CASE REPORT

LARYNGEAL SARCOCYSTOSIS ACCOMPANYING LARYNGEAL SQUAMOUS CELL CARCINOMA: CASE REPORT AND LITERATURE REVIEW

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Abstract. Laryngeal sarcocystosis is an uncommon zoonotic coccidian protozoal infestation of human beings. The authors reviewed the pathology of 1,063 laryngeal biopsies over the past 10 years (2000 to 2009). Only one case of laryngeal sarcocystosis accompanying laryngeal squamous cell carcinoma was identified. The overall prevalence of laryngeal sarcocystosis was 0.094%. The case was a 66-year-old man who presented with voice hoarseness for six months. Physical examination and computed tomography revealed an ulcerative exophytic mass on the right true vocal cord, suggestive of laryngeal carcinoma. He underwent a right frontolateral partial laryngectomy. Histopathology showed a nonkeratinizing squamous cell carcinoma with *Sarcocystis* spp in the vocalis muscle. He was followed up and enrolled in speech therapy. The authors briefly review the clinicopathologic features and pathogenesis of muscular sarcocystosis and concurrent laryngeal sarcocystosis and squamous cell carcinoma.

Keywords: larynx, sarcocystosis, sarcosporidiosis, squamous cell carcinoma, protozoa

INTRODUCTION

Sarcocystosis, previously known as sarcosporidiosis, is an uncommon zoonotic coccidian protozoal parasitic infestation of human beings caused by *Sarcocystis* spp, an intracellular protozoan parasite in the phylum Apicomplexa (Levine, 1986; Gutierrez, 1990). *Sarcocystis* spp have an obligatory two-host cycle with sexual reproduction (gametogony followed by sporogony) in the intestine of a carnivore or omnivore as a definite host, and asexual multiplication (schizogony) in the tissue of an herbivore as an intermediate host. Human beings may serve as both intermediate and definitive hosts. Muscular sarcocystosis was first reported by Miescher in 1843 (Fayer, 2004). The most common *Sarcocystic* spp causing human muscular sarcocystosis is *Sarcocystis lindemanni* (Gutierrez, 1990; Frenkel, 1997). To the authors' knowledge, there are only

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two published reports of human laryngeal sarcocystosis in the literature (Kutty and Dissanaike, 1975; Limsuwan and Bunyaratvej, 1978) and the prevalence of laryngeal sarcocystosis in Thailand is unknown. The authors report the clinical and histopathologic features and prevalence of laryngeal sarcocystosis over a ten-year period (2000 to 2009) at a tertiary care university hospital in Thailand.

CASE REPORT

A 66-year-old man presented to the otolaryngology department with a chief compliant of voice hoarseness for six months. His underlying diseases were hypertension, benign prostatic hypertrophy, dyslipidemia, and chronic obstructive pulmonary disease. The physical examination showed an ulcerative exophytic mass of the right true vocal cord. No palpable cervical lymph nodes were detected. Laryngeal biopsy was performed and pathology revealed squamous cell carcinoma (SCC). Relevant laboratory investigations included: hemoglobin 13.5 g/dl, hematocrit 38.4%, white blood cell count 8,210/mm^3 with a differential of 54% neutrophils, 31% lymphocytes, 12% monocytes, 2% eosinophils, and 1% basophils. Computed tomography of the larynx was done and exhibited an exophytic heterogenous enhancing mass measuring 1.3x0.9x0.6 cm of the right true vocal cord, suggestive of laryngeal carcinoma, T1N0M0. A right frontolateral partial laryngectomy was performed. The histopathological diagnosis was nonkeratinizing SCC with *Sarcocystis* spp in the vocalis muscle. Polymerase chain reaction (PCR) for *Toxoplasma gondii* was negative. The postoperative course was uneventful. The patient was followed up and enrolled in a speech therapy program. No additional antiprotozoal treatment was given. The patient was regularly followed up at the Ear-Nose-Throat clinic for 3 years without evidence of recurrence.

The pathological specimen included a part of the larynx consisting of the right thyroid cartilage attached to the true and false vocal cords. An exophytic mass measuring 1.3x0.9x0.6 cm was located on the middle one third portion of the right true vocal cord. The sections revealed nonkeratinizing SCC (Fig 1A, 1B) with a few sarcocysts in the vocalis muscle. The sarcocysts measured 154-315 m x 98-189 m and contained numerous banana-shaped bradyzoites with no surrounding tissue reaction (Fig 1C, 1D). The pathologic diagnosis was nonkeratinizing SCC and *Sarcocystis* spp infection of the vocalis muscle.

