CEREBRAL MUCORMYCOSIS IN A CHILD

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Mucormycosis is a disease caused by a group of fungi of the phycomycosis class which in its cerebral form involves the brain and its meninges mainly through vascular channels.

Although until the last decade there had been only eleven case reports,[1] increasing numbers of cases are being reported from the United States, Great Britain, Canada, Australia, Europe, Mexico, Africa and Asia. We believe this is the first case report from Turkey of mucormycosis occurring in a child. The disease in this four and a half year old child was complicated by uremia and acidosis. A steady rise in the incidence of the disease has been reflected by reports of sixty cases of the cerebral form which had been diagnosed at post-mortem; the estimated mortality rate is about 82 per cent.[2]

The course of infections of the brain due to other fungi are generally slower than cerebral mucormycosis which is rapid as in our case and which in our case terminated in the death of the child.

The first case of cerebral mucormycosis was described by Paltauf in 1885 in an adult[3] and its first occurrence in a child was reported by Kurrein in 1954.[4] The earliest reported age was twenty days.[5]

There have also been an increased number of reports[1,6-9] in which the diagnosis is made while the patient is alive. This may be due in part to the increasing awareness on the part of the clinicians of the disease, and its limited area of involvement. It is difficult to overlook characteristic histopathologic findings and numerous, large hematoxyphilic fungi.[10] But chances of culturing the fungi are difficult and are usually lost due to the fixation or freezing of the tissues obtained at post-mortem. In our case other mycologic studies were not made and our diagnosis depended on histologic examination. Ted Suie and W. H. Havaner[2] stated that among the phycomycetes, mucor and rhizopus were isolated in cerebral mucormycosis.

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Case Report

A four and a half year old boy was admitted to the Children's Hospital of Hacettepe School of Medicine on September 19, 1965 with complaints of somnolence, vomiting and diarrhea. He was the fifth child of parents who were both forty years old. No complications were present during pregnancy or at delivery. The other siblings were in good health. The patient had appeared in good health until twenty days prior to admission when he developed fever, cough, sore throat and an inability to recognize persons around him. He could neither eat nor drink, vomited continuously and had intermittent diarrhea. A local physician was called who diagnosed the disease as bronchopneumonia and five injections were given and syrup prescribed which the family could not identify. In spite of this treatment, the child's condition did not improve and a day prior to admission, somnolence deepened, edema of the face and eyelid developed and the child passed a tomato juice colored urine on one occasion.

Physical examination on admission revealed a fever of 36 C° and a pulse rate of 104 per minute. Respiration was 20 per minute, weight 10.500 Kg and blood pressure 75/50 mm Hg. He was in shock, comatose with a poor general condition and cloudiness of the cornea. Blood tinged fluid was observed in nose and mouth. Due to edema the left eye could not be examined. No abnormal findings were found on examination of chest and abdomen. Neurological examination brought forth no response to stimuli. DTR's and abdominal reflexes were negative, Babinski sign positive, bilaterally.

During hospitalization, ringer lactate and sodium bicarbonate were given for acidosis. Initial attempts to obtain urine by catheter were unsuccessful, and a direct x-ray of the pelvic area showed that the catheter failed to reach the bladder. After a few attempts the catheter entered the bladder and 240 cc of urine were obtained. To control convulsions on the left side of the body, phenobarbital and chloralhydrate were given.

Laboratory examination showed numerous WBC's and a few erythrocytes. Sugar and acetone were negative. Hb: 5.45 gm/100 ml, leukocytes: 9000/mm^3, platelets 28.000/mm^3. Anisocytosis and poikilocytosis were seen on the smear. NPN was 190 mgr per cent, total protein 5.5 gm per cent with 3.2 gm albumin, blood sugar: 120 mgm per cent, CO_2: 5.95 mEq/L, K: 4.1 mEq/L, Cl: 82.2 mEq/L. Throat and urine culture showed a growth of E. coli. On the second day of hospitalization, the dehydration and acidotic condition continued and the patient passed a little urine.

Laboratory examination (second day of hospitalization): Hb: 7.40 gm/100 ml. Leucocytes: 15.200/mm^3. Triangular and 0.1 per cent burr cells were seen. Platelets were 1 to 2 per high power field. Blood group A, Rh+, Coombs Negative, urinalysis was similar to that of the first day's examination.

