SHORT REPORT

Monosporium apiospermum meningoencephalitis: a clinico-pathological case

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Abstract

Twenty nine cases of central nervous system infection due to *Monosporium apiospermum* have been reported. Six of them occurred after an aspiration pneumonia following a near drowning. The case of a 53 year old man is reported: *M. apiospermum* was isolated from cerebrospinal fluid, sputum, urine and from the mud of the ditch where the patient had fallen. Though the treatment used recommended doses of intravenous, intrathecal and intraventricular amphotericin B, it was ineffective and the patient died 97 days after the near drowning. Necropsy showed that the ventricular infectious process was more prominent distant from the antifungal ventricular source.

Monosporium apiospermum is the asexual form of *Pseudallescheria boydii*. This ubiquitous fungus commonly found in soil, rivers, and polluted water is a well known cause of cutaneous, pulmonary and osteo-articular infections. However, 29 cases of CNS infections have been previously reported. Aspiration pneumonia following a near drowning is, after immunodepression, the main predisposing factor for *M. apiospermum* infections of the CNS.¹⁻⁶ The prognosis depends on the severity when the treatment is started,⁴ and is usually bad because of severe difficulties encountered in making an ante mortem diagnosis.⁷ We report the following case because of the rare occurrence of *M. apiospermum* infections of the CNS, the difficulties in making the diagnosis and the fatal evolution despite an adequate treatment.

Case report

A 53 year old previously healthy market gardener, developed an aspiration pneumonia after he was found lying face down in a ditch after a car crash. He had no head trauma. Clinical and radiological improvement of the pneumonia was obtained within 15 days under netilmicin (400 mg IM daily), cefotaxime (3 g IV daily), and methyl-prednisolone (40 mg IV daily) for seven days, then under pefloxacin (800 mg IV daily), erythromycin (4 g IV daily) and chloramphenicol (2 g IV daily) for 24 days. On the 30th day after the accident his temperature was 38.5°C and antibiotics were withdrawn to perform new bacteriological samples. Twenty four hours later confusion,

frontal headache and mild neck stiffness appeared while the remaining neurological examination was normal. CSF was clear with normal pressure and contained 280 leukocytes/mm³ (76% polymorphonuclear), 180 mg/dl proteins and 29 mg/dl glucose; CSF cultures were sterile. Brain CT scan revealed a left cerebellar lesion suggesting an abscess. Staphylococcus dermatitis was isolated from the blood cultures and catheter, and the patient was treated with rifampicin (1800 mg IV daily), vancomycin (1500 mg IV daily) and ornidazole (1 g IV daily). Hydrocortisone (50 mg) and chloramphenicol (50 mg) were administered intrathecally every three days. The temperature fell to 37°C within three days but the patient remained confused. Thrombocytopaenia (75,000 platelets/mm³) was seen between day 47-50, and on the fifty first day, transient macular rashes appeared on

Figure 1 CSF evolution under treatment from the 32nd to the 93rd day after car crash. (a) intrathecal chloramphenicol (50 mg every three then every two days); (b) intrathecal hydrocortisone (50 mg every three days); (c) intrathecal hydrocortisone (100 mg every two days); (d) intravenous therapy with rifampicin (1800 mg/d) and vancomycin (1500 mg/d); (e) intravenous ornidazole (1 g/d); (f) intraventricular amphotericin B (0.1 mg to 0.9 mg every four days) + intravenous amphotericin B (from 5 to 55 mg every two days) + intravenous flucytosine (5 g/d); (g) intrathecal amphotericin B (from 0.1 mg to 0.6 mg every two days).

