ENTOMOPHTHOROMYCOSIS DUE TO CONIDIOBOLUS

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Entomophthoromycosis due to Conidiobolus coronatus is a granulomatous infection characterized by lesions that originate in the inferior turbinate, spread through ostia and foramina to involve the facial and subcutaneous tissues and paranasal sinuses. The majority of the cases have been described from areas of tropical rainforest in West Africa, agricultural and outdoor workers (aged 20-60 years) being the ones most frequently affected. The fungus is common in soil and decaying vegetation. Infection probably occurs by implantation of the spores of the fungus in nasal mucosa. C. incongruus is a rare agent of the disease, so far known only from two cases with lesions involving the pericardium, mediastinum, lungs, liver, oesophagus and jejunum. C. coronatus is known to cause a clinically similar disease in horses, mules, a dolphin and a chimpanzee. A characteristic histological feature is the presence of thin-walled, broad, often septate hyphae or hyphal fragments with a thick eosinophilic sheath, frequently phagocytosed within giant cells. The fungus is known to produce in vitro several enzymes, e.g., elastase, esterase, collagenase and lipase, which have a possible role in pathogenicity. A concentrated brain heart infusion culture filtrate antigen is useful for immunodiagnosis. Several drugs e.g., potassium iodide, cotrimoxazole, amphotericin B, ketoconazole and itraconazole have been tried with varying success. Investigations on the immunology of disease and the role of proteases and lipases in the pathogenesis of infection is an important area of further research.

INTRODUCTION

Entomophthoromycosis is a general term for a mycosis caused by fungi of the order entomophthorales, class zygomycetes. Entomophthoromycosis due to Conidiobolus (generally C. coronatus and very rarely C. incongruus) is a granulomatous infection characterized by nasal obstruction and swellings of the soft tissues of the nose, face and lip. A histologically similar infection of subcutaneous tissues of several parts of the body caused by a morphologically related fungus, Basidiobolus ranarum, belonging to the same order entomophthorales is designated Entomophthoromycosis due to Basidiobolus (or subcutaneous phycomycosis or zygomycosis due to Basidiobolus). The zygomycetes, one of the six classes in which phycomycetes have been divided (1), also includes the order mucorales, some members of which cause mucormycosis, an infection of nasal mucosa, paranasal sinuses, meninges, brain and blood vessels (43). Zygomyces is a collective name used for infections caused by fungi of the order entomophthorales and mucorales. C. coronatus was first recognized as a pathogen of higher animals when it was recorded as an etiological agent of nasal granuloma in horses (16). The first case of human infection was reported in 1965 from Jamaica by Bras and co-workers (6). Since then numerous cases of the disease have been reported from tropical countries of Africa, Asia and America (31, 43). The first record of human infection due to C. incongruus was a case of pulmonary infection in an infant in the USA (15, 20). Later another case of disseminated infection due to this fungus was reported from Thailand (8). In this article, an attempt is made to review the epidemiology, clinical features, histopathology and immunology of entomophthoromycosis due to Conidiobolus and some aspects of the biology of the causative fungi.
Epidemiology

About 100 cases of the disease have been described, the majority from countries in West Africa, viz., Nigeria (23, 40), Cameroon (42), Cote de Ivoire (14), Congo (31) and Zaire (31), with a handful of reports from Central Africa (9, 49), Asia and the American continent (5, 6, 43, 45). The majority of the cases from West Africa have originated from areas of tropical rainforest, agricultural and outdoor workers being the ones most frequently affected (31, 34). The disease generally affects adults; over 80% of the cases have been males aged 20-60 years partly or wholly engaged in agricultural work (31, 34). The male to female incidence ratio is 8:1. The affected patients have otherwise been healthy without any debilitating or constitutional abnormality. There has been no history of previous use of steroids or prolonged use of broad spectrum antibiotics.