On the third and last admission day, the patient's general condition remained the same with acidotic respiration and dehydration little improved. The patient passed no urine. Lumbar puncture showed xanthocromia, protein 200 mgm per cent sugar : 145 mgm per cent and 72 cells of which many were polymorphonuclear. Hb : 6.40 gm/100 ml. Platelets : 36,000/mm^3, CO_2: 7.06 MEq/L, Cl: 116 MEq/L.

I. V. Gantrisin was given but the patient's condition gradually worsened and he died at 11.30 p.m. on September 21, 1965 after three days of hospitalization.

Post-mortem examination : Autopsy was performed three days after death. Externally, no developmental anomaly was present, but nutrition appeared to be poor. Length was 68 cm, circumferances of the head, chest, abdomen were 51, 53, and 51 cm respectively. There was general edema of the body. The left eye-lid was swollen and the pupil was not distinct due to cloudiness. The right pupil appeared dilated. Blood crust was seen in the nose and mouth. Subcutaneous fat was less than normal. No significant findings were observed in the chest nor in the abdominal cavity.

Main gross findings were in the urinary system and in the brain. The kidneys (Figure 1) showed bilateral hydronephrosis, somewhat more prominent on the right, and the ureters showed transversal incomplete valve-like foldings. The entrance of the ureters to the bladder was dilated. There was hypertrophy and dilatation of the bladder. The bladder neck was granular, dusky-red with some narrowing of the prostatic urethra.

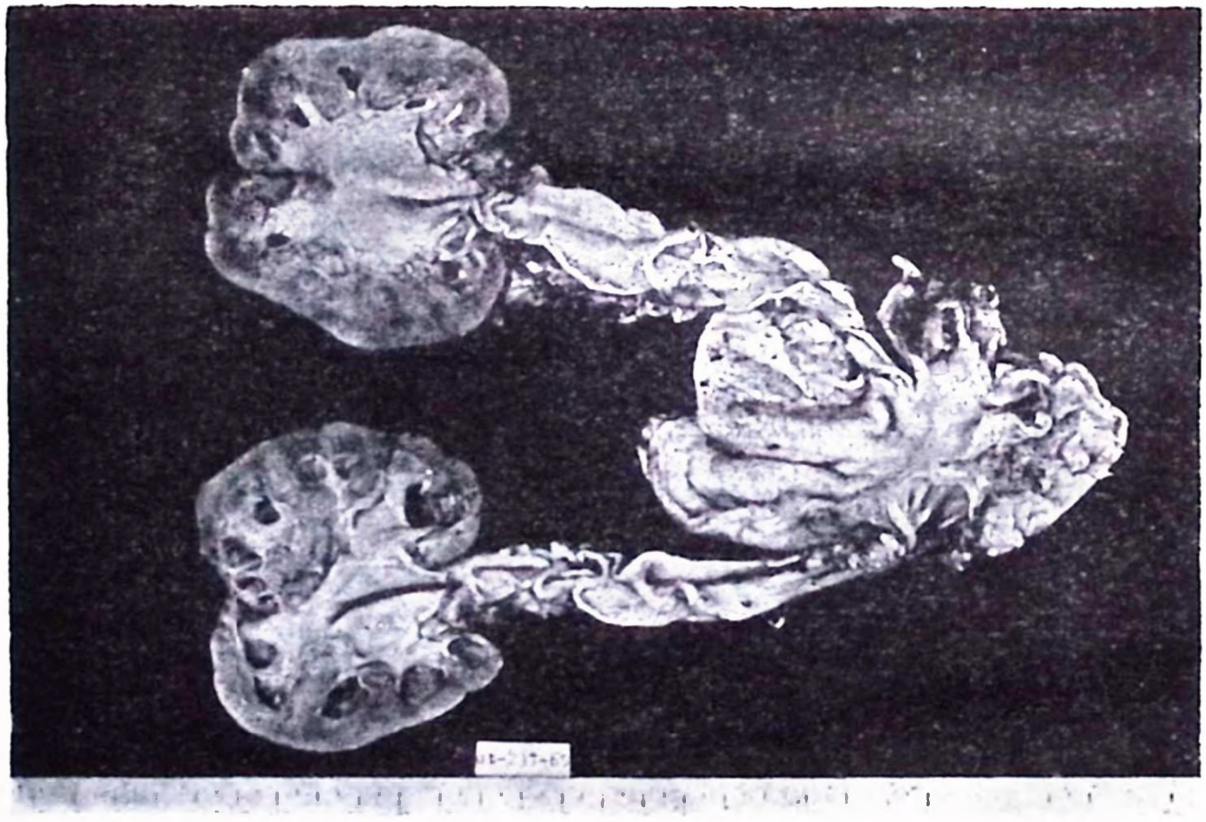

Figure 1. Kidneys showing bilateral hydronephrosis.

