Some deep mycoses diagnosed by histopathology in South Eastern Nigeria

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Summary

Twenty-three cases of deep mycoses were histologically diagnosed in 6500 surgical biopsy specimens examined during a three year period (1985-1988) in the Department of Pathology, University of Calabar Teaching Hospital, Calabar, Nigeria. These included 12 cases of African histoplasmosis, four of mycetoma, four of actinomycetoma, two of paranasal aspergilloma, and one of zygomycosis due to *Conidiobolus coronatus* (rhinoentomophthoromycosis). Involvement of tooth gum and colon in one case each of African histoplasmosis, and of maxillary sinus in two cases of paranasal aspergilloma were unusual clinical manifestations. The need for greater awareness of deep mycoses and for provision of adequate laboratory facilities in Nigeria is emphasized.

Key words

Deep mycoses, South eastern Nigeria, African histoplasmosis, Mycetoma, Actinomycetoma, Paranasal aspergilloma, Zygomycosis due to *Conidiobolus coronatus*

Algunas micosis profundas diagnosticadas histopatológicamente en Nigeria Sudoriental

Resumen

Se diagnosticaron histológicamente 33 casos de micosis profundas en 6500 muestras quirúrgicas durante un periodo de tres años (1985-1988) en el Departamento de Patología, University of Calabar Teaching Hospital, Calabar, Nigeria. Entre éstas se diagnosticaron 12 casos de histoplasmosis africana, cuatro de micetoma, cuatro de actinomicetoma, dos de aspergiloma paranasal y uno de zigomicosis por *Conidiobolus coronatus* (rinoentomoftoromicosis). La afectación de las encías y del colon en cada caso de histoplasmosis africana, respectivamente, y del seno maxilar en dos casos de aspergiloma paranasal fueron manifestaciones clínicas inusuales. Se enfatiza la necesidad de una mayor alerta respecto a la incidencia de las micosis profundas y de la provisión de recursos de laboratorio en Nigeria.

Palabras clave

Micosis profundas, Nigeria Sudoriental, Histoplasmosis africana, Micetoma, Actinomicetoma, Aspergiloma paranasal, Zigomicosis por *Conidiobolus coronatus*

There has been an increasing awareness about the occurrence of deep mycoses in Nigeria and other parts of West Africa. Epidemiological, clinicopathological and mycological features of certain deep mycoses, viz. African histoplasmosis, mycetoma, zygomycosis due to *Conidiobolus coronatus* (rhinoentomophthoromycosis) and aspergillosis have been described from some parts of Nigeria [1-6]. To the best of our knowledge, no information is available on the prevalence of deep mycoses in Cross River and Akwa Ibom States, a south eastern part of Nigeria. This communication describes clinicopathological features of twenty-three cases of deep mycoses from this geographic region.

MATERIALS AND METHODS

The diagnosis of the cases was based on a histological study of 6500 surgical biopsy specimens received at the Pathology Department of the University of Calabar Teaching Hospital (UCTH), Calabar over a three year period (1985-88). Mycotic/actinomycotic etiology was established in 23 (0.35%) of cases. The clinical data including the types and pattern of lesions, age, sex, race and geographical origin of the patients were abstracted from requisition forms, which accompanied the specimens. All specimens were fixed in 10% formalin and paraffin embedded sections were stained with H&E, PAS, Gram and Grocott stains.

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RESULTS

In all, 23 cases of deep mycoses were diagnosed histologically. The patients originated from Cross River and Akwa Ibom States of Nigeria. All cases were HIV negative. The salient clinicopathological and histological features of these cases are described below under individual mycoses.

African histoplasmosis. This was the most frequent mycosis in our series represented by twelve cases, eight males and four females, aged 8-80 years. The clinical presentations varied widely. The commonest manifestation was in bone, presenting clinically as osteomyelitis or osteosarcoma. X ray of the cases showed significant bone destruction. Localized bone destruction of tarsus, iliac, femur and tibia occurred in five cases, presenting as chronic painful swellings with or without discharging sinuses. One of these cases, a 12-year-old boy with disseminated and generalized bone involvement died within four months post diagnosis. In another case, tooth gum was involved with the appearance of cutaneous nodules in the back and lower limbs following after three months.

The second common presentation was the presence of firm, discrete, single or multiple painless subcutaneous nodules of variable size and shape. Two cases presented with solitary ulcerating nodules, and another one exhibited multiple subcutaneous nodules over the chest wall and the back. The clinical impression of lipoma, onchocerciasis, Kaposi's sarcoma, multiple fibromatosis was entertained. The lymphoreticular system was involved in two patients with cervical lymphadenopathy. These were queried as tuberculosis/lymphoma.

One female presented with chronic large bowel obstruction during surgery and an infiltrating tumour was identified at the splenic flexure, and the abdominal lymph nodes were enlarged. The clinical diagnosis suggested carcinoma of the colon. This particular case was described earlier in detail [7].

