,1 million m^3 dam near Nelspruit in the eastern Transvaal Lowveld. Both patients 1 and 2, who had not been exposed to infective water previously, developed Katayama fever, while the third patient, who is a keen watersportsman and has lived in the area for about 10 years, was only mildly affected.

Water-contact history

The event took place at noon on 21 February 1986. The weather was warm and the sky overcast but bright. It had rained the previous day, raising the water level and submerging the grassy fringes of the dam. The divers wore costumes, but only patient 3 wore a wetsuit jacket. Oxygen tanks and goggles were donned while lying in the shallows near a stream estuary along the upper reaches of the dam. The search began in water 4 m deep, 50 m from the shoreline. The engine was recovered in 2 m of water nearer the shore. The divers then lay back in the shallows to remove their equipment and total water-contact time was about 25 minutes for patients 1 and 2, whereas patient 3 was in the water 10 - 15 minutes longer. Because the weather was warm, the divers did not dry themselves thoroughly on leaving the water.

Signs, symptoms and treatment

The signs, symptoms and treatments are shown in Table I. The initial, clinical syndrome, characterised by a cercarial itch, presented in each patient shortly after leaving the water. The dermatitis was fairly general in patients 1 and 2 whereas in

TABLE I. SYMPTOMS IN 3 SCUBA DIVERS DURING INVASIVE AND ACUTE/TOXAEMIC PHASES OF SCHISTOSOME INFECTION

Phase	Symptoms	Duration of symptoms		
		Case 1	Case 2	Case 3
Invasive (< 21 d)	**Cercarial itch**	**Within 3 - 5 min, lasted 48 - 72 h**	**Within 3 - 5 min, lasted 48 - 72 h**	**Within 3 - 5 min, lasted about 48 h**
		+++	+++	++
	Dermatitis	+++	++	+
	Swelling/oedema	**Lower calf**		
		++	—	—
	Urticaria	**Periodic for 6 - 8 wks**		
		++	—	—
Acute/toxaemic (21+ d)	**Onset of K fever**	**21 d post-infection**	**21 d post-infection**	**'Unwell'**
		+++	+++	+
	Pyrexia and sweating	**2-3 → 6-7/d/8 wks, late afternoon — early evening**	**< 6/d/<8 wks, late afternoon — early evening**	**Pyrexial only at 9 wks and after first treatment**
		+++	++	+
	Rigors and delirium	+++	—	—
	Concentration affected	**At 4 - 5 wks**	**At 4 - 5 wks**	**At 8 - 9 wks**
		++	++	+
	Malaise	**After 4 - 5 wks**	**After 4 - 5 wks**	**—**
		++	+	—
	Tender spleen and caecal area	**At 5 - 6 wks** ++	—	—
	Arthralgia	**Wrists and elbows** ++	—	—
	Dry, unproductive cough, wheeze	**At 6 wks** +++	+	**At 4 - 5 wks** +
	Lethargy	**At 7 wks** +++	+++	—
	Headaches	**Frontal & peri-orbital**		
		++ → +++	+ → ++	—
	Concentration, speech affected	+ → ++	—	—
	Diplopia, gait affected	+ → ++	—	—
	Diarrhoea and constipation	**At 9 wks, alternating**		
		++	+?	—
	Positive diagnosis	**Rectal biopsy 9 wks**	**Stool at 7 wks**	**Symptoms**
	Nausea	++	+?	—
	Loss of appetite and weight	**By 11 wks, − 10 kg**		
		+++	++	—
	Itchy scrotum	**Intermittent, almost entire period**	**Intermittent, almost entire period**	**Infrequent**
		+++	+++	+

+++ = severe; ++ = moderate; + = mild; → = increasing; ? = probable; K fever = Katayama fever; — = not experienced.

patient 3 it was confined to his lower trunk; seemingly his wetsuit jacket had afforded him some protection. He assumed that his condition had been caused by grass hairs and seeds in the shallows where he had donned and removed his diving equipment. The swelling of patient 1's lower calf was fugitive, lasting only a few days.

