HOST TISSUE REACTION TO *GNATHOSTOMA MALAYSIAE* (NEMATODA : GNATHOSTOMIDAE) IN *RATTUS SURIFER* MILLER

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Abstract. The occurrence of adult *Gnathostoma malaysiae* in *Rattus surifer* and *R. tiomanicus* in Malaysia has been reported but there are no known reports on the host tissue reactions. This paper reports on the gross pathology caused by *G. malaysiae* in a red spiny forest rat, *R. surifer* and the tissue reactions caused. A tumor-like growth was located on the mid-stomach wall in a female rat captured in Gunung Bachock, Kelantan, Malaysia. This growth consisted of four tunnel-like structures containing sanguinopurulent fluid and leukocytes and this structure led into a central canal. The tissue surrounding the tumor was greatly inflammed and there was localized gastritis. The tunnel-like structure was surrounded by dense fibrotic tissue. The stomach wall was devoid of superficial epithelium and smooth muscle but mucinous glands were present. The midregion of the fibrotic scar contained eggs of *G. malaysiae* which had evoked a strong tissue reaction and were surrounded by pus. Blood vessels were empty, dilated and had undergone vasculitis and thrombosis.

INTRODUCTION

According to Miyazaki (1991) 20 species of *Gnathostoma* have been reported but only 10 species are probably valid. The most frequently encountered species, *G. spinigerum* Owen, 1836 has been reported from many carnivorous mammals (cats, civet cats, tigers and leopards) from many parts of Malaysia (Adams, 1933; Rhode, 1962; Miyazaki, 1960; Lim, 1976). Other species reported from Malaysia are *G. doloresi* from pig and *G. malaysiae* from wild rats, *Rattus surifer* and *R. tiomanicus* (Sandosham, 1953; Miyazaki and Dunn, 1965).

The species *G. malaysiae* was described by Miyazaki and Dunn (1965) from wild rats, *R. surifer* and *R. tiomanicus* and subsequently reported by Betterton (1978) in *R. surifer*. In the rat these worms are known to produce characteristic tunnel-like tumors or lesions on the stomach wall. We have not found any report of description of tissue response to *G. malaysiae* infections in mammals, especially rats. This paper describes the gross and microscopic host reaction to *G. malaysiae* and tissue pathology in *R. surifer*.

MATERIALS AND METHODS

In November of 1977 six live *R. surifer* were trapped from an area surrrounding the openings of several small bat caves in the jungle fringe area of Gunong Bachok, Kelantan, Peninsular Malaysia. Examination of one female *R. surifer* showed a large tumor-like growth consisting of four tunnel-like structures leading to a central canal or anterior chamber located on the midstomach wall. The worms within this tumor were removed and fixed. In all four adult worms, 2 males and 2 females, were found in the pouches (Fig 1, 2). The worms were identified as *G. malaysiae*. The anterior chamber opened into the lumen of the stomach. The tumor (without the worms) was excised, fixed in neutral formalin (80°F, pH 7.2) and the excised tumor was sent to the Armed Forces Institute of Pathology, Washington DC for deposit and processing.

RESULTS

Gross tissue pathology

The head bulb of the adult worms were attached to the burrows or canals of the tumor-like cyst in the anterior portion of the stomach wall.

The lumen of the stomach wall was penetrated by four adult worms. These worms were found in both the central anterior chamber and in the four accessory tunnel-like structures (Fig 3A; the

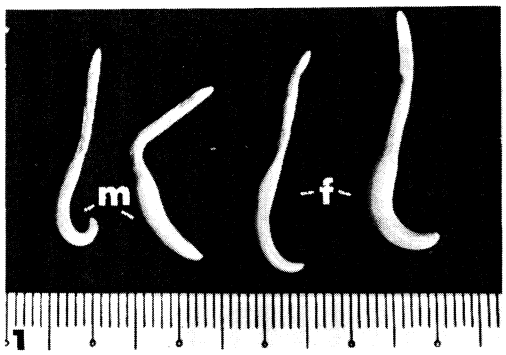

Fig 1—Adult males (m) and females (f) of *Gnathostoma malaysiae*.

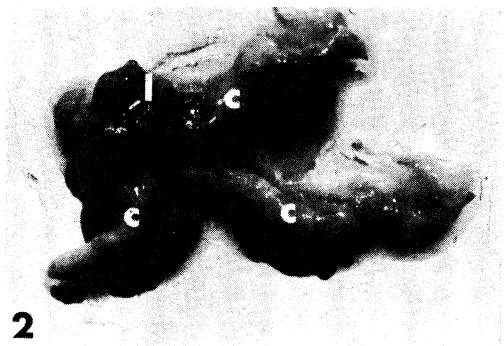

Fig 2—Tumor-like cyst containing *G. malaysiae* in canals (c) occupied by worms in the lumen (l) of stomach of *Rattus surifer*.

worms have been removed) measuring 1.5 to 2.5 cm in length. The central anterior chamber was filled with sanguinopurulent fluid containing many leukocytes. The canals approached but did not open into the peritoneal cavity. The tissue surrounding the tumor was greatly inflamed and showed a localized but marked gastritis. The tissue surrounding the area occupied by the worms was dense and fibrotic.