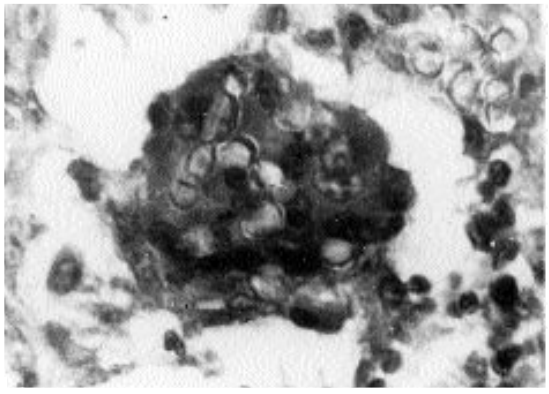

Figure 1. Tissue section (H&E) from a subcutaneous nodule in a 20-year-old male patient of African histoplasmosis showing a giant cell containing yeast cells of *H. capsulatum* var. *duboisii.* 525x.

Tissue biopsies in all cases revealed granulomatous inflammatory reaction with numerous giant cells of a foreign body and Langhan's type, most of them containing numerous oval yeast cells, 8-14 µm in diameter, characteristic of *Histoplasma capsulatum* var. *duboisii* (Figure 1). Clusters of yeast cells were also observed extracellularly in tissue sections of all cases. The wall of yeast cells stained intensely with Grocott stain. Other inflammatory cells included macrophages, plasma cells, lymphocytes, and a few neutrophils. Fibroblastic reaction was seen in the case of colonic involvement, partially obliterating the lumen.

Mycetoma. This was represented by eight cases, four of eumycetoma (caused by true fungi) and the other four of actinomycetoma (caused by actinomycetes). The patients were between 15-65 years of age; six of them were males. All affected patients were farmers. The site of involvement was the foot in seven cases, and the right hand in the other one. All patients presented clinically with painless, slowly enlarging swellings with multiple nodules, some of them ulcerating and discharging pus containing granules. The duration of illness ranged from one to three years. X-ray of the lesions in all patients revealed bone involvement in four cases. Mycetoma was suspected in seven of the cases. In the other involving a 65-year-old male with dark brown nodules on the sole of right foot melanoma or Kaposi's sarcoma was queried.

Histology of biopsies confirmed the diagnosis of mycetoma in all the eight cases. A study of the morphology of the granules in the tissue sections established the diagnosis of eumycetoma (mycetoma caused by true fungi) in four cases, and actinomycetoma (mycetoma caused by actinomycetes) in the other four cases. H&E stained tissue sections in the cases of eumycetoma revealed mycotic granules surrounded by numerous polymorphs and occasionally mononuclear and multinucleate giant cells. In two of the cases, the granules were lacking cement; they were oval-lobular or somewhat horseshoe shaped, 145-260 x 125-180 µm with a deeply stained eosinophilic periphery and a pale centre (Figure 2), characteristic of mycetoma due to *Pseudallescheria boydii* [8]. The granules comprised of septate hyphae forming vesicles, particularly at the periphery. In the other two cases of eumycetoma, tissue sections showed irregularly oval, black granules embedded in hard brown cement matrix. The grains comprised of dark brown, branching septate hyphae tending to swell i.e. form vesicles towards the periphery, an appearance not unlike of *Madurella mycetomatis*. The H&E stained tissue sections in the cases of actinomycetoma showed multiple microabscesses, centrally containing actinomycotic granules. The granules were relatively smaller, elongated, slightly curved with a homogenous interior and a fringed and clubbed periphery, surrounded by polymorphonuclear leukocytes and peripheral monocytes, a feature characteristic of nocardial mycetomas. Gram stained sections revealed the grains to be comprised of compact masses of thin mycelium fragmenting into rods and cocci.

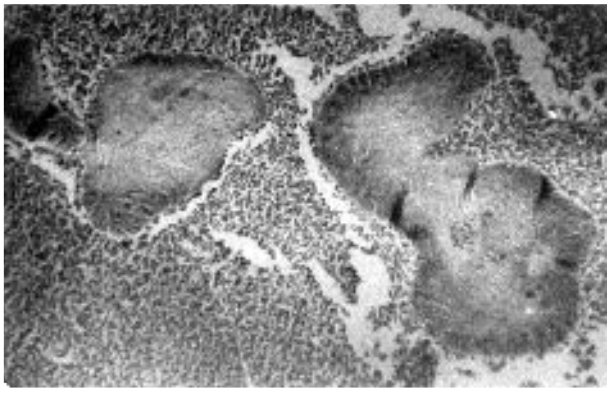

Figure 2. H&E stained tissue section from a case of eumycetoma in a 35-year old female showing granules suggestive of *P. boydii*, surrounded by inflammatory cells. 250x.

Nasal aspergilloma. This was detected in two male patients aged 25 and 26, respectively. The clinical presentation was right maxillary sinusitis and chronic nasal obstruction with frequent nasal discharges. The right antral washings yielded fragments of greyish brown soft tissue. Histological examination revealed necrotic tissue with acute inflammatory reaction and a mass of abundant septate, hyphae growing radially with repeated dichotomous branching, frequently with globose to oval cells at the tips and in intercalary positions. The morphological appearance of the hyphae was considered suggestive of *Aspergillus* [9].

