Sparganosis

K. Vanathy

Learning Objectives

1. To emphasise the various modes of transmission of infection to the human beings.
2. To understand danger of ocular and central nervous system involvement.
3. To know about the challenges in the clinical and laboratory diagnosis of this condition.

Introduction

Sparganosis is a zoonotic infection in humans caused by plerocercoid larvae of Pseudophyllidean cestodes of the genus *Spirometra.* The plerocercoid larval form (L3) *Spargana* causes the infection. Humans are the accidental hosts. *Spargana* in infected humans can invade the eyes, brain, subcutaneous tissue, breast or spinal cord and can cause a threat to human health. Many species of the genus *Spirometra* including *Spirometra mansoni, Spirometra ranarum, Spirometra erinaceieuropaei* and *Spirometra proliferum* and recently described *Spirometra decipiens* cause sparganosis.

History

The parasite was first described by Patrick Manson in 1882 from China. He identified the most common species of Asia, *S. mansoni* during the post-mortem examination. The first case of human sparganosis was reported by Stiles from Florida, USA, in 1908. In 1959, *S. erinaceieuropaei* was identified and considered as a single species which was previously considered as separate species like *S. mansoni* and *S. erinacei.* This is one of the most common species worldwide. Morphologically, *S. erinaceieuropaei* and *S. decipiens* were differentiated by the presence of a number of coils in the uterus which was 5–7 and 4.5, respectively. *S. mansonoides* was reported by Mueller in 1935. It was found that *S. erinaceieuropaei* was distributed in the Asian region and *S. mansonoides* in North America. A few cases of *S. theileri* was reported in 1974, among the Masai tribe of East Africa. It was identified from excised nodule which contains sparganum.

The first case of *S. proliferum* was reported by Ijima in 1905. The parasite was found to multiply inside the host and hence it was also known as proliferating sparganum. It tends to proliferate with one plerocercoid in one lesion and thus disseminated throughout the body involving all

K. Vanathy (✉)
Department of Microbiology, Mahatma Gandhi Medical College and Research Institute, Pondicherry, India

S. C. Parija, A. Chaudhury (eds.), *Textbook of Parasitic Zoonoses*, Microbial Zoonoses,
https://doi.org/10.1007/978-981-16-7204-0_34

visceral organs and subcutaneous tissue. The parasite causes infection in immunocompromised hosts, such as AIDS patients, is fatal and can be identified during autopsy. The first case of *S. proliferum* was reported from the USA by Stiles in 1908, but the most common species identified later in 1935 was *S. mansonoides*. *S. decipiens* was another species reported in humans in the year 2015.

Taxonomy

The genus *Spirometra* belongs to Family, Diphyllobothriidae; Order, Pseudophyllidea; Sub-class, Eucestoda; Class, Cestoidea and Phylum, Platyhelminths. Species of two genera, *Diphyllobothrium* and *Spirometra,* are closely related. Phylogenetic studies based on ribosomal internal transcribed spacer 2 sequences are carried out to know the relationship between different species of the genus *Spirometra* with that of *Diphyllobothrium.*

Genomics and Proteomics

S. erinaceieuropaei possesses the largest genome among tapeworms of 1.26 Gb. The beta tubulin gene analysis demonstrated that this particular species may not respond to treatment with albendazole. The nucleotide variations were very minimal among strains found in Australia, Asia and New Zealand. DNA sequence analysis of mitochondrial dehydrogenase, cytochrome oxidase, iron sulphur protein analysis has shown that although *S. proliferum* is closely related to *S. erinaceieuropaei,* both the species are quite distinct.

The Parasite Morphology

Adult Worm

Spirometra are long, segmented and flattened dorso-ventrally. The worm is 60–110 cm long and 0.5–0.8 cm in width. Adult worm consists of head or scolex, neck and body or strobila (Fig. 1). The scolex is elongated and spoon-shaped, does not have any suckers and possesses a pair of longitudinal grooves called bothria. This groove is helpful for their attachment to the intestinal tissue. The neck is followed by body or *strobila* which contains many, nearly 1000, proglottids that may be immature, mature and gravid. The worm is hermaphrodite, both well developed male and female reproductive organs are found in the worm.