Microscopic tissue pathology

Histological examination of the stomach wall showed portions devoid of both superficial epithelium and smooth muscle while mucinous glands were present. The remaining infected tissue consisted of loose connective tissue with numerous patches of fibrotic scarring. Examination of the midregion of fibrotic scar revealed several highly keratinized, pitted nonoperculate nematode eggs (25 by 56 μm) whose size and morphology were consistent with those of *G. malaysiae* as reported by Miyazaki and Dunn (1965) (Figs 3C, 3D). Pus, adjacent to the eggs, consisted of necrotic cells, leukocytes, and cellular debris. Surrounding this area was a granulation tissue of polymorphonuclear leukocytes, eosinophils, lymphocytes, plasma cells, histiocytes and fibroblasts. Many fibrocytes, fibroblasts, and both thick and thin bundles of collagen enveloped the granulation tissue, and formed a fibrotic boundary for the lesion.

Several elongated clefts, which were seen grossly as tunnel-like pouches, were bordered by granulomatous fibrotic tissue. The lumen of the canal, which contained several eggs and much necrotic material, was lined by severe fibrinoid necrosis of the connective tissue (Fig 3A). Acute and chronic inflammatory cells, mainly histiocytes, were evenly distributed along the canal wall. This layer bordered laterally on dense fibrotic tissue.

Throughout the connective tissue that grossly formed the tumor of the stomach wall, specimens with diffuse infiltrates of inflammatory cells comprised polymorphonucelar leukocytes, lymphocytes, plasma cells and histiocytes. A most striking feature of this tissue was the many mast cells. Almost all blood vessels were empty although some were dilated and some of these had undergone vasculitis and thrombosis.

Fragments of lamellar cuticle and hooklets of an arthropod/insect material were found in the centers of some of the fibrotic areas (Fig 3B) probably portions of a recent meal. No internal structure of the organism was discernible.

DISCUSSION

There are no detailed description of host tissue reaction to *Gnathostoma* sp. in mammals, particularly in rats and earlier reports have focused on parasitological aspects of *Gnathostoma* infections (Swanson, 1976; Miyazaki and Dunn, 1965; Betterton, 1978). In this report the histopathological reactions are described. The pathology in the present case may have been caused by two factors. Firstly it may have been due to the mechanical damage caused by the penetration of the worms having broad, hook-like multitoothed spines in the cuticle. Secondly it could have been caused by the cervical glands of the larval stages of worms which have tissue lytic enzymes consisting of hemolysin,

