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Ectopic Bilharziasis

By AHMED FATT-HI, M.D.* and ISMAIL KAMEL, Ph.D.† (Cairo, Egypt)

BILHARZIASIS is a very old disease. It was known to the ancient Egyptians as a disease causing haematuria and they called it 'â a â' disease. They also described it as an incurable malady inflicted by the God of Death which tortured both men and women and was caused by a worm named Heltu. Calcified eggs were found in the kidneys of two mummies of the new Empire which were dissected in 1910 (Attiah, 1958).

Tiodor Bilharz was the first to discover the worm in 1851, in the blood of the mesenteric veins of an Egyptian boy and he mentioned that these worms were the cause of the endemic haematuria. In 1856, the worm was named 'Bilharzia' by Michael, but his publication was not known to the zoologist until later because it appeared in scientific journals dealing with Geology. Since Weinland's designation in 1858, it has been agreed to call the disease 'Bilharziasis' and the parasite 'Schistosoma' (Arafa, 1962).

This discovery was confirmed by the studies of Pierre Joseph, Van Beneden and Rudolph Leuckart, but it was not until 1903 that Patrick Manson showed that the eggs found by Bilharz actually belong to two different species, 'haematobium' and 'mansoni'. The life-cycle of this parasite was not clear until in 1915, when Robert Thomas Leiper discovered that certain snails served as intermediate hosts (Diamantis, 1928).

Bilharziasis, apart from being a very old disease, is also one of the most important public health problems in Egypt, where at least 16 million or more farmers have been afflicted. It is also seen in varying degrees of endemicity in East and South Africa, in the Middle East, in the Far East and in South America; about 200 million persons are infected throughout the world.

Ectopic Bilharziasis is defined by Faust (1948) as a specific local granulomatous reaction to the worms or their eggs occurring outside the porto-caval venous circulation. Most ectopic lesions occur in childhood. The exact route by which the parasite can reach such ectopic sites as the brain, spinal cord, ocular adnexae, skin, heart or lung, is not definitely known, but many postulates have been advanced to explain such occasional clinical entities. These postulates may be summarized as follows:

(1) Cercariae may penetrate the skin or mucous membrane, to develop indirectly into adults in nearby local veins, without the necessity for an incubative stage in the liver (Zawahry, 1956). Bilharz himself

* Professor of Oto-Rhino-Laryngology.
† Professor and Head of Pathology Department, Kasr Aini Hospital, Faculty of Medicine, Cairo University.

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reported one case of a bilharzial mass in the skin of the back of a water-carrier, which was due to the oozing of infected water from the bag (Cahill and El-Mofty, 1964).

(2) Other workers have proposed that a patent foramen ovale may explain how the eggs reach unusual sites, but the likelihood of such an abnormality is too infrequent to serve as an explanation in many cases (Bird, 1965).

(3) Eggs may be deposited by the worms in the gastrointestinal and genito-urinary tracts and filtered through the capillary barriers in the liver and lungs, to get into the general circulation and thence to be filtered out in the terminal arterial capillaries; but ova are usually deposited in the peri-venous tissues, not in the peri-arterial tissues (Badir, 1946).

(4) The worms may migrate from their usual habitat and circulate against the blood stream (Black, 1945). The presence of the worms in venules near to an ectopic lesion would lend some support to this theory (Badir, 1946).

(5) The fifth postulate depends upon the vertebral venous plexus system which consists of thin-walled, usually valveless plexuses, which have connections with the veins of the body cavities at each intervertebral space, as also with veins in the spinal canal, veins in the girdle, the azygos system, veins of the brain, skull and thoraco-abdominal wall, and veins of the pelvic viscera. Ova which are free in the portal or caval system may be pushed through these connections (by any effort or strain) and may be deposited in distant localities (Batson, 1940).