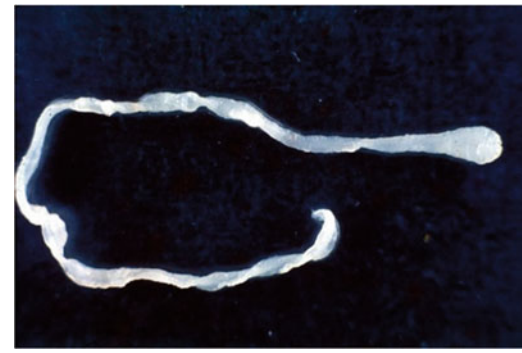

Fig. 1 Adult worm of *Spirometra* (Courtesy: CDC)

Eggs

Eggs are ovoid in shape and measure about 65 × 35 μm in size (Fig. 2). Each egg contains an embryo inside which has three pairs of hooklets. The egg is surrounded by a thin membrane or capsule and it has an operculum at one end. The egg is not embryonated when hatched. Embryonation occurs in water.

Larva

Sparganum is the larval stage of the parasite. It is wrinkled, white, ribbon-shaped measuring 3 mm in breadth and 30 cm in length. The larva does not have any suckers, but instead have two longitudinal grooves at the anterior end called bothrids. It has a solid body with no bladder. The larva has unsegmented strobila of 20–30 cm in length. The strobili consist of the scattered longitudinal

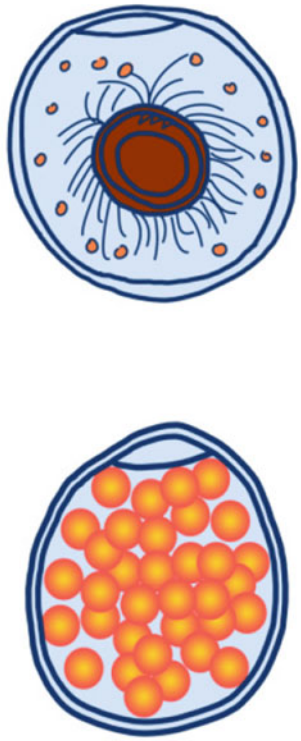

Fig. 2 Embryonated and unembryonated egg of *Spirometra*

muscle fibres in the mesenchyme and a thick tegument.

Cultivation of Parasite

S. mansonoides has been cultivated in vitro, in primary cell culture or cell lines. Those monolayer cell cultures include human amnion, rhesus monkey kidney, rat or hamster embryo. WI-38 and L-cells are the cell lines used in vitro culture. They are maintained in eagle's medium or medium 199 containing 10% calf serum.

Laboratory Animals

The plerocercoids can be maintained by serial passage in BALB/c mice every 10–12 months. The mice can be infected orally with sparganum infection. This model has been used for immunological and other studies.

Life Cycle of *Spirometra* spp. Hosts

Host

Spirometra spp. completes its life cycle in a definitive host and in first and second intermediate hosts (Fig. 3).

Definitive Hosts

Dogs, cats, birds and wild carnivores. Humans are the accidental hosts.

First Intermediate Hosts

Cyclops and fresh-water crustaceans.

Second Intermediate Hosts

Frogs, snakes, birds, mammals and other amphibians.

Infective Stage

Plerocercoid larva, L3 larva, (Sparganum) is the infective stage.

Transmission of Infection

Humans, the accidental hosts, acquire infection by (a) ingestion of contaminated water with Cyclops harbouring procercoid larva (L2) which develops into sparganum in human intestine and (b) ingestion of raw or undercooked reptiles and birds infected with plerocercoid larva (L3), the *sparganum*. (c) The infection is also acquired by application of the infected flesh of the second intermediate host over the human skin, conjunctiva or vagina as a poultice on the infected wound. In either of the above modes of transmission, man acts as a definitive or second intermediate host. Man acts as a dead-end host.