DISCUSSION

Sarcocystosis is an intracellular protozoal parasitic disease caused by cocidea of the genus *Sarcocystis*. It is endemic in Southeast Asia, including Malaysia and Thailand (Bunyaratvej *et al*, 1982; Wong and Pathmanathan, 1992). The most common species are *S. hominis*, *S. suihominis* and *S. lindemanni* (Frenkel, 1997; Fayer, 2004); the first two *Sarcocystis* spp commonly occurring in the intestinal tract. *S. lindemanni* commonly causes muscular sarcocystosis (Bunyaratvej *et al*, 2007). In Malaysia, the overall incidence of both intestinal and muscular sarcocystosis is 19.7%, with the highest prevalence rate being reported among Aborigines (39.7%), followed by Malays (17%), Indians (8.7%) and Chinese (3.6%) (Kutty and Dissanaike, 1975; Thomas and Dissanaike, 1978; Kan and Pathmanathan, 1991). The incidence of muscular sarcocystosis was 21% of tongue-tissues obtained from consecutive

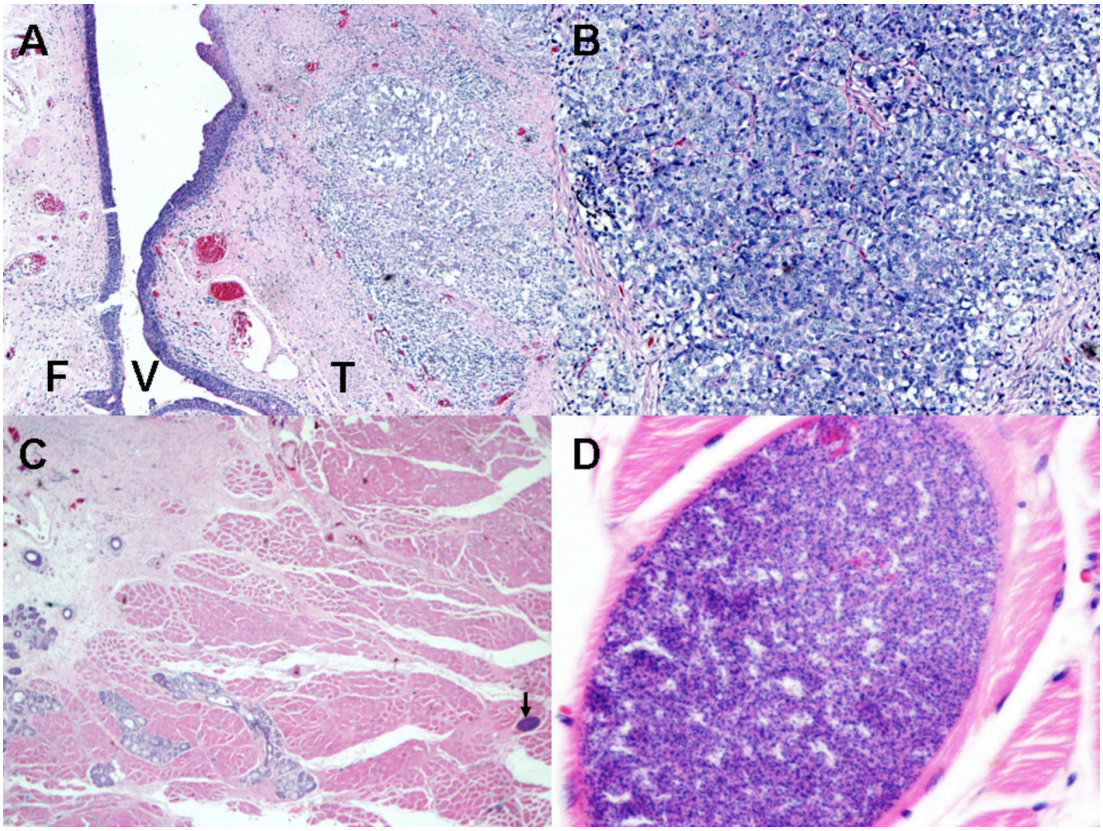

Fig 1–Cross-section of a sarcocyst in the vocalis muscle and squamous cell carcinoma. A) This section shows squamous cell carcinoma of the true vocal cord; "F", "V", and "T" represent the false vocal cord, laryngeal ventricle and true vocal cord, respectively. H&E, x40. B) This section shows nonkeratinizing squamous cell carcinoma; H&E, x100. C) This section shows a sarcocyst (arrow) in the vocalis muscle. H&E, x40. D) The sarcocyst measures 315 m x 189 m and has a thin, smooth cystic wall. Several small bradyzoites are seen within the sarcocyst; H&E, x400.

