CASE REPORTS

Allescheria boydii—Unique Systemic Dissemination to Thyroid and Brain

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ALTERED reactivity of tissues, allowing invasion by organisms of low virulence, is becoming more frequent with the increasing utilization of immunosuppressive agents. *Allescheria boydii* is a fungus which under normal circumstances produces suppuration only of skin and subcutaneous tissues. It is the principal agent responsible for "Madura foot". The report which follows describes a case in which there was dissemination of this fungus to the thyroid and brain. So far as is known, no other case of hematogenous dissemination of Allescheria has been reported.

A 19-year-old salesgirl was well until November 1963, when she developed tonsillitis for which she received an injection of penicillin. One week later, she noted tea-coloured urine and puffiness of her eyes and hands. These symptoms cleared gradually. However, towards the end of January, increasingly severe swelling of the legs, hands and periorbital tissues developed and the urine again became tea-coloured. She was admitted to hospital in Moncton, New Brunswick. After 20 days' treatment with penicillin, the urine became normal and she was discharged. Several weeks later, she again developed increasing edema and hematuria, as well as dyspnea, orthopnea and leg cramps.

Her terminal admission was to the Toronto General Hospital on May 9, 1964. Physical examination revealed edema of the face, hands, feet and sacrum. The fundi were normal. Both lung bases were dull to percussion. The pulse was 84 per minute and regular, the blood pressure was 155/90 mm. Hg and a Grade 3/6 systolic murmur was heard along the left sternal border. There was no cardiomegaly. The liver was palpable 5 cm. below the right costal margin. The uterus was enlarged to a size consistent with a pregnancy of four months' duration.

Investigations.—Urinalysis revealed a specific gravity of 1.006. 4+ albumin, and many red blood cells, white blood cells and granular casts. The hemoglobin level was 12 g. % and the white blood cell count 9900 per c.mm. Serum proteins were 3.6 g. %, with albumin 1.3 g. and globulin 2.3 g. The serum cholesterol value was 236 mg. %. The blood urea nitrogen (BUN) was 21 mg. % and the serum creatinine 1.8 mg. %. Creatinine clearance was 9.6 ml./min. Lupus erythematosus cell preparations were negative on five occasions. Renal biopsy, performed on May 26, revealed marked proliferation of glomerular epithelium, with the formation of huge crescents, many of which were at least 10 cell-layers thick and almost totally obliterated the capsular space (Fig. 1). In addition, numerous acute inflammatory cells were present. A diagnosis of severe subacute glomerulonephritis was made (Dr. S. Ritchie).

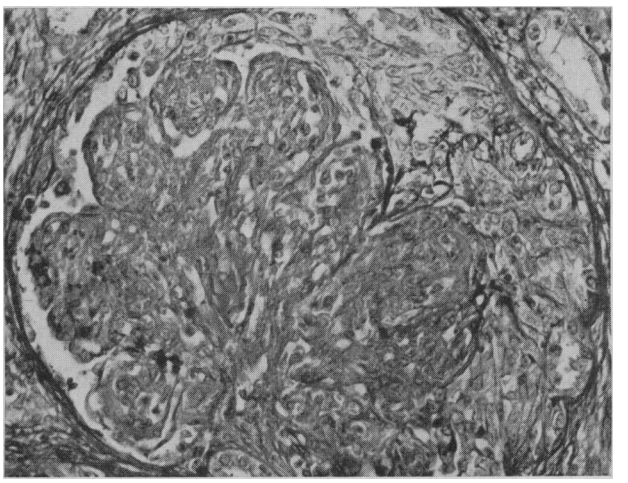

Fig. 1.—A single glomerulus shows disorganization with the formation of extensive crescents, as well as thickening and fusion of the glomerular tufts. (Phosphotungstic acid hematoxylin stain, × 300.)

Course in hospital.—The patient was placed on a low sodium diet and treated with diuretics and steroids. Even so, her BUN continued to rise and she was placed on azathioprine (Imuran) in an effort to diminish her immunological responsiveness. A cation exchange resin (Kayexalate) was given for hyperkalemia, and packed red cells for her increasing anemia. On June 22, a stillborn male fetus was passed spontaneously. Generalized purpura developed with aphthous ulcers, which did not respond to nystatin. Terminally she developed severe congestive heart failure and died on July 9 with a BUN of 300 mg. %.