The brain weighed 1150 grams. There was an opaque, red-grey thickening of the meninges of the inferior surface of the frontal and temporal lobes. The lepto-meninges over the cerebral convexities appeared thin and transparent except in the depth of the cerebral sulci where they had a slight grey-white exuda-like appearance around the blood vessels. Basilar and anterior cerebral arteries showed thrombosis. The coronary sections of the brain showed large areas of the purplish red and irregular discoloration of the frontal and temporal lobes, bilaterally (Figures 2 and 3). A similar appearance was noted on the

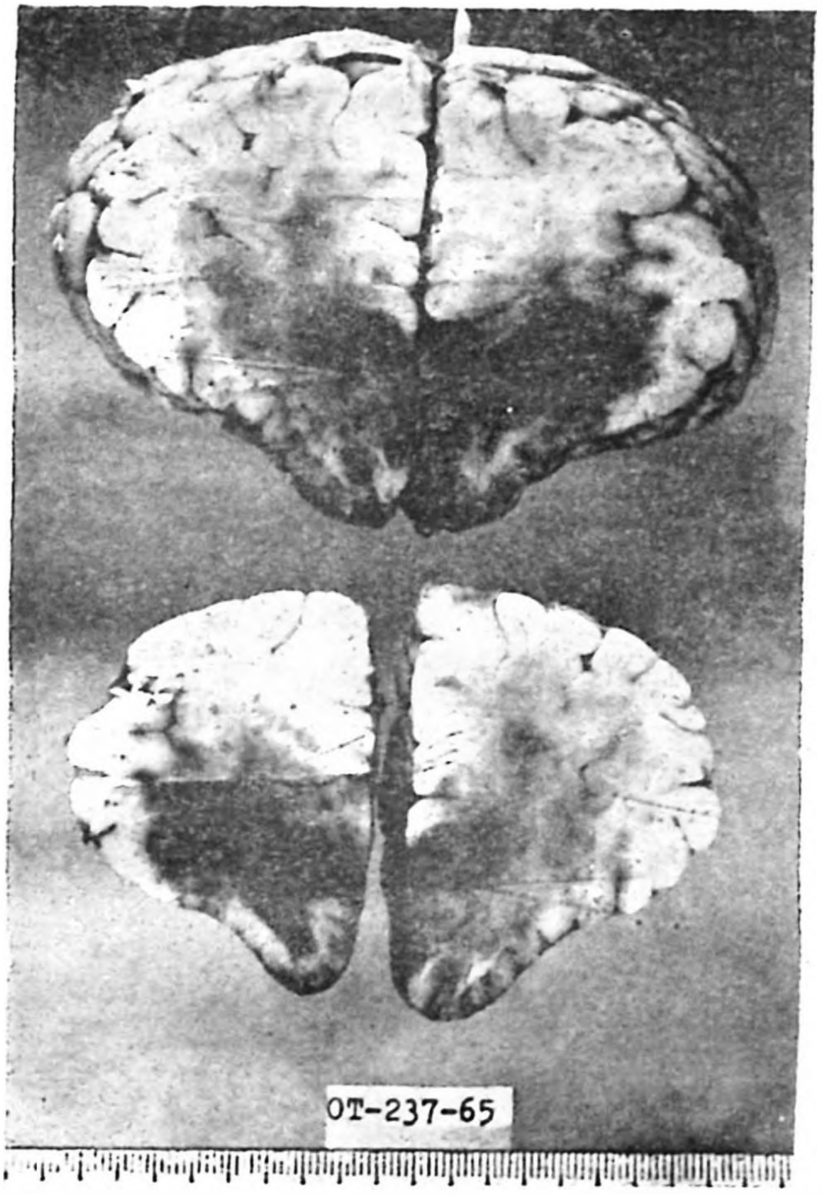

Figure 2. Coronary section of the frontal lobes showing bilateral hemorrhagic necrosis.

left side of the pons (Figure 4). On the removal of the brain, the distribution of the meninges suggested trauma. Gross and post-mortem x-ray examinations, however, showed no sign of fracture or other significant finding related to mucormycosis. Other gross findings were: esophagitis, numerous ascarides in the lumen of the small bowel, colitis, atrophy of the thymus, edematous lungs and an accessory spleen.