It seems that the most widely accepted concept is the last. It has been postulated that straining, coughing or lifting heavy weights may prevent the blood from entering the thoraco-abdominal cavity and may also squeeze the blood out of the cavities. Thus masses of schistosoma eggs may be carried via the vertebral venous system and deposited in the vessels of the brain, spinal cord, and elsewhere. The development of collaterals in hepatic fibrosis will assist this mechanism and worms may leave their normal habitat, to migrate into distant areas whenever irritated, as by incomplete chemotherapy or by surgical intervention (El-Garem, 1962). The same route of infection was also suggested by Cahill and El-Mofty (1964), as an explanation for extragenital cutaneous Bilharziasis, and by Attiah (1958), for ocular affections.

Schistosoma ova are mainly responsible for the formation of such ectopic lesions, but adult worms may occasionally be found. Immuno-allergic reactions have also been blamed for some of the manifestations of such ectopic cases (Mostafa, 1977; Ezzat *et al.*, 1979). The ova may be found dispersed at random, thus indicating that they have been conveyed to the area by the blood stream. However, they may be found in a linear arrangement along a blood vessel, this suggesting that the ova may have been deposited by an adult female. The deposition of ova usually induces a specific granulomatous inflammatory reaction which will be responsible

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for the pathological condition; but in some cases these infiltrating ova are seen without any surrounding inflammatory reaction. However, such patients are not suffering from a generalized immunological defect, because ova in other sites have produced the characteristic granulation tissue (El-Mofty and El-Zawahry, 1962).

Lesions in the nervous system, ocular adnezae or skin are by far the most common ectopic manifestations of Bilharziasis. Other rare sites include cardiac muscle, thyroid and salivary glands. A search of the literature has failed to disclose any record of ectopic lesions in the upper respiratory passages, ear, nose and throat. In 1913 Fujinami and Narabayashi (Badir, 1946) found the worms in gastric, oesophageal, splenic and renal veins in experimentally affected monkeys.

Pharyngeal Bilharziasis

No case has been previously reported of ectopic lesions in this area. We have seen two cases of ectopic Bilharziasis presenting as masses in the posterior pharyngeal wall. In such cases, it may be suggested that the cercariae can penetrate the pharyngeal mucosa to complete their life-cycle or to develop in the veins of the locality. That the cycle can be completed away from the normal habitat is, however, doubtful, and experiments are still in progress to prove or disprove such an assumption (Attiah, 1958).

No specific clinical picture can be claimed to be characteristic for ectopic pharyngeal bilharziasis. The two cases seen in the pharynx were in patients aged seven and 14 years.

The first case was a male child aged seven years complaining of a nasal tone in his voice. Clinical examination showed a mass protruding behind the soft palate. Digital examination revealed a hard, smooth non-bleeding mass attached to the posterior wall of the pharynx. The cut section of the hard mass was gritty, and fibrous bands divided it into loculi.

Microscopic examination showed subepithelial lymphocytic infiltration together with plasma cells, eosinophils, macrophages and fibroblasts (Fig. 1). The ova observed in the section showed various stages of degeneration and calcification. Further investigations demonstrated heavy urinary bilharzial infestation.

The second case was a female aged 14 years who presented with a sensation of a lump in the throat. Clinical examination showed a large non-pedunculated mass in the left side of the pharynx behind the tonsil. The mass was non-ulcerated, firm in consistency and attached laterally and posteriorly, and it extended from the masopharynx above to the hypopharynx below. The mass was removed and the pharyngeal mucosa was reconstructed.

Macroscopic examination showed lymphocytic infiltration and scattered granulomatous formation, with macrophages surrounding the terminal spined ovae (Fig. 2). Plasma cells and eosonophils were present,