Dogs and cats acquire the infection by eating frogs, snakes, amphibians or mammals which contain sparganum larva. *Spirometra* adults live in the small intestine of mammals and other definitive hosts. The nutritive materials absorbed through their tegument are transferred to internal tissues and they get metabolised. They are

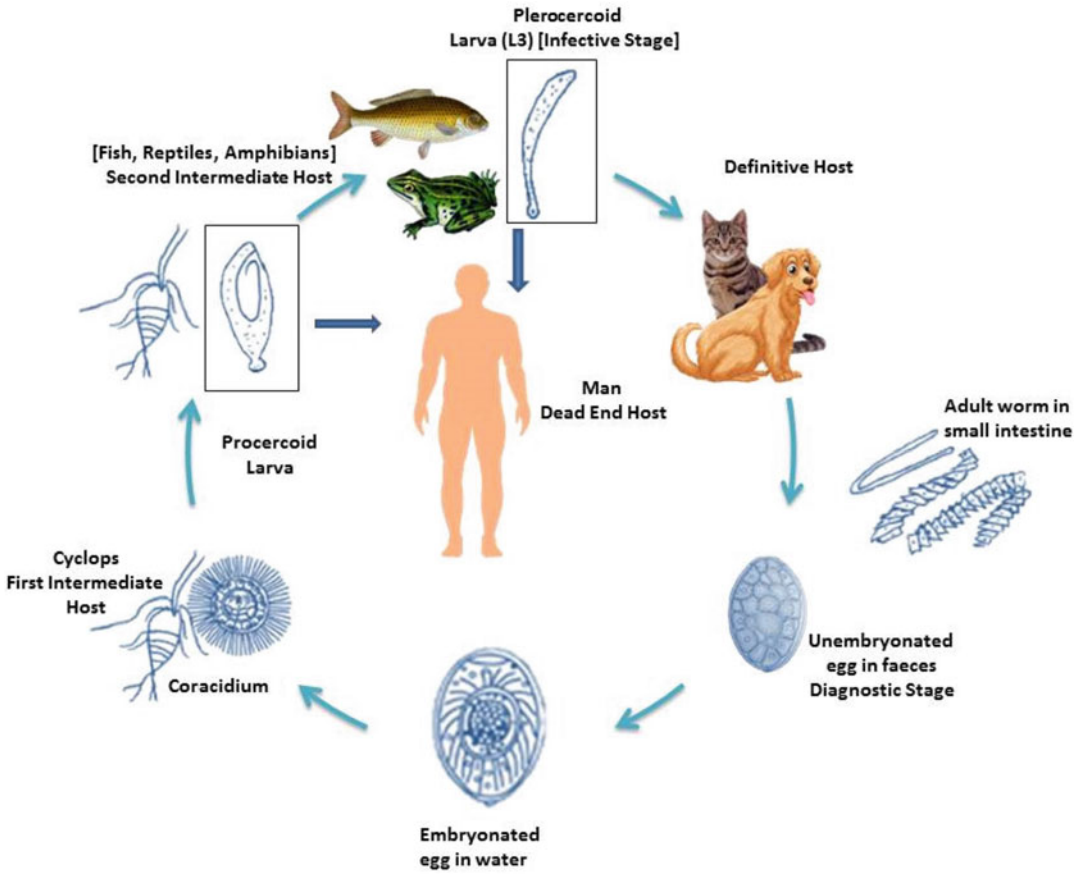

Fig. 3 Life cycle of *Sparganum*

hermaphroditic. The adult worms live for many years inside the host and release the eggs in faeces.

The eggs hatch in fresh water as coracidia. Coracidium is around 80–90 μm in diameter and is covered by the ciliated membrane. They are ingested by Cyclops, the copepods in water, in which they develop into the procercoid larvae (L2) in 3–11 days. Procercoid larvae are oval in shape and vary from 260 ×44–100 in size.

Frogs, snakes, mammals and amphibians, among others, acquire the infection by ingesting the infected cyclops. On ingestion, the larvae which are released in the intestine penetrate the intestinal wall, migrate to the tissues and develop into sparganum larvae. The life cycle is repeated by ingestion of these infected hosts.