Zygomycosis due to Conidiobolus coronatus *(Rhinoentomophthoromycosis).* This was represented by a single case. The patient, a 45-year-old male presented with painless firm swellings of the nose, upper lip and right cheek of nine months duration. The swellings were attached to the underlying structures but not to the overlying skin. Histology showed chronic inflammatory reaction with abundant eosinophils forming microabscesses. The fungal hyphae were thin walled broad often septate, 4-10 µm in diameter with a thick eosinophilic sheath staining intense pink in H & E sections (Figure 3). Frequently the hyphal fragments were phagocytosed by the giant cells. The eosinophilic material had a satellite of fringe-like disposition, which was particularly striking when seen surrounding cross sections of fungal filaments.

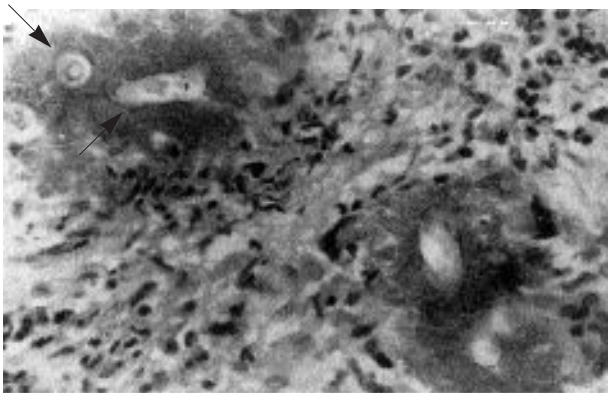

Figure 3. Tissue section (H&E stain) from a case of zygomycosis due to *C. coronatus* in 45-year-old male showing wide thin walled hyphae (cut across and longitudinally) with eosinophilic sheath in a microabscess. 650x.

All cases of deep mycoses were diagnosed retrospectively, except the two of the cases of actinomycetoma due to *Nocardia* sp. Treatment could be tried only in the latter two cases. The patients were put on cotrimoxazole (trimethoprim 80 mg, sulphamethoxazole 40 mg) tablets, 6 hourly for 12 weeks. Following this the lesions almost cleared in both the patients and they were put on a further course of the drug for another six weeks. Only one of the patients turned up for a follow-up, his lesions had healed completely.

DISCUSSION

The present report serves to focus attention on the prevalence of certain deep mycoses and their varying clinicopathological features in south eastern Nigeria. These twenty-three reported cases represent an incidence rate of 0.35% deep mycoses in our biopsy series during the three-year period (1985-1988) reviewed. This is close to 0.4% incidence in the series reported by Onuigbo and Gugnani [4] from an area covering some eastern States of Nigeria. African histoplasmosis is one of the most frequently recognized deep mycoses in Nigeria [3-5,10]. It is not surprising, therefore, that as many as 12 of the 23 cases of deep mycoses under review were of this type. Majority of our patients showed lesions of the bone, skin, subcutaneous and lymphoreticular tissues. With some differences, this essentially conforms to the general pattern of the disease described in Nigeria [2,3,10]. Intestinal involvement recorded in one of our cases is a rarely described condition [11,12]. Involvement of gum noticed in another case is noteworthy as gum lesions in African histoplasmosis are rarely known. The consequent development of subcutaneous nodules in this case lends support to the possibility of haematogenous spread of infection suggested by Williams *et al.* [3].

Mycetoma is known to be common in West Africa [13] but the number of cases so far reported in Nigeria is relatively small [14,15]. The detection of seven cases in our series representing both eumycetoma and actinomycetoma adds to our knowledge of the distribution of mycetomas and its etiology in Nigeria. If properly looked for, both types of mycetoma may be common in south eastern and other tropical areas of Nigeria. Aspergilloma of paranasal sinuses is endemic in Sudan [16,17]. Several cases of this disease have also been reported from Malawi in east central Africa [18]. Aspergilloma is very rarely known in Nigeria. Martinson *et al.* [19] reported one case of aspergilloma of the ethmoid. The two cases involving maxillary sinus in our series constitute the first recorded cases in Nigeria. The solitary case of zygomycosis due to *C. coronatus* originating from Cross River State of Nigeria extends the distribution of this disease already known in several other parts of Nigeria [20-22].

In conclusion, we would like to mention that the cases included in this report represent only a tip of the iceberg of deep mycoses prevalent in Nigeria. Many more cases of deep mycoses possibly occur in several parts of Nigeria but are not detected or recognized due to several factors, viz. lack of awareness, paucity of medical specialists, inability of patients to seek proper medical attention due to their poor socioeconomic conditions. Thus, there is need to consider the possibility of deep mycoses in patients with chronic granulomas. Also provision of basic mycology laboratory facilities and trained personnel in all the University Teaching Hospitals in Nigeria may help uncover the great variety of deep mycoses possibly prevalent in the country.

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