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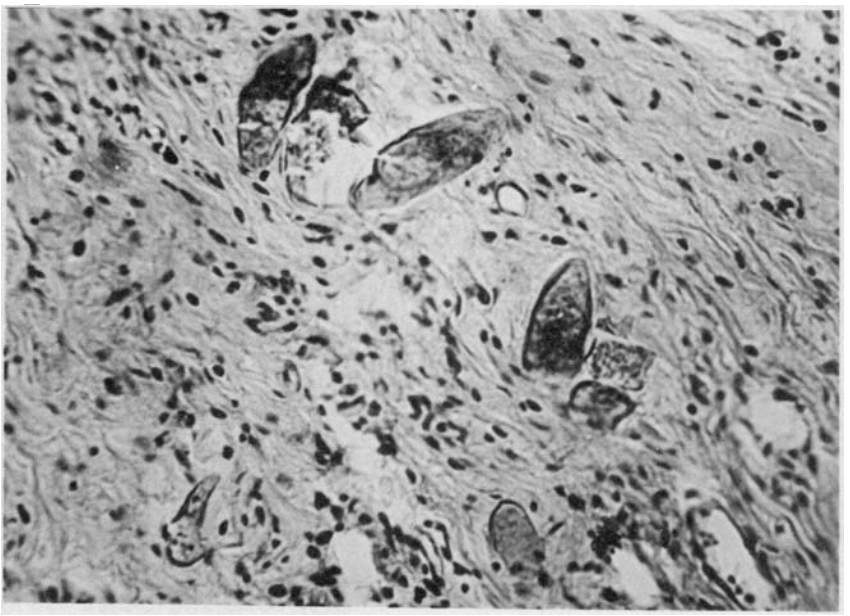


FIG. 1

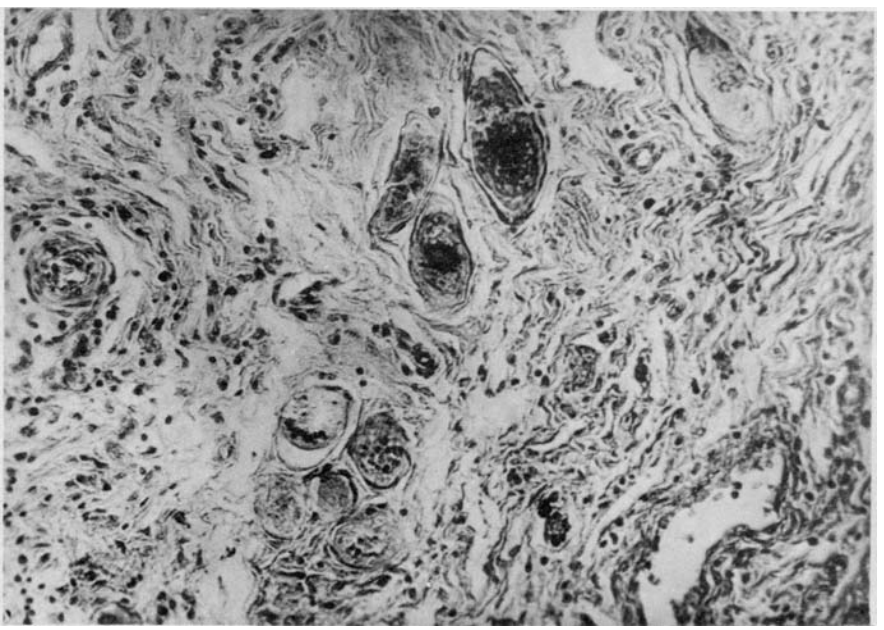


FIG. 2

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with few giant cells. No worms were seen in the mass examined. The post-operative follow-up showed normal healing of the pharyngeal wound. Further investigations of the patient showed heavy bilharzial infestation of both urinary tract and intestines with hepato-splenomegaly.

Broncho-Pulmonary Bilharziasis

Belleli, in 1885, was the first to describe bilharzial ova in the lungs (El-Garem, 1970). Shaw and Ghareeb (1938) discussed isolated parenchymatous tubercles as well as focal necrotizing pneumonia from dead embolized worms. Massive eosinophilic granulomata round bilharzial ova were also described (Mallah and Hashem, 1953). Nor-El-Din and El-Baz (1954) reported the presence of bilharzial ova in the sputum. Erfan and Deep (1957) described transient pulmonary infiltrations of the Loeffler type as well as miliary bilharzial lesions. Ragab and Hashem (1962) performed experimental work to show the different lesions in the lungs in the various stages of bilharzial infestation, and they described two main groups: the first includes early lesions produced by cercariae as they pass from the skin to the lungs on their way to their final destination in the portal circulation; the second group includes late lesions produced after maturation of the worms and deposition of the ova. These are due either to the ova or to the worms, usually in the form of bilharzial follicles. The very well-known presentation of bilharzial pulmonary hypertension with secondary heart failure (Bilharzial cor pulmonale) has been described by many authors, who included in its pathology bilharzial parenchymatous tubercles and obliterative endarteritis with secondary angiomatoid formations (Salah, 1961).