The etiological agent Conidiobolus coronatus has a world-wide distribution in soil and plant detritus, though human and animal infections have occurred generally in tropical and subtropical climates (12, 36, 43). In fact, Conidiobolus coronatus is the commonest species of Conidiobolus in plant detritus (12). Clark (11) found it to be very common in decaying vegetation in Nigeria and demonstrated that its concentration varied with the season, being at its peak in the period of regular rainfall. Yendol (54) found that conidial germination in Conidiobolus coronatus does not occur below 95% humidity and was maximum at 100% humidity. These findings support the predominance of infections due to this fungus in rain-fed forest zones of the tropics. In a monthly survey of Conidiobolus in field soils and beach litter at Keele, Staffordshire, UK, during 1983 and 1984, Conidiobolus coronatus was found to be a very common species (47). The fungus has also been found to be associated with several insects (7, 27). Conidiobolus incongruus has been reported from soil in North Carolina, US, and from India (43).

The exact mode of human infection has not been established. Infection probably occurs by implantation of the inhaled spores of the fungus in nasal mucosa or through minor trauma e.g., insect bites. The habit of frequent picking of the nose in some people may also cause minor trauma providing a mean of entry of the causative agent. In order to investigate if the habit of taking snuff frequently could be a contributing factor, we cultured several samples of snuff but could not isolate the fungus from any of the samples.

Natural infections have been observed in animals including horses (16, 32, 50), a dolphin (43) and a mule (10). There have been no reports from Africa of Conidiobolus coronatus infection in these animals, though the condition is very common in humans. However, a case of Conidiobolus coronatus infection in a chimpanzee has been reported from Tanzania (44). Attempts at experimental infection of several laboratory animals have been unsuccessful (18, 30).

Clinical features

Human infection: Infection generally begins unilaterally in the nasal mucosa, usually in the region of the inferior turbinate and spreads through suture and foramina to the dorsum of the nose, the glabella, forehead and cheek or along the facial planes into alae nosae and upper lip. Due to intranasal swellings, the patient has a feeling of nasal obstruction (31). Epistaxis has been reported in a few patients (31, 34).

The lesions are usually painless, firm and attached to the underlying structures and tissues but are not attached to the overlying skin. The development of subcutaneous nodules in the cheeks, eyebrows and upper lip may give the patient an appearance of a tapir or hippopotamus (42). Generally subcutaneous tissue and submucosa are affected; in rare cases the dermis is also involved. A case of submental lymph node involvement has been reported (24). Spread of the disease into the pharynx and the larynx resulting in dysphagia and laryngeal obstruction has been reported in a few cases (31, 35). Chronic extensive lymphedema has also been recorded in a few cases.

Infection due to Conidiobolus incongruus: Only 2 cases are known so far. The first case, reported in an infant in USA (15, 20), affected the lungs and caused signs of respiratory obstruction and, later, heart failure. Radiography showed areas of increased density in one lung and mediastinum. The diagnosis of entomophthoromycosis was made following thoractomy and a biopsy of the granuloma which involved the lung, mediastinum and pericardium (20). The fungus was correctly identified by King & Jong (29).

The second was a fatal case of disseminated infection in a 20 year-old Thai male presenting a subcutaneous mass accompanied by fever, weight loss, cough and haemoptysis (8). Histological examination of lesions in the subcutaneous tissues, lungs, liver, oesophagus and jejunum showed a granulomatous reaction with a bright eosinophilic amorphous material surrounding the hyphae. The fungus was identified in culture.

Clinical features of the disease in animals

Horses: The disease in horses manifests as a nasal granuloma with bilateral nasal swellings with epistaxis and symptoms of dyspnoea (32, 50). Presence of gross proliferative lesions in the rear limbs is a frequent sign. The symptoms of infection in mules are similar (10). Inhalation of spores from the environment has been suggested as the mode of infection (50).

Chimpanzee: The only case reported in the literature (44) was from a wild chimpanzee in the Gombe Stream Reserve of Western Tanzania. The lesions occurred as tumourous swellings on the exterior and in the interior of the nose and on both eyebrows. The subcutaneous tissue was indurated, oedematous and gelatious, similar in appearance to that observed in human lesions. With the onset of sexual maturity, the lesions in the animal exacerbated.