Antemortem diagnosis and attempted treatment of (*Halicephalobus*) *Micronema deletrix* infection in a horse

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An eight-year-old, 345 kg, Arabian gelding was referred to the University of Wisconsin Veterinary Medical Teaching Hospital for evaluation of bilateral facial swelling and concurrent weight loss and dysphagia of 30 days duration. The horse was unresponsive to previous treatment with procaine penicillin G and phenylbutazone.

On physical examination, the horse was depressed and cachectic. There was bilateral, asymmetric (more pronounced on the left) facial swelling over the maxillary sinuses. Examination of the oral cavity revealed long enamel points on the premolars and molars of both upper and lower dental arcades. Linear erosions were noted on the hard palate, and gingival hypertrophy of the lingual and buccal aspects of the maxillary oral mucosa was apparent. The left submandibular lymph node was enlarged, and skin abrasions were observed in the area of the throat latch where the halter would normally be located. Neurological examination was unremarkable.

Differential diagnosis included facial trauma, neoplasia, secondary nutritional hyperparathyroidism, and mycotic or bacterial sinusitis. Complete blood count revealed a normocytic normochromic anemia with hyperglobulinemia (5.6 g/dL, normal = 3.1–5.2 g/dL). Serum chemistry and electrolyte evaluations were normal. Strongyle type eggs were found on fecal examination. Radiographs of the skull demonstrated bilateral, lateral displacement of the upper dental arcade and osteopenia of the nasal, incisor, and maxillary bones. Endoscopic examination of the middle and ventral meatus revealed numerous, 3–10 mm in diameter, raised, sessile lesions and grade II lymphoid hyperplasia of the pharynx.

The horse was sedated by IV administration of 250 mg of xylazine (Rompum, Haver/Diamond, Shawnee, Kansas, USA) and 20 mg butorphanol tartrate (Torbugesic, Fort Dodge Laboratories, Fort Dodge, Iowa, USA) for a biopsy of the left maxillary sinus. A square area (10 × 10 cm) was clipped, aseptically prepared, and locally infiltrated with 5 mL of 2% lidocaine (Elkins-Sinn, Cherry Hill, New Jersey, USA). A 6 mm Michel trephine was introduced through a 2 cm stab incision in a lateral to medial direction to a depth of 7 cm. A 4 cm core biopsy sample was harvested and submitted for histopathological evaluation, and the skin was closed with simple interrupted sutures of 2-0 nylon.

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Numerous microgranulomas separated by dense fibrous connective tissue were seen on histopathological examination. Microgranulomas were characterized by a necrotic center, an intermediate zone containing large numbers of macrophages and giant cells, and an outermost zone with focal collections of lymphocytes and eosinophils. The necrotic centers of the microgranulomas had numerous nematode segments and were occasionally mineralized. The parasite had a smooth cuticle, a sharply tapered tail, and inapparent celom. A rhabditiform esophagus was present within the digestive tract. Granulomatous sinusitis secondary to a (*Halicephalobus*) *Micronema deletrix* infection was diagnosed.

The horse was treated orally with 50 mg/kg of fenbendazole (Panacur, Hoechst-Roussel Agri-Vet, Rahway, New Jersey, USA) and IV with 1.1 mg/kg of flunixin meglumine (Banamine, Schering-Plough Animal Health, Somerville, New Jersey, USA) daily for three consecutive days. An attempt to remove sharp points on the molars and premolars by "floating" was unsuccessful because of the gingival hypertrophy. The horse was discharged to the owner 24 hours after cessation of treatment. Discharge instructions included providing a high quality, palatable diet and observing the horse's mental activity. Thirty-six hours after discharge (five days after initiation of treatment), the horse began to develop hind limb ataxia. The neurological status of the horse continued to deteriorate over the next 48 hours. With the suspicion of neurological involvement of *M. deletrix* and a grave prognosis, the horse was euthanized at the owner's request.

Necropsy findings consisted of firm, markedly enlarged, submandibular lymph nodes. The maxilla contained a destructive, infiltrative, and proliferative yellowish-brown, firm mass which infiltrated the maxillary and nasal sinuses and displaced the dentition. Within the maxillary sinuses, there were numerous firm, yellowish-brown, 3–5 cm in diameter, polypoid masses. The hard palate was thickened (4 cm) with dense fibrous connective tissue (Figure 1). All other organs appeared normal on gross pathological evaluation.

Histopathological evaluation of the polypoid masses of the maxilla and hard palate was identical to that described in the maxillary sinus biopsy. The submandibular lymph nodes were diffusely hypercellular and characterized by large coalescing nodules with increased collagen density. The lymph nodes were heavily infiltrated with mixed mononuclear cells consisting of plump macrophages, giant cells, lymphocytes, and plasma cells. Wide bands of fibrous connective tissue coursed through the lymph node and the germinal centers were depleted of lymphocytes.

