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Relato de caso

Aspergillus infection causing cerebral aneurysm: case report and review of the literature

Infecção por Aspergilose provocando aneurisma cerebral

Moisés Heleno Vieira Braga[1],
Juliana Naves Ravanini[2],
Sergio Rosemberg[2],
Maurício Brígido Mandel[3],
Bernardo Assunção de Mônaco[3]

ABSTRACT

Background: *Aspergillosis infection of the central nervous system (CNS) is a rare disease and corticosteroid use has increased the number of cases. It presents a high lethality rate and has to be aggressively treated.* ***Methods:*** *A review of literature was done and 38 cases were identified involving cerebral aneurysms caused by this fungus to date.* ***Conclusion:*** *Aspergillus infection is very rare worldwide but its frequency is currently in expansion because immunocompetence failure is growing up: it has no specific presentation, making diagnosis difficult. Its prognosis is poor, so the disease has to be treated as early as posible.*

Keywords: *Mycotic aneurysms, Aspergillus fumigatus, Intracranial aneurysms*

RESUMO

Resumo: *Aspergilose do sistema nervoso central (SNC) é uma doença rara. O uso de corticosteróides tem elevado o número de casos na atualidade. Trata-se de uma doença com uma elevada taxa de letalidade e deve ser tratada de forma agressiva.* ***Métodos****: A literatura foi revisada, sendo identificados 38 casos envolvendo aneurismas cerebrais causadas por Aspergillus.* ***Conclusão****: A infecção por Aspergillus é muito rara no mundo, mas sua freqüência vem se elevando porque a falha de imunocompetência está crescendo. Não há uma apresentação específica desta doença, tornando o diagnóstico muito difícil. O prognóstico é ruim, portanto a doença deve ser tratada precocemente.*

Palavras-chave: *Aneurisma micótico, Aspergillus fumigatus, Aneurisma intracraniano*

Introduction

Aspergillosis of the central nervous system (CNS) is a rare disease; however, it has recently increased in frequency due to wider use of antibiotics, corticosteroids and immunosuppressants[3,8,18]. We report a case of Aspergillus arteritis that presented with repeated temporal infarction and a giant fusiform aneurysm. Few studies regarding mycotic aneurysms caused by Aspergillus have been published in the literature to date.

Case report

A previously hypertensive patient sought attendance at the Otorhinolaryngology (ORL) clinic in January 2009 complaining of facial pain associated with left nasal obstruction initiating in January 2008. In addition, she presented with infrequent nasal itching, but no sneezing, consistent purulent nasal secretion since January 2008 and epistaxis, hyposmia and left frontotemporal headache.

Magnetic resonance imaging (MRI) revealed a solid lesion in the left maxillary sinus extending into the temporomandibular joint, pterygoid fossa and the left temporal gyrus (Fig. 1).

1. Peripheral Nerve Unit, Department of Neurosurgery, FHEMIG Fundação Hospitalar do Estado de Minas Gerais , Minas Gerais MG, Brazil;
2. Department of Pathological Anatomy, University of São Paulo Medical School, São Paulo SP, Brazil;
3. Department of Neurosurgery, University of São Paulo Medical School, São Paulo SP, Brazil.

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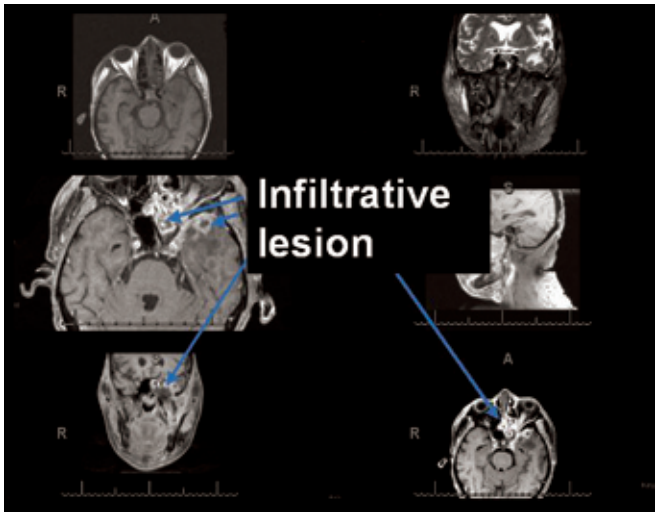

Figure 1. MRI (T1 weighted) - hyperintense lesion invading ethmoid sinus, middle fossa, maxillary sinus and left temporal lobe (blue arrows)

In January 29th 2009, a left middle meatus lesion biopsy was done: a granulomatous lesion material was found and forwarded for microscopic analysis and culture. Microscopy revealed the presence of symmetrical septate hyphae and 40 days after processing, growth of Aspergillus fumigatus was observed in culture (Fig. 2).