Microscopic examination of the kidneys showed pyelonephritis in addition to the hydronephrosis. Sections of the brain showed thrombi in the vessels with many fungi both in the lumina and in the wall extending to the surrounding tissue (Figure 5). Numerous fungi could be seen under medium power (Figure 6). High power (Figure 7) showed large, branching and nonseptate fungi of a hemotoxophilic character. These may be seen in the sections stained by H+E. In the brain sections there were local areas of hemorrhage, necrosis and polymorphonuclear infiltration in the adjacent areas of vascular channels. Meninges also showed polymorphonuclear infiltration and fungi of a similar character. Microscopically, the presence of acute inflammation in the meninges and

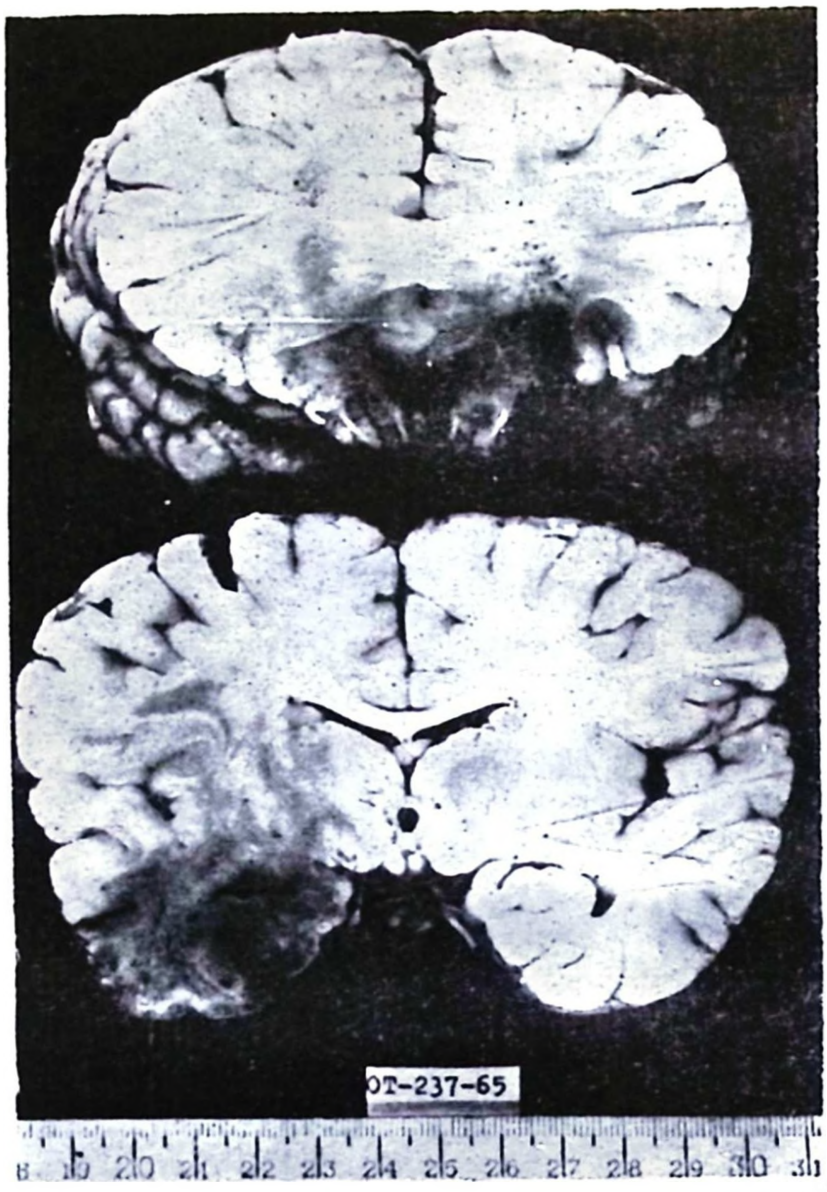

Figure 3. Coronary section of the brain showing extension of the hemorrhagic necrosis.

the brain, with thrombosis resulting in a necrotizing type of encephalitis in some areas, and nonseptate, thick and branching filiments of fungi led to the diagnosis of cerebral mucormycosis. Since the diagnosis of mucormycosis was made after microscopic examination, no culture studies for fungi were made.