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Figure 2 Pathological findings; (a) cerebellar nodule (arrow); (b) intraventricular purulent material (arrow); (c) intraluminal isolated spicule (arrow); (d) periventricular nodule (arrow); (e) fungal filaments isolated from purulent material in occipital horns (PAS stain $\times 400$); (f) culture of *Monosporium apiospermum* in Sabouraud medium showing single conidia arise on the tip of conidophores (lactophenol cotton blue preparation $\times 400$).

the trunk. CT scan revealed the same cerebellar lesion and multiple nodules appeared in the periventricular white matter together with an enhanced ependymal reaction within the occipital horns. CSF follow up under antibiotics is reported in figure 1. On day 55, his confusion deteriorated but the temperature was 37°C and neurological examination remained otherwise normal. After a second break from medication, CSF contained 2560 leukocytes/mm³ (80% polymorphonuclear), 3540 mg/dl proteins and 10 mg/dl glucose. *M. apiospermum* was isolated from the CSF, sputum and urines, but blood cultures remained sterile. *M. apiospermum* was also isolated from a sample of the mud from the ditch where the patient had fallen two months earlier (Sabouraud's culture medium, lactophenol cotton blue). The isolated strain was susceptible to amphotericin B, flucytosine, miconazole, ketoconazole and itraconazole. Treatment started with increasing doses of amphotericin B, beginning with 5 mg the first day up to 55 mg. Amphotericin was administered each two days (one day with and one day without), with effective blood levels. The patient also received intrathecal and intraventricular amphotericin B (respectively from 0.1 mg to 0.6 mg and from 0.1 mg to 0.9 mg per injection), and intravenous flucytosine (5 g daily). CSF cultures were negative within 10 days, whereas urine and sputum cultures were still positive. The level of consciousness rapidly worsened, and hydrocephalus appeared. On day 94, the acute hydrocephalus was reduced by a ventricular puncture through the subcutaneous device. Three days later, the patient suddenly died. He had received total intravenous doses of 853 mg amphotericin B, 150 g flucytosine, intraventricular doses of 6.6 mg amphotericin B, and an intrathecal dose of 2.7 mg amphotericin B.

General necropsy revealed a bilateral bronchopneumonia with rare mycelial filaments in

the bronchiolar lumen. The other organs had no fungal elements: kidneys, spleen, myocardium and endocardium were normal. We found also a chronic aspecific pachyvaginitis. The immediate cause of death was not clearly established.

The fixed brain weighed 1300 g. Necropsy (fig 2) revealed a generalised cerebral oedema, with right temporal herniation. The thickened leptomeninges had an inflammatory aspect, but they were free of any filament. The left cerebellar lesion (8 mm) was at a chronic stage, without any fungal filaments. An easily separated material filled the occipital ventricular horns, including the purulent choroid plexus. A well circumscribed lesion overlapped the roof of the right ventricular horn to lie in the periventricular white matter. In the anterior part of the lateral ventricles, this material was less invasive and was developed from the roof of the ventricle. Microscopic examination of the yellowish material showed an acute suppurative necrosis bordered by granulomatous reaction with new vessels containing mycelial filaments: these were septate hyphae, with little branching, sometimes rigid or regularly dilated, but no sporulation.

Discussion

Isolation of *M. apiospermum* from the ditch where the patient had fallen and from the sputum made the lungs the probable route of entry. The causative agent was not detected in blood cultures but blood dissemination was probable since we found *M. apiospermum* in the urine and CSF cultures. Initially clinical improvement with antibiotics was misleading for the diagnosis. However, the improvement was too slow, and the appearance of CT abnormalities, within the white matter, made us consider a fungal infection in spite of negative results of CSF cultures performed 15

days before the diagnosis. Unfortunately, intrathecal hydrocortisone probably made the fungal dissemination easier. Systemic steroids, initially given for the pneumonia, probably favoured the pulmonary dissemination of *M apiospermum*. The fungal septicaemia probably occurred when cutaneous manifestations and transient thrombopaenia appeared as reported in a previous case.² Local and systemic amphotericin B made CSF cultures negative within 10 days. Necropsy examination revealed that CT scan signs of ventriculitis were due to the infectious process, and not to the toxicity of intraventricular amphotericin B. There was more purulent material at a distance from the local source of antifungal therapy, in the right frontal horn. This posterior predominance of fungal ventriculitis far from the catheter emergence, leads us to believe that our local therapy was partially effective but was not sufficient to stop the infectious process spreading posteriorly. However, posterior areas were initially more severely involved than anterior areas and the position of the patient in his bed might have favoured the posterior predominance of infection too. Cerebral localisation

makes fungi particularly inaccessible to treatment,⁸⁻¹⁰ and total recovery is unusual.¹⁰

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