routine autopsies (Wong and Pathmanathan, 1992). In Thailand, the incidence of intestinal sarcocystosis has been reported as 23.2%, detected by stool examination (Wilairatana *et al*, 1996). Muscular sarcocystosis was detected in skeletal, laryngeal and cardiac muscle specimens from 15 autopsy cases (Limsuwan and Bunyaratvej, 1978). Laryngeal muscle sarcocystosis accompanying laryngeal SCC has never been reported.

Muscular sarcocystosis is acquired by ingestion of infected oocysts from the feces of an infected carnivore or omnivore. Each oocyst releases four sporozoites which penetrate the intestinal mucosa and develop into schizonts in the capillary endothelium. Asexual multiplication occurs first in the endothelium of small vessels in the mesenteric lymph nodes. Subsequent hematogenous dissemination leads to merozoites invading the microcirculation

of muscular tissue of intermediate hosts which harbor sarcocysts or zoitocysts in their muscles. Muscular sarcocystosis commonly occurs in the adult tongue (Pathmanathan and Kan, 1981; Wong and Pathmanathan, 1992). Histopathology often shows sarcocysts measuring 40 to 456 m in length and 26 to 142 m in width (Wong and Pathmanathan, 1992; Wong *et al*, 1994). The cystic wall is composed of hyaline eosinophilic monomorphous material and is well demarcated from the surrounding muscle fibers. Muscular sarcocystosis causes a wide spectrum of clinical manifestation including myositis, myalgia, localized painful muscular swelling, low grade fever, weakness, vasculitis, and eosinophilia (Pamphlett and O'Donoghue, 1990; Frenkel, 1997; Fayer, 2004). Serum erythrocyte sedimentation rate and creatinine kinase levels are usually elevated (Arness *et al*, 1999). The muscular symptoms with muscular sarcocystosis are associated with the inflammatory reaction mainly composed of lymphocytes followed by eosinophils (Mehrotra *et al*, 1996). Symptoms were detected in only 10 out of 52 patients (19.2%) with biopsy-confirmed muscular sarcocystosis (Arness *et al*, 1999).

The diagnosis of muscular sarcocystosis from endemic areas of Thailand is usually made from biopsy or autopsy material. Biopsies are usually taken for other reasons, then sarcocystic infestation is found, such as in the present case. The parasites are always found incidentally and identification is made with the histopathologic findings. Sarcocysts should be differentiated from the tissue cysts of *Toxoplasma gondii*. Sarcocysts are often larger and can be visualized grossly. On histopathology, sarcocysts usually have thicker cystic walls, may be striated and often present with compartments, metrocysts and microvilli in the wall of some parasites. The bradyzoites of *Sarcocystis* spp are larger and more prominent. With *Toxoplasma gondii*, the entire bradyzoite (except the nucleus) is periodic acid schiff (PAS) positive, whereas with *Sarcocystis* spp it is negative. Therefore, routine histopathologic examination is of value for identifying this unsuspected conditions. However, some species and earlier developmental stages of *Sarcocystis* spp are difficult to distinguish from *Toxoplasma gondii*. Additional diagnostic studies, such as PCR and checking antibodies against *Toxoplasma gondii* should be performed. Serological testing can provide evidence of prior exposure to *Sarcocystis* spp but does not differentiate between intestinal and muscular sarcocystosis.

Muscular sarcocystosis has no specific treatment. Corticosteroids may provide symptomatic relief in cases of vasculitis or eosinophilic myositis. The overall prognosis is excellent. Proper disposal of human feces and careful animal husbandry are necessary to control muscular sarcocystosis. Public health education regarding transmission, combined with proper diagnosis are crucial. There is no risk of recrudescence, because the intracystic bradyzoites are incapable of infecting other host cells.

Sarcocystic infestation may accompany and/or complicate head and neck carcinomas. Clinicians should be aware of the possibility of muscular sarcocystic infestation.

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