Microscopic observations in other organs were: edema of the lungs, cystic dilatation of the pancreatic acini, all compatible with uremia. The liver had the periportal mild fatty metamorphosis seen in malnourished children. There were fungi in the esophagus and colon which in their morphologic characteristics seemed consistant with Candida infection.

Discussion

Mucormycosis is a disease caused by a group of saprophytic fungi which are widely distributed in nature, occurring in soil, and on fruit and bread.[11] The fungi belong to the class of phycomycetes

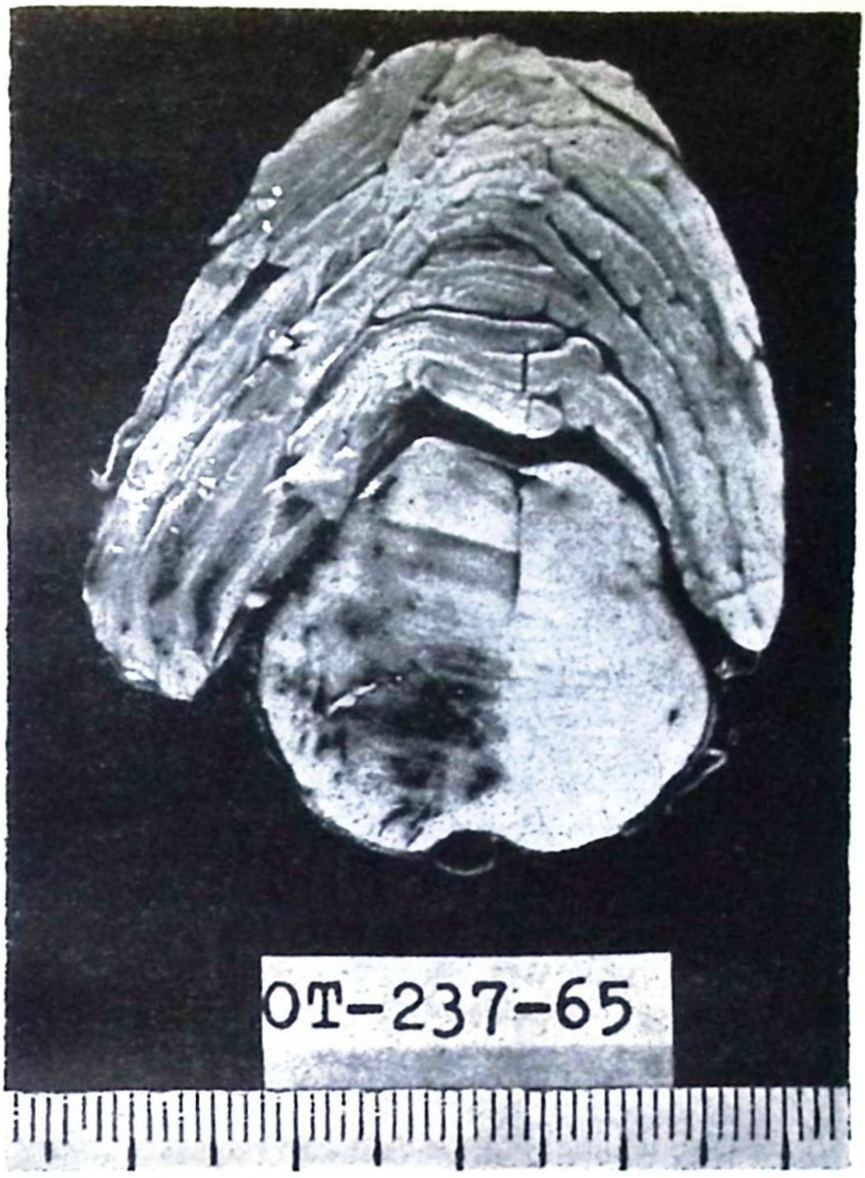

Figure 4. Section of the pons showing thrombosis of the basilar artery with hemorrhagic necrosis of the left side.