Postmortem findings.—Autopsy revealed marked pitting edema of the legs, and ascites of 2400 ml. Petechiae were present in the lungs, heart, bowel and skin. There was a patchy uremic pneumonitis and mild cardiomegaly of 360 g. with left ventricular hypertrophy. The kidneys weighed 270 g. each and were pale and swollen. The cortex of each measured between 1.5 and 2 cm. in thickness, and the corticomedullary junction was indistinct. Microscopically, the glomeruli all displayed changes identical to those seen in the renal biopsy. In the mouth, pyriform sinuses and esophagus were grey pseudomembraneous plaques 3 to 4 mm. in thickness. Microscopically, the squamous epithelium was lost and the plaques consisted of a fibrin

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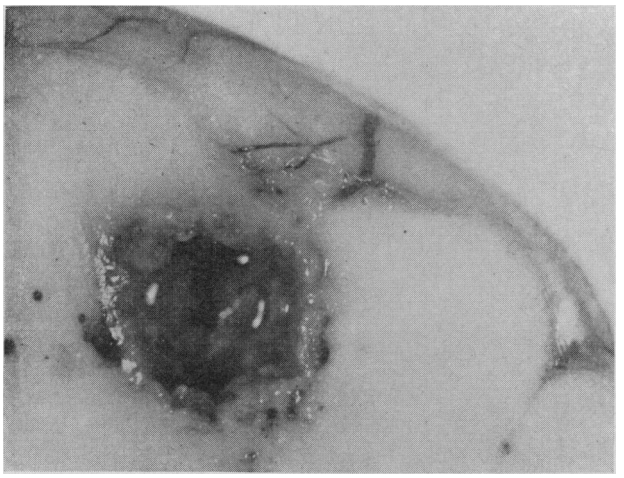

Fig. 2.—The larger cerebral abscess lies in the white matter but extends through the cortex to abut on the subarachnoid space. (×4.)

network containing red blood cells, necrotic debris and clusters of Gram-positive cocci, but careful search failed to demonstrate any fungi. The inflammatory reaction did not extend through the wall of the esophagus.

An abscess measuring 2 x 1.5 cm. was present in the left lower lobe of the thyroid gland. It was pale, grey, semisoft in consistency and surrounded by a zone of hyperemia. Two abscesses were present in the brain. The larger, 1 cm. in diameter, lay partially in the cortex abutting on the pial surface of the parietal lobe, and was filled with soft, grey material. Beneath it, extending down through the white matter, was a zone of brownish discolouration containing scattered recent petechiae (Fig. 2). A similar, but smaller, abscess was present in the left parietal lobe. Microscopically, the abscess cavities, both in the brain and in the thyroid gland, contained fungi with septate hyphae which occasionally branched and bore chlamydospores (Fig. 3). A portion of the thyroid abscess was cultured; the brain abscesses were unsuitable for culture because of previous formalin fixation.

Mycology.—Material from the abscess in the thyroid gland was grown on Sabouraud's glucose agar at room temperature. Colonies with a furry beige mycelium appeared while the agar beneath them showed a dark brownish pigmentation. Microscopically, these colonies consisted of branching septate hyphae bearing small conidia of about 3 to 6 μ, either at their terminal end or arising on short projections from the sides of hyphae. Large thin-walled sacs (perithecia) measuring up to 150 μ in diameter grew deep within the colonies. When crushed, these perithecia ruptured and exuded large numbers of elliptical ascospores measuring 4 to 6 μ in size. Though the original culture was no longer available, Fig. 4 shows an example of a ruptured perithecium exuding ascospores which was obtained from another culture of *A. boydii* (Mr. J. B. Fischer). The presence of these perithecia and the ascospores that they contained, allowed identification of this fungus as *Allescheria boydii*.