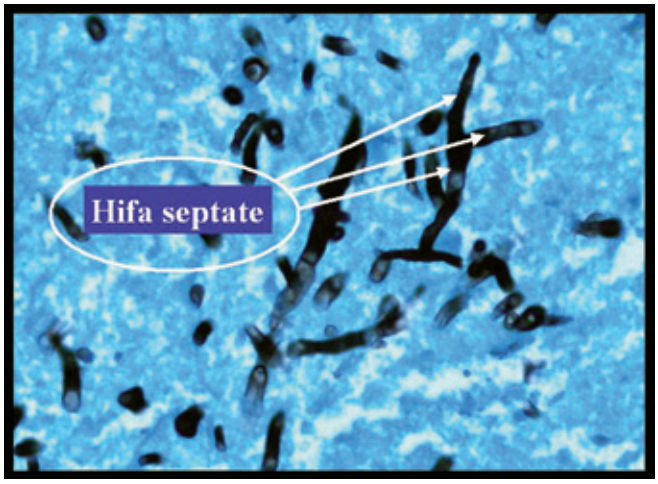

Figure 2. symmetrical hyphae suggestive of Aspergillus (methenamine silver staining)

One month later, the patient was admitted to the Hospital das Clinicas of the University of São Paulo Medical School (HCF-MUSP) for a new biopsy of the lesion detected in the maxilla and partial resection of the lesion.

The patient experienced a very intense facial pain and edema, which needed administration of high dosis of medications, including gabapentin, amitriptyline and oxycodone. She was discharged for outpatient follow-up on February 27th 2009.

In March, the patient presented with recurrence and was again admitted to hospital for reoperation of the lesion. Amphotericin B was administered for 8 days, when treatment was altered to ambisome (liposomal amphotericin B), in order to combat the infection. Hydrocortisone was maintained throughout the treatment.

Surgery was performed, involving resection of the lesion with partial excision of the small meningeal branch and left temporal lobectomy.

The patient presented with Pseudomonas meningitis, and, while continuing to receive liposomal amphotericin B, hydrocortisone and clindamycin, cefepime and meropenem were added.

Later, she presented with diminished level of consciousness (GCS 11) and was transferred to the intensive care unit with abundant bleeding through the right nostril, which was stopped by the Otorhinolaryngology team. Cranial computer tomography (CT) was performed, which revealed a Fisher Grade IV subarachnoid hemorrhage (SAH). Angiography showed right internal carotid artery (ICA) pseudoaneurysm (Fig. 3).

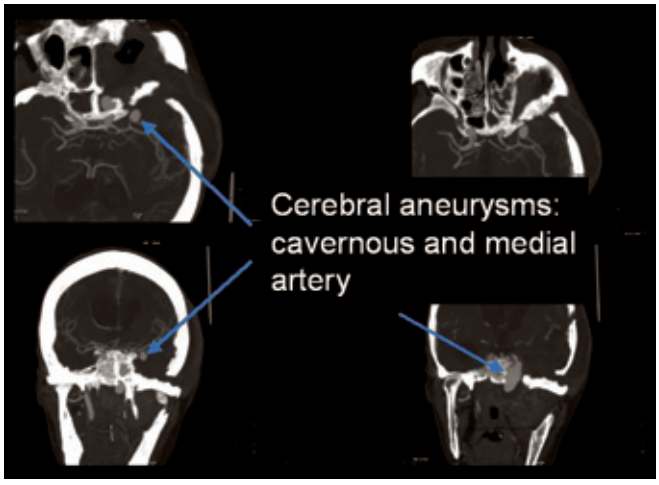

Figure 3. Angio CT - fusiform mycotic aneurysm of the right internal carotid artery and the left middle cerebral artery (blue arrows).

Neurological examination showed a GCS 8 (AO2 MRM5 MRV1) , anisocoria (R> L pupil), right semi ptosis involving also the 7th cranial nerve and right upper limb monoparesis (strength grade II).

The patient was transferred to a recovery hospital for rehabilitation and maintenance of antimicrobial and general care, but unfortunately died due to progressive deterioration of level of consciousness.

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Discussion

Only a few of the 350 types of Aspergillus are pathogenic to humans. A. fumigatus, A. flavus, A. sjdowi are more often involved in CNS pathology, though A. fumigatus commonly affects the brain[12]. Various sites may be involved by aspergillus, such as the parenchyma, meninges, vascular and ventricular systems[22].

Patients who have been treated with prolonged administration of antibiotics, corticosteroids or immunosuppressants and those who are immunocompromised as a result of diabetes mellitus, alcoholism, leukemia or AIDS are predisposed to fungal infections[3,8,9,18]: the reported patient did not present any known predisposing factors.