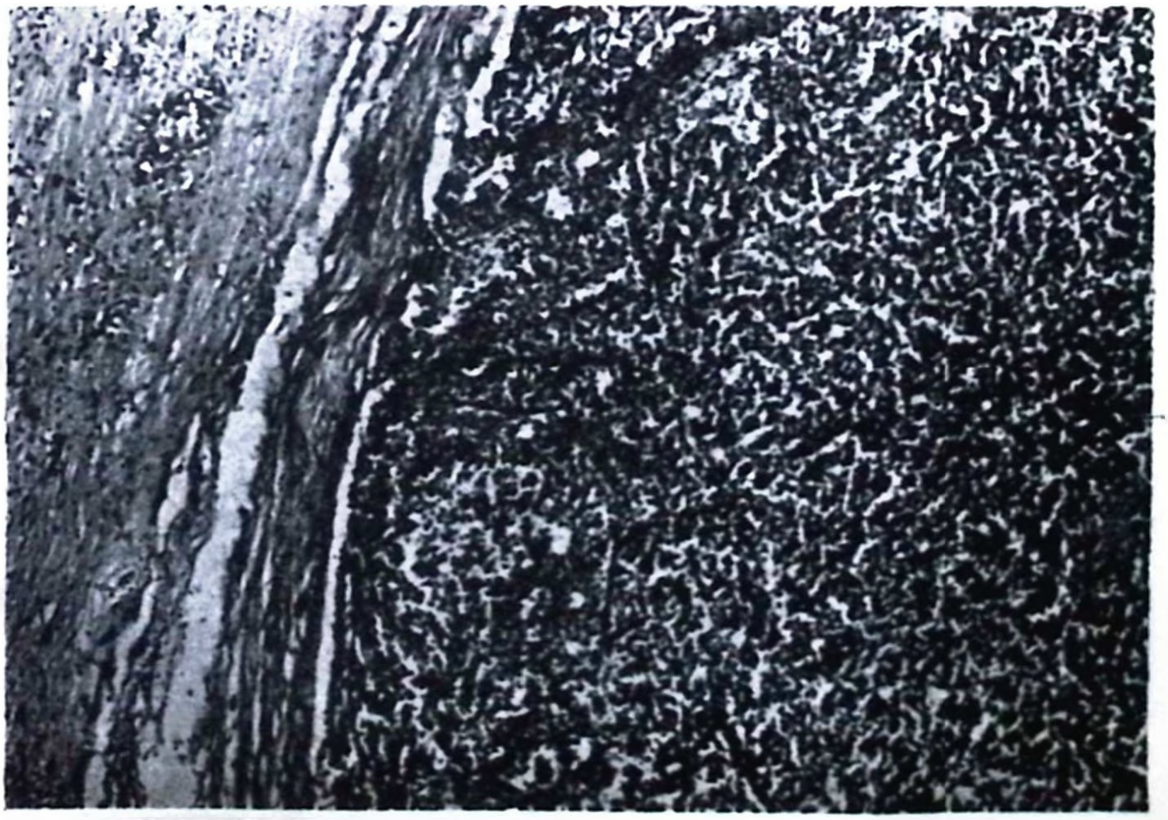

Figure 5. Brain section showing thrombi in the vessels.