DISCUSSION

In recent years, the advent of immunosuppressive therapy has markedly altered the picture of

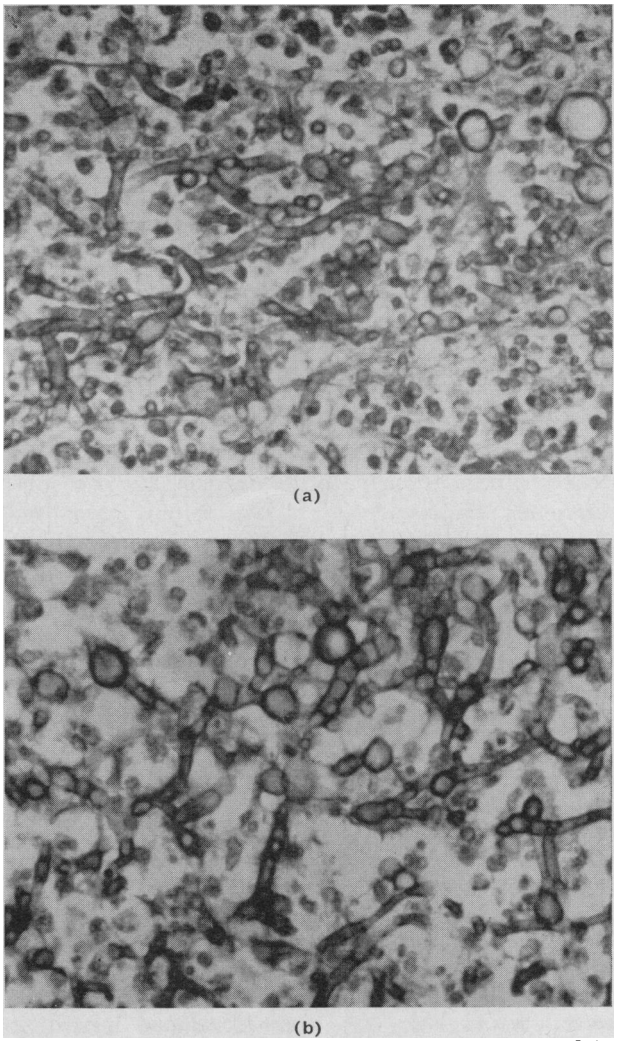

Fig. 3.—Hyphae and chlamydospores as they appeared in the abscesses. (a) represents the hyphae and chlamydospores in the thyroid gland abscess from which the cultures were obtained. (b) shows the morphologically identical hyphae and chlamydospores in the right parietal lobe abscess. (Periodic acid-Schiff stain, × 720.)

terminal infections in debilitating diseases.[1] Reports of infections with various micro-organisms such as *Nocardia asteroides*, Aspergillus, *Pneumo-*

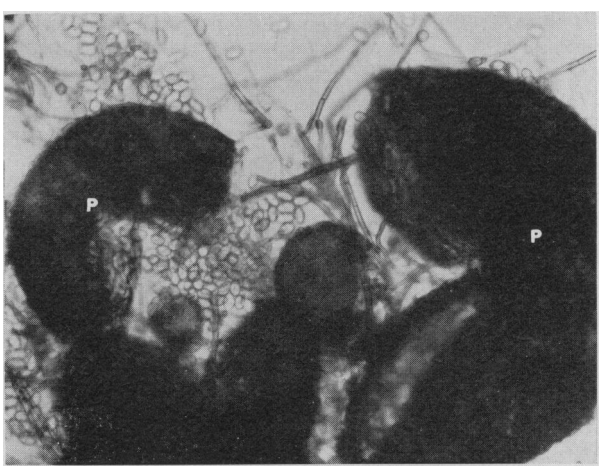

Fig. 4.—Two perithecia (P) have ruptured, releasing large numbers of ascospores among the septate hyphae. (× 390.)

cystis carinii, cytomegalovirus and *Pseudomonas aeruginosa* are becoming more and more numerous in the medical literature.[2, 3] Infections by a mixture of micro-organisms are also common.[4] Indeed, in the present case, in addition to the fungal abscesses, a pseudomembranous inflammation of the mouth and esophagus, presumably staphylococcal, was also present.