Aspergillus may reach the CNS via hematogenous dissemination from a remote extracranial site (usually the lung) or extension from a contiguous extracranial focus, such as the paranasal sinuses or the orbits. It has also been reported that neurosurgical procedures can induce direct fungal invasion[8,10,11,22]. Fungus infection can produce hemorrhage, thrombosis, infarction, necrosis, meningitis and ventriculitis[17]. CNS aspergillosis appears as meningitis, encephalitis, brain abscesses, subdural abscesses or mycotic arteritis. In arteritis, Aspergillus invades the cerebral blood vessels and causes intense inflammation of the arterial wall, leading to thrombosis, dilation, rupture and mycotic aneurysm formation. Previous cases of subarachnoid hemorrhage (SAH) caused by ruptured mycotic aneurysms exhibited poor prognosis[2,3,6,9,11,18,22].

Although a focus was not detected during autopsy, for several reasons, we suspect that Aspergillus spread hematogenously from an extracranial focus. First, Aspergillus invaded almost all of the main intracranial arteries. Second, fungal hyphae show greater invasion of the inner layer of the arterial walls than in the outer layer. Moreover, autopsy and analysis of MRI did not reveal any granulomas or abscesses in the nasal cavities, paranasal sinuses, orbits or brain parenchyma. These findings support the concept that hematogenous dissemination is the most likely cause; however, it is possible to treat CNS induced aspergillous aneurysms using vascular clipping.

Matsumura et al. 18 classified CNS aspergillosis as follows: 1) brain abscesses and granulomas, 2) meningitis and encephalitis, 3) intracerebral hemorrhage, 4) SAH, 5) cerebral infarction foci and 6) occlusion of a major artery. Two mechanisms have been reported as causes of SAH, i.e., rupture of mycotic aneurysms and collapse of vessel walls due to Aspergillus arteritis. To the best of our knowledge, 38 cases caused by CNS aspergillosis have been documented.

The mortality rate for intracranial aspergillosis is extremely high. Walsh et al.[40] reported that only 1 out of 17 patients with this condition was successfully treated. Mortality rate ranges from 80 to 90%[18]. Good outcomes were obtained only with early diagnosis, prompt surgical drainage and aggressive antifungal therapy[31,40].

CNS aspergillosis is difficult to diagnose. In most cases, cerebrospinal fluid (CSF) culture results are negative and CSF analysis reveals only nonspecific findings, such as pleocytosis and increased protein content[17,31]. Radiological findings are often nonspecific and do not yield enough information to confirm the diagnosis. Recently, it was reported that typical MRI features of cerebral Aspergillus produce a hypo- to isointense image of the lesion on T1-weighted and very low T2-weighted MRIs, with regular presentation when using post-gadolinium contrast[43].

It is often difficult to differentiate aspergillosis-related mass lesions (such as granulomas or abscesses) from other lesions, even when using MRI[4,17,35,36]. In such cases, diagnosis can only be confirmed through biopsy and culture of resected specimens.

Diagnosis of mycotic aneurysms is also established only with histological examination of specimens, although cerebral angiography can yield useful information[1,4,23]. In the present case, however, aspergillosis progressed without demonstrating an obvious infectious focus or forming mycotic aneurysms. Therefore, the cause of repeated SAH was not detected by angiography. These circumstances made it extremely difficult to establish an early diagnosis for this patient. The differential diagnosis for progressive cerebral infarction should include Aspergillus arteritis, to permit early aggressive treatment in order to improve patient prognosis.

In this report, irregularity in the features presented by patients was clearly observed. Analysis verified that the presence of mycotic aneurysms caused by Arpergillus occurred in the following vessels: 16 cases (42.1%) were located in the internal carotid artery; 12 cases (31.6%) presented in the basilar artery; only 6 (15.8%) were located in the middle cerebral artery; 5 (13.2%) or 4 (10.5%) presented in the vertebral artery; and that the presence of mycotic aneurysm in the superior cerebellar artery and anterior cerebral artery is much more rare, presenting only 1 case (2.6%) each in this review, with some cases showing more than one artery affected (Table 1).

Conclusion

Aspergillus infection is very rare worldwide but its frequency is currently in expansion because immunocompetence failure is

increasing: it has no specific presentation, making diagnosis difficult. This is a serious disease presenting with high mortality and poor prognosis, such that diagnosis must occur as early as possible to provide the patient with the best chance of survival.

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Corresponding author

Moisés Heleno Vieira Braga
Herculano de Freitas 237/ 157
01308-020, Bela Vista São Paulo
Fone :+55 (11) 6693 2270 +55 31 88143616
moizeusss@yahoo.com.br