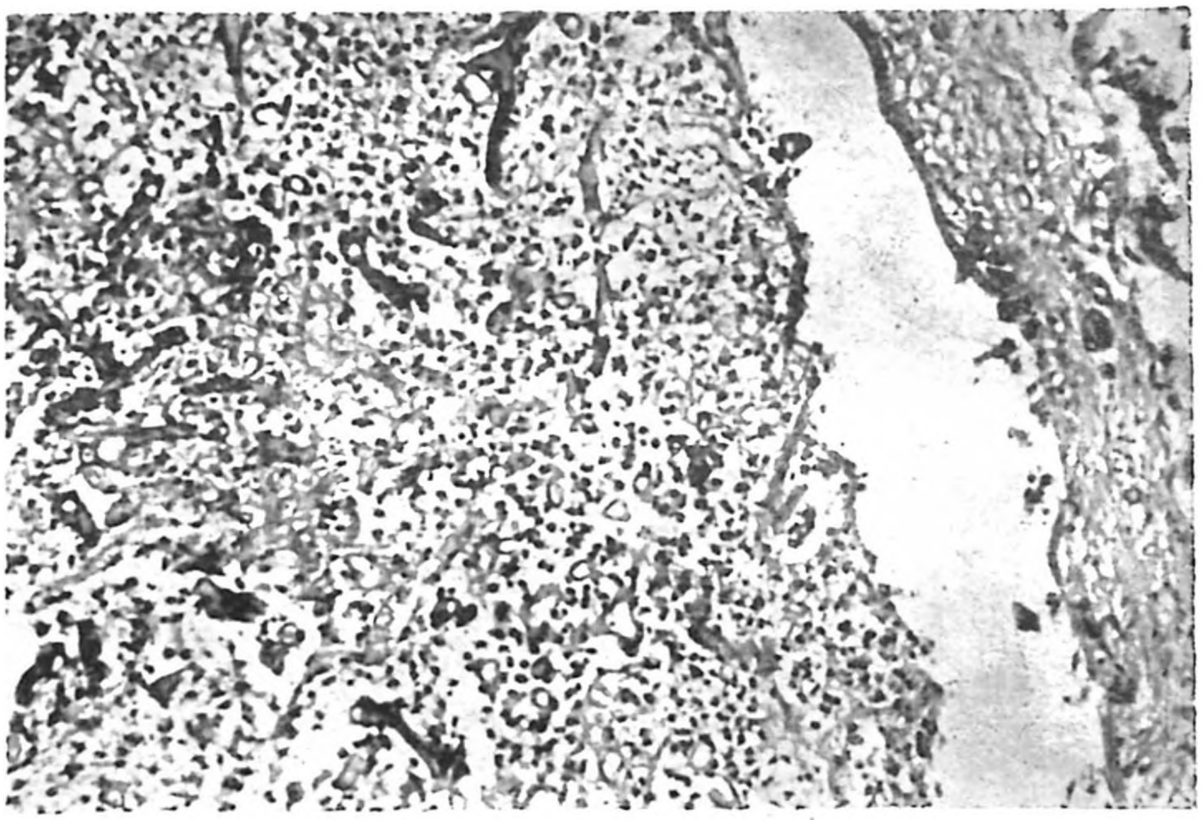

Figure 6. Medium power microscopy showing numerous fungi.