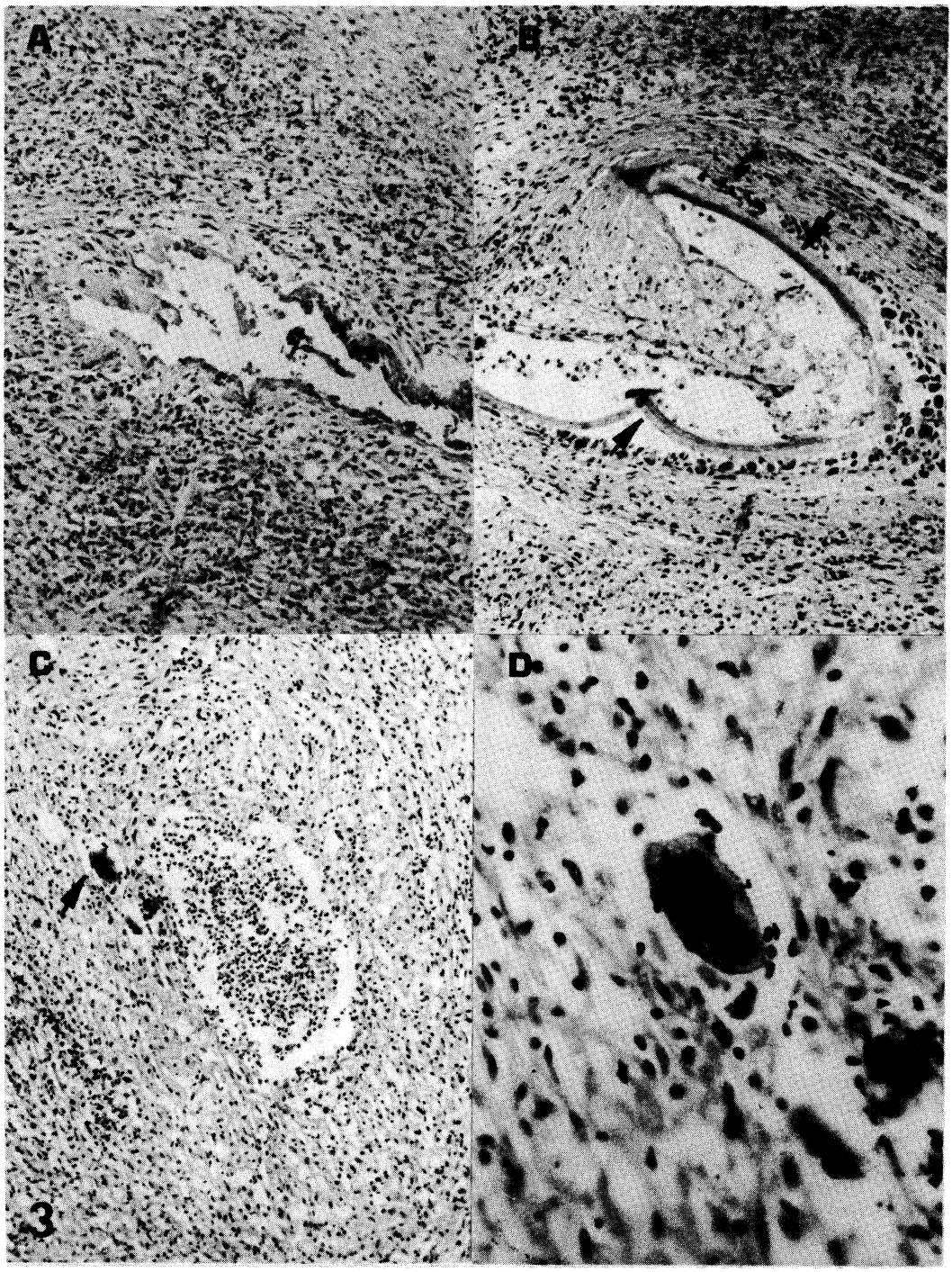

Fig 3—Pathology of tumor-like structure caused by *G. malaysiae* in the stomach of *R. surifer*. A. Elongated cleft lined by fibrinoid necrosis of connective tissue, containing necrotic material. Surrounding the cleft are dense inflammatory cells. (X 53). B. Fragments of mite material (between arrows) infiltrated by macrophages and surrounded by foreign body giant cells. (X53). C. Keratinized pitted nonoperculate egg of *G. malaysiae* (arrow) adjacent to collection of pus and enveloped by granulation tissue (X 53). D. Detail of egg of *G. malaysiae* found in the center of a fibotic scar (X 132).

hyaluronidase, a protease and an acetylcholine-like substance (Swanson, 1976). When these worms penetrate and form a tunnel, the host tissue is broken down and toxic waste products from digestion and gland secretions are released. These products could have resulted in the host inflammatory reactions reported by Beaver (1984).

The intense inflammation along the tunnels and central canal seen in this case is probably caused by the digestive excretions. The dense fibrotic tissue at the rim of the central canal indicated the site where the parasite had penetrated the stomach and formed the tunnels and remained within for some time. Histopathological changes (pus formation, granuloma and fibroblastic proliferation) near parasite egg deposits indicated strong irritation and destruction of the host tissue. Despite the peripheral fibrous tissue, pus that formed around the egg material suggests that even after the eggs are deposited, they continue to provoke necrosis. Neither eosinophils nor foreign body giant cells were abundant in the granulomatous tissue.

Cuticular fragments of arthropod/insect material found in the stomach wall of the *R. surifer* could have been eaten by the rat as these animals feed mainly on insects, fruits and leaves (Wang *et al,* 1976). These could have been inadvertently forced into the central canal by the parasite during its penetration.

In Malaysia only two cases of human gnathostomiasis have been reported (Samy, 1918; Sandosham, 1949). In Thailand, however, gnathostomiasis is considered an important zoonosis (Daengsvang, 1980) and as many as 400 to 500 persons per year suspected of suffering from gnathostomiasis visited a major hospital in Bangkok (Sethasuban, 1990). The parasite is frequently found in the eye region and rarely enters the central nervous system, and when this does occur eosinophilic neuritis, meningitis, or encephalitis with bizarre variable symptoms can occur (Swanson, 1976). In Japan four species, *G. spinigerum, G. hispidium, G. nipponicum* and *G. dolorensi* are responsible for gnathostomiasis (Miyauchi *et al,* 1992).

Hitherto there were no reports of *G. malaysiae* in humans from Malaysia and Thailand where this parasite is found in *R. surifer.* Setasuban *et al* (1991) however believe that it is possible that cases are occurring among humans in Thailand.

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