Ocular Bilharziasis

Attiah (1962) mentioned that ocular complications may occur indirectly through allergic reactions to probable toxins of the parasite, or through functional disturbances of the organs affected, as well as being due to ectopic lesions. The ocular tissues were affected in children aged 4–12 years, mostly in males and in all except two with unilateral involvement. The site was in either the palpebral conjunctiva or the caruncle. The globe and lacrimal system were not involved in any of the cases reported. The lesion was in the form of a granuloma which presented either as a polypoid mass, or as a diffuse swelling, or as multiple pinpoint or large discrete nodules. Ova were present in all the lesions except one (Badir, 1946).

Cerebral and Spinal Cord Bilharziasis

Day and Kenawy (1936) were the first to report a case of transverse myelitis due to schisosoma haematobium. Bayoumi (1939) reported another case. Ova and not worms were responsible for the involvement of

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the nervous system. The following is a list of reported cases due to schistosoma Japonicum, haematobium or mansoni, whether the diagnosis was pre-operative or port-mortem. A similar collection was presented by El-Garem (1962).

The pathological and clinical pictures of cerebral bilharziasis include space-occupying granulomas, Jacksonian epileptic fits, softening of parts of the cortex or medulla, and symptomatic psychosis (El-Garem, 1962). Involvement of the spinal cord may present either with transverse myelitis, a granulomatous mass or radiculitis, especially of the cauda equina (Bird, 1965). The myelogram in spinal bilharziasis is specific and is characterized

TABLE

LIST OF REPORTED CEREBRAL AND SPINAL CORD BILHARZIASIS

Year	Author	Schistosoma						Year	Author	Schistosoma					
		Japonicum		Haematobium		Mansoni				Japonicum		Haematobium		Mansoni	
		C	S	C	S	C	S			C	S	C	S	C	S
1980	Jamagiwa	PM						1946	Billings	2P					
1906	Tsunode	PM	E					1946	Resende						P
1910	Houghton	P						1946	Faust	PM					
1910	Aoyogi	PM						1946	Gulter	P					
1913	Ferguson			PM	OV			1946	Swanson	OP					
1917	Ferguson				PM			1947	Malting	OP					
1930	Multer						PM	1947	Tillman	7P					
1930	Maciel					PM		1947	Speigel	OP					
1931	Chu	2P						1947	Watson	OP					
1935	Nieva	P						1947	Chasnoff	OP					
1935	Schimidzu	OP						1947	Palmer	OP					
1935	Taveres					P		1947	Reeves	OP				7P	
1935	Simoes					P		1948	Faust					PM	
1936	Edgur	OP						1948	Raper	P					
1936	Day				PM			1948	Tungho	OP					
1936	Egan	2P						1948	Saunders	20P					
1936	Spiridon	3P						1948	Garrera			P			
1937	Greenfield	20P						1948	Hunt	PM					
1939	Bayoumi					PM		1950	Gelfand			28 è OV			
1939	Hoff				3P	P		1951	Smith	P				OP	
1939	Santacruz	PM						1952	Ross					PM	
1940	Manson				OV			1953	Abbott					P	
1941	Espin						PM	1956	Hovvax					OP	
1941	Vitug	PM						1957	Chang	P9M					
1942	Ponde					P		1958	Alves			40 è OV			
1945	Gama						OP	1958	Janes	40P					
1945	Thomas	PM						1960	Hutton			PM			
1945	Syra					P									
1945	Pints					P		PM & OP		34		2	2	6	3
1946	Carrol	5P						P (Pre-Op)		30		1	3	15	
								Present Ova			1	68	2		

C = cerebral.
PM = Post Mortem.
P = Pre-operative.
S = spinal cord.
OP = Operative.
E = Eggs.