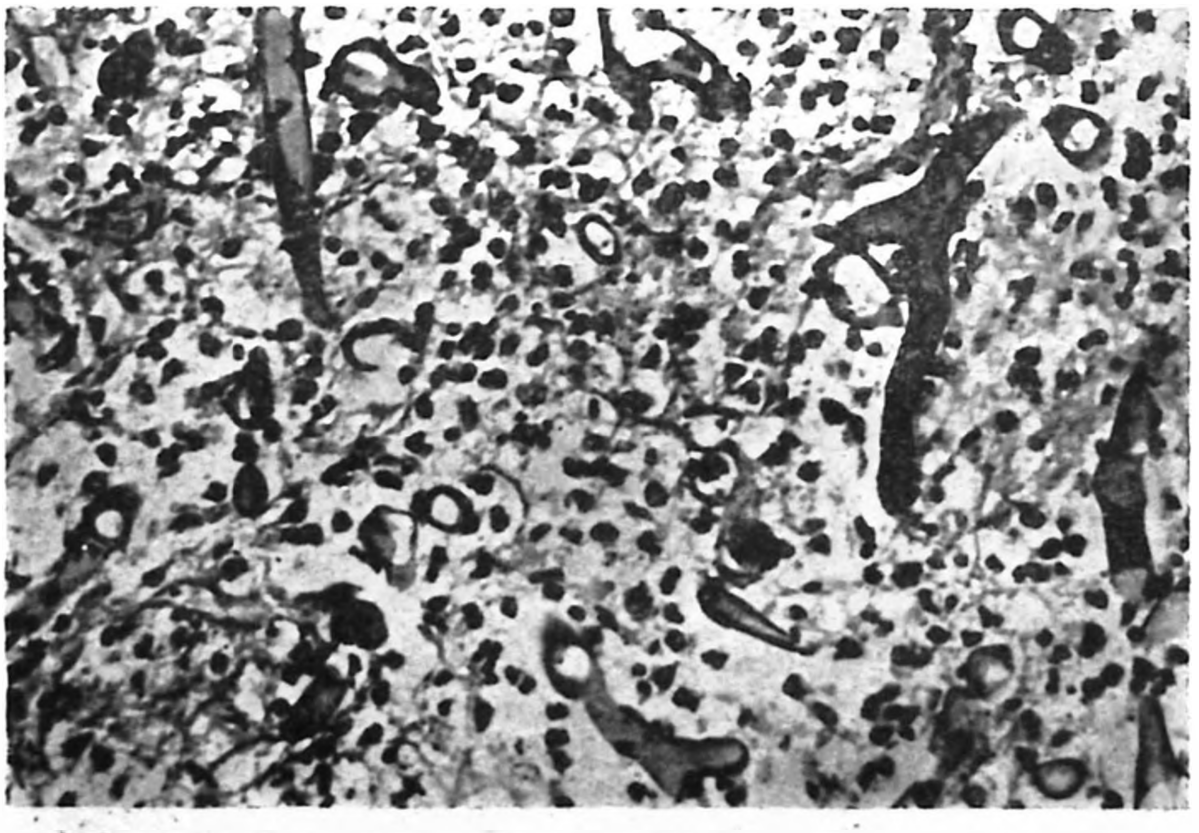

Figure 7. High power microscopy showing hemotoxophilic, large nonseptate fungi.

which include several genus of fungi such as Rhizopus, Absidia, Cunningamella, Martierella, Basidiobulus and Mucor.[12]

In histologic sections all of these fungi have similar characteristics of broad, nonseptate hyphae and exact identification can only be made by culture studies. The name Phycomycosis includes all these species of Phycomycetes.[13] They are known as laboratory contaminants and have been grown from human feces and nasal swabs free of the disease.

The diagnoses then, depend upon the invasive character of the fungi. This can only be made after histologic examination. Diagnostic features are: 1. Mycotic invasion of vessel walls and thrombosis. There is only one case of aneurysm of the cerebral vessels of which mucor was said to be a cause.[14] 2. Hemorrhage and necrosis. 3. Polymorphonuclear cell infiltration and fungi. 4. Granulomatous inflammation (rare).[15–17] 5. Cultural identification.

In our case, as we did not suspect fungus infection until after the histologic examination of the brain sections, cultural studies were not made. However the case of this four and a half year old boy presented some interesting findings. There was thrombocytopenia and second fungus infection in the gastrointestinal tract. Case reports of these conditions in association with mucormycosis have been mentioned in a recent review article.[12]

Our patient showed anatomically a condition of congenital hydronephrosis with superimposed pyelonephritis and enteritis, clinically, acidosis and uremia were present. Previous case reports listed kidney disease as the predisposing factor[1, 5, 17–10] and diarrhea.[19, 20] The role of acidosis in the pathogenesis of the disease appears as an important factor in many case reports. Diabetes mellitus is more frequently a predisposing factor in the cerebral form in which again acidosis may occur.[1, 6, 12, 13, 15, 23, 24] Experimental evidence also gives a significant role to acidosis in the pathogenesis of the disease.[25]

The other frequently associated factor is disorder of the hemopoietic system.[12, 14, 17–20] With the increasing frequency of the disease, the probable role of the wider use of antibiotics, corticosteroids, and other chemotherapeutic agents has also been reported.[28, 26, 27] In our case the role of these agents could not be determined, since we did not know the medication given to the patient prior to admission to the hospital. In our hospital no such therapy was given until a few hours prior to death (Gantrisin R). The common factor

appears to be metabolic abnormality as has been shown in experiments with animals.[30] Involvement of the central nervous system occurs usually in one of three ways: 1. There is involvement of other viscera (lungs, gastrointestinal tract, etc.). 2. There is involvement of cranial structure (eyes, nose or paranasal sinuses). 3. There is involvement of no other structure than the brain and its meninges. In our case, visceral involvement was not present. However involvement of the cranial structures could not be determined in the absence of microscopic examination. In cerebral mucormycosis, involvement of eyes, nose or paranasal sinuses is the most common form. Proptosis and homolateral ophthalmoplegia were demonstrated in approximately 65 per cent of the cases.[31] Clinical characteristics of the disease are eye signs (ophthalmoplegia), nasal signs (black turbinate), meningo-encephelitis in the presence of the above mentioned predisposing diseases.

Summary

A case of cerebral mucormycosis in a four and a half year old boy with uremia and acidosis due to kidney disease and enteritis has been presented with a brief review of pertinent literature. Rare observations were thrombocytopenia and second fungus infection (Candida) in the gastrointestinal tract. A postmortem diagnosis was made. This case also demonstrated the usual rapid death of a patient with cerebral mucormycosis.

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