The cerebellum contained multifocal, granulomatous infiltrates within the meninges. Some of the meningeal

vessels contained *M. deletrix* organisms. In one area, the neuropile contained an intense inflammatory reaction consisting of dense sheets of macrophages and giant cells along with gliosis and gitter cells. No lesions were found in the spinal cord, brain stem, or cerebrum.

Of the 21 reported cases of *M. deletrix* infection in horses, only one other case was diagnosed antemortem (2). Similarly to our case, the diagnosis was made by a biopsy of a granulomatous mass of the mandible; however, treatment was attempted with a single dose of ivermectin (0.2 mg/kg IM, MSD Agvet, Rahway, New Jersey, USA). As in our case, the horse remained stable for a period of four days, and on the fifth day, began to develop mild neurological signs of ataxia. Within 24 hours, the neurological signs continued to progress to a state of recumbency and the horse was subsequently euthanized.

Our treatment protocol, (fenbendazole at 50 mg/kg for three days), was based on recommendations for treating verminous encephalitides (9). Some of the horses reported to be infected with *M. deletrix* were routinely or empirically treated with various antihelmintics consisting of ivermectin (2,5) or benzemidazoles (8). Little is known about the efficacy of antihelminitics to verminous encephalitides. Unsuccessful treatment of *M. deletrix* infections may be due to either the inability of antihelmintics to cross the blood brain barrier and penetrate granulomatous lesions of the nervous system or a lack of sensitivity of *M. deletrix* organisms to antihelmintic therapies. Flunixin meglumine was also used as an anti-inflammatory agent in anticipation of massive parasite demise and potential parasitic thromboembolism. No lesions were found on necropsy suggestive of parasitic thromboembolism secondary to treatment.

Three reports have partially summarized the clinical and pathological findings of these cases (1-3). Most lesions have been confined to the central nervous system (1-4). Extraneural lesions have also been reported in the kidneys (1,2,4,5), oral/nasal cavities (1,2,6-8), regional lymph nodes (1,5,7,8), lungs (3,5), adrenal glands (5), stomach (5), and bone (5). A definitive diagnosis of *M. deletrix* infection is difficult to confirm in the absence of accessible granulomatous lesions. This is because most cases of *M. deletrix* infection have clinical signs suggestive of neurological disease. Horses with neurological manifestations of *M. deletrix* infection have generally undergone a rapid and progressive neurological deterioration (2,3,4). *Micronema deletrix* nematodes have not been observed antemortem in body fluids (cerebrospinal fluid, blood, urine, saliva, milk, joint fluid) and subsequent diagnosis is made by histopathological evaluation of tissues.

Micronema deletrix has traditionally been regarded as a saprophytic nematode. Other investigators suggest that, since the parasite has only been reported in living tissue, it be considered a facultative parasite to man and equidae (3). The etiopathogenesis of *M. deletrix* infection is not known. Reports of human cases have been associated with decubital ulcers and a laceration with manure contamination (10). Involvement of the brain and kidneys suggests a hematogenous route of infection. Reports involving the nasal and oral cavities, in addition to the lungs, are suggestive of inhalation as a possible route of transmission. Based on the report of Spalding *et al*, involving infection of two half-sibling foals (3), prenatal, perinatal, and transmammary routes of transmission must also be considered.

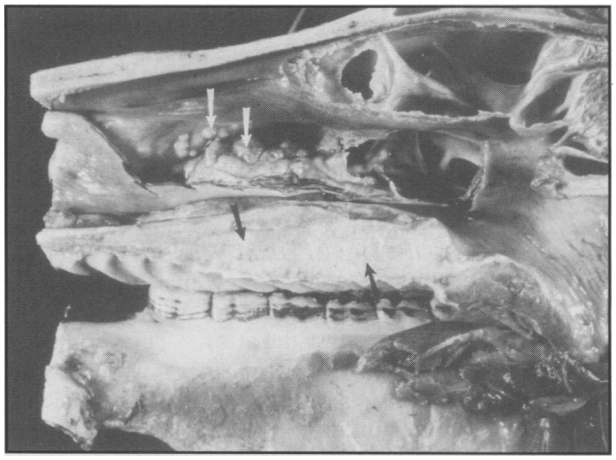

Figure 1. Sagittal section of the skull at postmortem. Note the markedly thickened hard palate (black arrow) and the polypoid masses in the maxillary sinuses (white arrows).

Micronema deletrix should be considered in the differential diagnosis of granulomatous lesions of the oral and nasal cavities in horses. A definitive diagnosis can be made by biopsy of accessible granulomatous lesions. The prognosis for recovery is poor, and this may in part be due to an apparent inability of antihelmintics to penetrate the granulomatous lesions caused by *M. deletrix*. The potential for neurological disorders with rapid progression with or without attempted treatment exists.

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