Pathogenesis and Pathology

Pathogenesis of sparganosis depends on the migration of the larva (Sparganum) and its subcutaneous location. The migratory larvae, during the course of infection, are found in the muscle or tissue in the extremities, the chest and abdominal wall. Eyes, pleura, pericardium, brain, spinal cord, lymph nodes, intestinal wall, urinary tract and scrotum are the other sites. Sparganum at these sites typically causes an inflammatory reaction in the tissues surrounding the subcutaneous site, subsequently resulting in nodules. These discrete subcutaneous nodules are the typical pathology of sparganosis that may appear and disappear during the course of infection. These nodules cause various clinical manifestations depending on their presence on various sites.

Table 1 Distribution of *Spirometra* species

Spirometra species	Distribution	Intermediate hosts	Definitive hosts
Spirometra erinaceieuropaei	Far East, Europe, Asia	*First intermediate hosts*: Cyclops and other crustaceans *Second intermediate hosts*: Frogs, snakes, birds, mammals and other amphibians	Dogs, cats, foxes, birds and wild carnivores. Humans are the accidental hosts
Spirometra decipiens	Korea, China		
Spirometra mansonoides	North America		
Spirometra theileri	East Africa — among Masai tribe in Kenya and northern Tanzania		
Sparganum proliferum	Far East and America		

Immunology

Limited immunological studies in experimental mice have revealed the important role played by T-regulatory cells which are initially up-regulated, followed by down regulation and final up-regulation. Regarding the cytokines, Interleukin-6 first increases and then returns to normal levels. There is a decrease in the levels of Interleukin-2, interferon-γ and IL-17α production but an increase in IL-4 and IL-10 levels.

Infection in Humans

There are two forms of sparganosis in humans: proliferative and non-proliferative.

In humans, the plerocercoid larva migrates to various organs, subcutaneous tissue and forms tender nodular mass. They are slow growing. Pleural cavity, brain, lung, CNS, eyes, subcutaneous tissue, breast, abdominal viscera and urogenital viscera, among others, are frequent sites of infection by the larva. Depending on the site of the location of the larva, the symptoms vary from non-specific discomfort, pruritus, elephantiasis and brain abscess to peritonitis and so on. Ocular sparganosis may involve conjunctiva and orbit of the eye causing periorbital oedema, lacrimation, orbital cellulitis, ptosis and movement disorder. Involvement of anterior chamber can cause hypopyon, synechia and secondary glaucoma. The nodules resemble a tumour mass in genital sparganosis involving labia, testes, scrotum, vagina, ureter and urinary bladder. Cerebrospinal involvement causes symptoms such as limb weakness, hemiparesis, paresthesias, headache and confusion. It mainly involves cerebral hemisphere mainly the fronto-parietal lobe extending to cerebellum. The lesion over the skin is a clear, rubbery, cystic swelling which remains painless for many years and may result in sudden pain.

Aberrant sparganosis caused by *S. proliferum* is called proliferative sparganosis in which the parasite continues to grow by branching and budding. Proliferating sparganosis involves subcutaneous tissue, bone and spinal cord. The larva may undergo continuous branching and budding to form many plerocercoids at single site. They begin as small tumour-like mass in the subcutaneous tissue of thigh and neck and then extent to involve internal organs like brain, lungs, abdomen, skin and muscles. They form cutaneous nodules and their adult form is unknown.

Epidemiology and Public Health

After the first reported case of sparganosis in China in 1882, many cases of sparganosis have been reported worldwide with a large number of cases in China, Thailand, Korea and the USA. In Thailand, the reported cases were seen involving the eyes, cerebrospinal region and viscera. The cutaneous and ocular sparganosis was due to the application of frog flesh as poultice for the treatment of sore eyes and also drinking contaminated water. Reports of human sparganosis have also been documented in Japan, India and Sri Lanka (Table 1). The liver sparganosis was first reported in India and was cured by aspiration of the worm from abscess followed by treatment with metronidazole.