The second clinical syndrome, involving Katayama fever, manifested in the afternoon as a sudden onset of severe pyrexia and sweating in patients 1 and 2. The pyrexial condition persisted in the ensuing weeks and was confined to late afternoon and early evening times, but was normal by morning. One of patient 1's initial attacks, which was particularly violent with rigors and delirium, occurred while he was taking a bath and he nearly drowned. A timely visit by a colleague saved his life. He recalled a previous occasion when he suffered heatstroke after severe sunburn and considered this to be the reason for his reactions.

At 5 - 6 weeks the dry cough experienced by patient 1 continued as a persistent 'tickle in the throat' and he felt 'tight-chested'; his stomach also felt distended ('bloated') but he was not aware of any oedema in his body. At 9 weeks he noted blood in his stool and had a proctoscopy and biopsy and blood tests. The proctoscopy revealed bloody lesions in the rectum and the biopsy material was positive for *S. mansoni* ova; he was also infected with paratyphoid and treated accordingly. After treatment with praziquantel he felt better, but had a recrudescence about a month later and was treated again. He was slightly nauseous for most of the time and lost his appetite, which probably accounted for some of his loss of 10 kg mass. After his initial 2 treatments he had a further 7 with praziquantel, since symptoms recurred every 2 - 3 months for more than 2 years. After his second treatment, those following seemed to exacerbate his condition; but he persevered. Recovery was slow, but improved after treatments with a homeopathic preparation (see footnote, Table II). In March 1989 he felt his normal self again.

At 7 weeks, patient 2 presented with *S. mansoni* in his stool. He was treated with praziquantel and went on leave to Australia where he had a recrudescence and was treated again. Over a 30- — 36-month period he had 4 treatments with praziquantel, 1 with niridazole and, lastly, one with the homeopathic preparation mentioned above; after the latter he felt much improved. Recovery was slow, since symptoms, particularly lethargy and malaise, seemed to recur within a few

TABLE II. TREATMENT DRUGS, NUMBER OF TREATMENTS AND APPROXIMATE RECOVERY PERIODS

Treatment drug	No. of treatments Case 1	Case 2	Case 3
Cortisone	**1 at 21 d**	**1 at 21 d**	—
Niridazole	—	1	—
Praziquantel	9	4	3
Bilharzia Nosode*	2	2	—
Recovery period (approx.) (mo.)	**30-36**	**30-36**	**11-12**

*Bilharzia Nosode is a homeopathic preparation containing: antimony tartrate DH6; cantharis DH6; hamamelis DH6; hydrastis DH6; methylene blue DH6. Due to persistent recrudescence of clinical symptoms, 2 patients were given courses of treatment with Bilharzia Nosode by B.D.G. At this stage of their condition no further tests were conducted to confirm whether or not they had an active infection before treatment. Importantly, both patients responded positively to treatment, with a marked decline and eventual disappearance of the clinical symptoms. Interestingly, antimony tartrate is a well-known schistosomacide, which reportedly kills eggs and adult flukes.

months of treatment. In March 1989 he was in normal health.

During the early acute phase, patient 3 who had been previously exposed was mostly symptomless. His visit to a doctor and subsequent treatment was prompted by the news of his colleagues' extreme reactions at the 21-day post-contact stage, and because he was feeling 'slightly unwell' at the time. Between 5 weeks and 6 weeks after his first treatment, he presented with a mild unproductive expirational cough, which continued for a few weeks. At 8 - 9 weeks he was aware of being inattentive and was mildly pyrexial without profuse sweating. On these grounds he sought further treatment, which was followed by a recrudescence and a third treatment, all within a year of contact. In May 1988, he reported he was in good health.

The intermittent itch in the scrotum, which developed in all 3 patients during the acute phase, persisted for almost the entire period of their medication, but for patient 3 it was mild and infrequent.