Allescheria boydii is the commonest of the many organisms which cause maduromycosis, a chronic suppurative condition of the feet ("Madura foot") or, rarely, the hands or other parts of the body. This disease occurs usually in the tropics, and over 50% of patients give a history of previous injury to the affected part.[5] *A. boydii* was first isolated from a case of "Madura foot" by Boyd and Crutchfield[6] in 1921 and has been isolated from the soil, where it is a saprophyte.[7]

Reports of *A. boydii* affecting parts of the body other than subcutaneous tissues are few. Belding and Umanzio[8] reported a case of otomycosis caused by this fungus. Creitz and Harris[9] described a case of chronic suppurative pneumonia in which it was isolated from the sputum, and Meyer and Herrold[10] isolated the same fungus from prostatic secretions of a patient with chronic prostatitis.

The only reported case of *A. boydii* affecting the nervous system was described by Benham and Georg[11] in 1948. This report concerned a middle-aged white woman who was given a spinal anesthetic in Trinidad for a herniorrhaphy. Four weeks later she developed signs of meningitis with papilledema, hypotonia and muscular wasting, leading to death after eight months. Repeated cultures of cerebrospinal fluid grew *A. boydii*. At autopsy, the spinal subarachnoid space was distended and, in places, obliterated by masses of granulation tissue. This meningeal reaction extended through the foramen magnum up the ventral surface of the brain stem and filled both cerebellopontine angles. No actual invasion of brain or spinal cord parenchyma was found. Though one of the abscesses in the brain of our patient abutted against the pia, there was in our case only localized involvement of the overlying subarachnoid space by the inflammatory process and both middle ears were free of infection.

To our knowledge, this is the first case in which fungal abscesses caused by *A. boydii* have been found in the parenchyma of internal organs, and it represents the first instance of the isolation of this fungus from the thyroid gland. At autopsy, no obvious site of entry of the fungus into the body was found. No fungi were present in the larynx or trachea or within the inflamed areas of the esophagus. The abscess within the thyroid gland lay entirely within the capsule while the inflammation in the esophagus was confined to the mucosa. Thus, we can only conclude that this organism reached both the brain and the thyroid gland by hematogenous spread, though its site of entrance into the body is unknown.

SUMMARY

A case of subacute glomerulonephritis in a 19-year-old girl is reported. Autopsy revealed abscesses in the brain and thyroid gland due to the fungus *Allescheria boydii*. This case is the first known example of hematogenous dissemination of *A. boydii* which, under normal circumstances, produces only a superficial mycosis, "Madura foot". The unusual dissemination is attributed to the therapeutic use of the immunosuppressive drugs cortisone and azathioprine (Imuran).

We wish to thank Drs. K. J. R. Wightman and W. T. W. Clarke for making available their clinical information, and Dr. P. G. Tuffnell and Mr. J. B. Fischer for identifying the fungus.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

DE HABITU DECENTI

"His manner must be both elegant and virtuous, manifesting to all both dignity and benevolence. . . . And he should appear thoughtful in demeanour but not austere, since austerity may appear to imply malevolence. On the other hand he who gives way to mirth and unseemly hilarity is regarded as vulgar. He must be strictly on his guard against this." And in another treatise, *de habitu decenti*, Hippocrates adds the following admonitions: "It is necessary that the physician should possess a certain amount of urbanity, since austerity repels both the sick and the well. . . . He should not converse more than is necessary with those unskilled in the art. For if he does it will be regarded as a challenge of his treatment. And he must above all things avoid officiousness and ostentation."

What a paragon of perfection would be the man who could comply with all these requirements demanded by our medical ancestors twenty-three hundred years ago. And yet who can deny the appositeness of each and every demand. Medical practice is not alone a matter of diagnosis and treatment; it brings the practitioner into such intimate relations to his fellow-man that it demands the exercise of all the social virtues. The author of the *de habitu decenti* has well said that "there is little difference between medicine and philosophy. For all those qualities demanded by the one are required by the other."—J. Playfair McMurrich, *Canad. Med. Ass. J.*, 5: 956, 1915.