Diagnosis

Human sparganosis is often misdiagnosed since the clinical features are not specific. Proper history taking and examination serves as a guide to some extent. Patients from endemic regions, eating undercooked frog and snakes and drinking contaminated water add to the suspicion of sparganosis. Also, they may present with migratory, painful, subcutaneous nodule. The diagnosis can be made by surgical excision of the nodule and removal of the worms. The absence of suckers and hooklets differentiates sparganum from cysticercus and coenurus. Definitive diagnosis can be made by inoculation of adult worm into the definitive host and collecting the worm or faeces specimen from the intestine (Table 2). But this is time consuming and cumbersome procedure.

Microscopy

The tissue section of the organ involved shows proliferating sparganum in H & E stain. The morphology of the larva removed at surgical resection reveals white, ribbon-shaped structures with a wrinkled surface ranging in size from a few millimetres to a few centimetres.

Serodiagnosis

The diagnosis can be made by antigen-specific IgG antibodies by ELISA from peripheral blood or crude somatic antigen. Antigenic polypeptide 28.7 kDa (SmAP) that is expressed by the sparganum stage increases the sensitivity and specificity of the test. Serological diagnosis may be used to confirm a suspected radiological finding.

Molecular Methods

Molecular techniques are considered to be superior to other procedures. PCR is used for the *Spirometra* species identification and the gene targets are small subunit (18S) and large subunit (28S) ribosomal RNA, ribosomal internal-transcribed spacer 1 and ribosomal internal transcribed spacer 2, *cox1*, *nad3* and nuclear *sdhB* genes.

Other Diagnostic Modalities

These include CT, MRI and USG. It is useful for cerebral and ocular sparganosis where CT shows hypodensity, ventricular dilatation and calcifications. It has to be differentiated from brain mass, cysticercosis and paragonimiasis.

Treatment

The main modality of treatment of sparganosis is surgical removal. It is necessary to remove the entire body of sparganum without leaving scolex which may lead to recurrence. The complete removal can be confirmed by repeated serological tests. A decreasing titre of anti-sparganum IgG

Table 2 Diagnostic methods of human sparganosis

Diagnostic approaches	Methods	Targets	Remarks
Microscopy	Biopsy	Tissue section-H & E stain	Primary method of diagnosis limitation: invasive
Serology	IgG antibodies by ELISA	Antigenic polypepetide 28.7 kDa (SmAP)	*Limitation*: Cross-reactivity with *Clonorchis* and *Paragonimus*
Molecular technique	PCR	Small subunit (18S) and large subunit (28S) ribosomal RNA, ribosomal internal transcribed spacer 1 and ribosomal internal transcribed spacer 2, *cox1*, *nad3* and nuclear *sdhB* genes	High sensitivity and specificity *Limitation*: Require skilled personnel

antibody confirms the complete removal of the worm. Localised chemotherapy is preferred if surgical removal cannot be done. The drug that may be used is praziquantel 120 mg/kg in divided doses. Mebendazole can also be used. For proliferating sparganosis, surgical removal is the only choice of treatment.

Prevention and Control

Preventive measures include avoidance of undesirable cultural practices such as consumption of raw or undercooked flesh of frog or snakes or application of fresh frog flesh as poultice over skin or sore eye or drinking contaminated water with infected copepods. It is also controlled by treatment of cestodiasis. Preventing hunting and sale of wildlife especially frogs and snakes, and increased public awareness on mode of the transmission, clinical presentation, treatment and prevention mainly for people travelling to endemic region, also contributes to control of the infection.

Case Study

A 33-year-old woman came with a history of painful migratory swelling over the left thigh for the past 6 months. Erythema was seen around the swelling. Initially it was diagnosed as a soft tissue tumour. Later MRI revealed several elongated tubular tracts in the medial aspect of the left thigh from which a long, wrinkled, whitish worm was removed. The diagnosis was made by histopathological examination as *Spirometra* Spp.

1. What are the modes of transmission of the infection in humans?
2. What are the measures necessary to prevent infection?
3. How to make a pre-operative diagnosis of sparganosis?

Research Questions

1. How to elucidate the pathogenesis and virulence factors of *Spirometra* Spp. which remains largely unknown?
2. What medical treatment may be useful which can obviate the need for surgery?

Further Readings

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