Discussion

Within 5 minutes - 24 hours or more, following exposure to water containing human or non-human[18] schistosome cercariae, individuals may experience itching, which is sometimes followed by a papular rash or cercarial dermatitis. The dermatitis, which is a characteristic of the first clinical syndrome or invasive stage of the disease, can be present for 2 - 3 days, as was experienced by these 3 patients. It is reasonably assumed that there was a concentration of cercariae in the shallows where the divers had donned and removed their equipment. Intermediate host snails favour areas of submerged vegetation for their foraging and breeding, and the warm and bright weather conditions were ideal for the emergence of cercariae from the snails, which tend to peak about midday — the time the search took place. The 25 minute exposure time of patients 1 and 2, including the short period spent in the shallows, bears witness to the remarkable ability of the microscopic-sized organisms to penetrate human skin within a short space of time.

The second clinical syndrome involving the migratory phase of the larvae and onset of oviposition, which was particularly severe in patient 1 but less so in patient 2, and scarcely noticed in patient 3, represents an intense allergic reaction to the developing parasite.[19] The unproductive cough, experienced by all 3 patients, was caused by the immature parasites passing through the lungs on their way to the liver, during the early stages of migration.[16] The liver invasion was marked by abdominal discomfort, a distended feeling and tenderness about the caecum and the eventual anorexia and nausea which was particularly evident in patient 1.

The systemic involvement, which usually manifests in the early invasive stage, started at 3 weeks with pyrexia and profuse sweating and later included intermittent itch of the scrotum, experienced by all 3 patients, and also the occasional diarrhoea, constipation and arthralgia as experienced by patient 1.

Besides the allergic reaction due to the presence of maturing and enlarging parasites after paired migration to predestined locations, their production of ova merely adds to and intensifies the immune complexes that are important to the pathogenesis of acute disease.[19] In patients 1 and 2, the allergic reaction was particularly severe.

It is generally accepted that the severity of the illness usually varies with the intensity of infection as measured by faecal or urine ova counts but this is not always the case, since mild infections, as reflected by ova output, can also be associated with severe illness, especially in older people.[20] In our cases, no quantitative ova assessments were carried out. However, importantly, it would appear that prior exposure has a modifying influence on the severity of the disease, as evidenced in patient 3, who was probably partly immune, having been infected on a previous occasion while partaking in watersports. It may also be true to say that by wearing his wetsuit jacket he was afforded some protection against cercarial penetration when compared with his 2 colleagues, who wore only costumes.

Acute schistosomiasis usually affects tourists or other visitors exposed to infection for the first time,[10,21,22] as was seen in patients 1 and 2. It is important to note that the clinical and immunological manifestations can be readily confused with malaria, and that many are similar to those of serum sickness, suggesting that immune complexes are important in the pathogenesis of acute disease.[19] It is therefore crucial for diagnosis in Katayama fever to obtain a recent travel and water-contact history, since there is an increasing number of people who travel to, or holiday in, endemic regions. This is particularly important in people returning to western Europe from the tropics[21,22] and subtropics or, for example, from the Transvaal Lowveld and eastern Cape Province to Cape Town or Johannesburg.

Antischistosomal drugs have no immediate effect on the course of acute illness,[24] which became evident in patients 1 and 2. They may in fact be contra-indicated because of a release of antigens and aggravation of the underlying immunopathology. Instead, steroids and symptomatic treatment are indicated, as was the procedure for both patients. It is important to realise that deterioration can occur after chemotherapy.[21,23]

Praziquantel remains the drug of choice for schistosomiasis. It is claimed to be active against the early stages as well as the mature stages of the parasite but, as found in our 3 patients and in the experience of others (J. H. S. Gear — personal communication), its efficacy against cercariae and schistosomules is uncertain and needs confirmation. In view of this it seems that specific treatment should be delayed until after the acute phase and oviposition.

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