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by intramedullary irregular trifid-edged swelling starting and ending abruptly, with a size equal to the length of a vertebral body, opposite D12 or L1 (El-Banhawy, 1971). Circumoral precipitin test (C.O.P.) is performed by incubating the schistosoma ova against the cerebro-spinal fluid and is claimed to be specific (Seif El-Din *et al.*, 1973). Operative treatment is indicated in space-occupying lesions preceded and followed by specific schistosomicidal therapy (El-Garem, 1962).

Cutaneous Bilharziasis

This has been classified into four categories (El-Mofty and El-Zawahry, 1962):

(1) Early cercarial dermatosis, mostly produced by non-human schistosomes mainly of the avian species, while the human type produces mild dermatitis in the form of erythema, urticaria and itchy papules. These usually disappear within seven days, leaving pigmented spots.

(2) Late non-specific allergic manifestations during the parasitaemic stage, and caused by the products of schistosomes. Allergic anaphylactoid reactions appear causing allergic erythemata and prurigenous lesions and fever. Joint pains, headache, enlargement of the liver and spleen and eosinophilia are the usual manifestations of this stage.

(3) Remote schistosomal infiltrative granulomata produced by schistosoma ova inducing an inflammatory and fibrotic reaction, usually around the genito-urinary tract.

(4) Extragenital infiltrative lesions which are caused by the deposition of schistosoma ova in the dermis in distant foci on the trunk. Fresh lesions appear as small firm rounded or oval papules with the same colour as the skin or a little darker. Older lesions aggregate and make papules or nodules of rough appearance. These masses are symptomatic and are neither itchy, tender nor painful.

Discussion

Ectopic Bilharziasis may affect different parts of the body e.g. ocular adnexae, brain, spinal cord, skin, heart or lung. A laryngeal mass which was thought to be bilharzial was mentioned by Shaheen (1942). However, ectopic pharyngeal Bilharziasis has not been reported before.

All three species of schistosoma can produce ectopic lesions. It has been mentioned that since schistosoma japonicum is more acute and its female worm is more prolific, its daily output of eggs is 50–300, while in haematobium it is 20–30, and in mansoni it is only 1–4 eggs; this may explain the higher incidence of japonicum cases (El-Garem, 1970). Also, the relative sizes of the ova may offer a further explanation; those of japonicum are the smallest, being 70–100 × 55 μ, while haematobium ova are 112–170 + 40–70 μ. Sixty-five out of 167 cases reported in the literature as bilharziasis in the nervous system were due to japonicum (El Garem,

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1970). Most authors agree that ectopic bilharziasis occurs more frequently in a later stage of the infection rather than earlier in the disease (Bird, 1965).

Adults are less prone to develop ectopic lesions as they may have developed some immunity, or have been treated. On the other hand, children may be unaware of the symptoms and do not seek early treatment. This may allow heavy infestation and give a chance for ectopic lesions to occur. Children are usually in more contact with infected water, and so are more liable to be infected than adults.

The diagnosis of ectopic pharyngeal bilharziasis is made by histopathological study. The presence of active Bilharziasis in the body is assumed by the fact that both our cases had excessive bilharzial ova in their urine and one case also had positive stools.

Ectopic lesions in the pharynx or elsewhere may be symptomless unless they are located in vital organs e.g., the heart, brain or spinal cord. They may be of minute size and may resolve under treatment before they attain a size that can be detected clinically. The lesion may remain unnoticed for a long time, until an increase in size necessitates surgical removal, as in ocular or cutaneous lesions.

The fact that no recurrence occurred in the two cases of ectopic pharyngeal bilharziasis after surgical removal of the masses, may be due to the anti-bilharzial treatment and the prevention of further exposure. The therapeutic response of ectopic ocular lesions reported in Egypt has been noticed to be good. It is claimed to prevent recurrence of granulomata which have been surgically removed (Attiah, 1962).

Summary

Ectopic Bilharziasis is discussed and two cases of ectopic pharyngeal affections are reported. The five theories advocated to explain how ectopic lesions can develop outside the portol-caval system are discussed. The clinical picture, age, diagnosis and follow-up of such lesions are mentioned.

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Address for correspondence:
Dr. Ahmed Fatt-hi (M.D.),
35 Sayeda Zenab Square, Cairo, Egypt.

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