B. Pfausler, A. Kampfl, K. Berek, H. Maier, F. Aichner, E. Schmutzhard

Syndrome of the Anterior Spinal Artery as the Primary Manifestation of Aspergillosis

Summary: Aspergillosis of the central nervous system (CNS) is an uncommon infection, mainly occurring in immunocompromised patients. Beside cerebral involvement spinal cord lesions are extremely rare. To our knowledge, aspergillosis initially presenting with acute paraplegia due to mycotic thrombosis of the anterior spinal artery in a formerly healthy patient has, so far, not been reported. Neither a primary focus nor an underlying disease had been detected.

Introduction

Aspergillosis of the nervous system is a rarely observed, life threatening condition [1]. It occurs most frequently in a setting of immunosuppression [1–4]. Meningitis, intracranial granuloma and abscess formation, hydrocephalus, mycotic aneurysms and intracranial arteritis have been described [5–10], as well as epidural abscess formation [11], spinal arachnoiditis [12], and spinal cord involvement [13]. The presented case describes the invasion of the anterior spinal artery by *Aspergillus* spp. hyphae and subsequent thrombosis leading to spinal cord infarction as the primary presentation of central nervous system aspergillosis in a previously healthy patient.

Case Report

A previously healthy 37-year-old male forest worker – having paid no attention to preceding minor splinter injuries – was admitted to a district hospital with sudden onset of flaccid paraplegia and sensory level at the fifth cervical vertebra. Cerebrospinal fluid (CSF), myelography, X-ray of the chest and the entire spine as well as a computed tomographic (CT) scan of the brain were normal. All routine laboratory parameters were within normal limits. In particular no leucocytosis was found. Since the patient did not show any improvement of the complete paraplegia, he was transferred within 2 days to our University Hospital. Flaccid paraplegia was unchanged, Babinski signs showed bilateral extensor response, hypalgesia was found below C 5. The patient was incontinent for defecation and micturition. He was febrile, temperature reaching 39.3°C. Leucocyte count in the peripheral blood was up to 19,000/mm^3 with 93% polymorphonuclear leucocytes (PMN).

Spinal tap was repeated, but CSF did not show any pathological findings; Gram stain, cultures for bacteria and fungi, serological examinations for neurotropic viruses (including HIV), examination for bacterial and fungal antigens were negative. Magnetic resonance imaging (MRI) of the cervical and upper thoracic spine revealed an intramedullary high signal intensity on proton density (PD) and T2 weighted images (Figure 1); the cervical cord was swollen from the second to the seventh cervical vertebra. The findings were interpreted as intramedullary edema. Administration of paramagnetic contrast agent (Gadolinium DTPA, 0.1mmol/kg body weight) did not add any further information, especially no epidural mass could be detected. MRI of the brain did not show any abnormalities. Transverse myelitis could not be excluded, tentative therapy with dexamethasone (8 mg t.i.d. for 1 week with slow tapering off), mannitol (100 ml 20% q.i.d. for 3 days) and ceftriaxone (2 g o.d. for 6 days) was started. Repeated chest X-rays and CSF examinations on day 6 and 10 after admission as well as repeated blood examinations for bacteriological, serological, virological as well as mycological pathogens remained negative. On the 17th day after onset of disease, subacute deterioration necessitated respiratory assistance due to signs and symptoms of septic shock with multiorgan failure. White blood cell count had risen to 79,000/ml with 95% PMN, maximum C-reactive protein was 29.4 U/l. On the 19th day for the first time pulmonary infiltration within the right upper lobe was detected in the chest X-ray. At this day CSF analysis was again within normal limits, in particular neither intrathecal IgG production nor oligoclonal bands were present. Repeated blood, sputum and CSF cultures remained negative as well. Finally the patient developed fatal multiorgan failure on the 27th day of disease. Because of the patient's critical condition throughout the last 10 days further neuroimaging workup was considered impossible. Figure 2 summarizes the most important inflammatory parameters and decisive therapeutic management steps.

The gross neuropathological examination showed multiple cerebral abscesses in the basal ganglia, in the frontal white matter and in both cerebellar hemispheres. Within the brain abscesses hyphae of *Aspergillus* spp. were found.

Cross section of the cervical spinal cord showed infarction in the blood supply area of the anterior spinal artery. The posterior spinal tract was spared (Figure 3).

The anterior spinal artery was totally occluded, microscopic examination demonstrated invasion of branching septate fungal hyphae, identified as *Aspergillus* spp., into the blood vessel lumen resulting in thrombosis (Figure 4).

Additionally there was focal fungal meningitis in the posterior fossa. Liver, lungs, spleen and lymphnodes showed multiple abscesses, within which hyphae were found.

Received: 20 October 1995/Revision accepted: 10 March 1995

Bettina Pfausler, M. D., *A. Kampfl*, M. D., *K. Berek*, M. D., Prof. Dr. *E. Schmutzhard*, M. D., Universitätsklinik für Neurologie; *H. Maier*, M. D., Institut für Pathologie; *F. Aichner*, M. D., Institut für Magnetresonanztomographie und Spektroskopie, Universitätskliniken, Anichstr. 35, A–6020 Innsbruck, Austria.

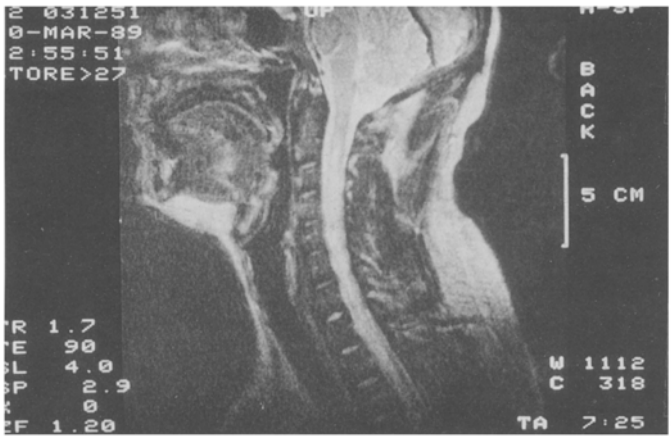

Figure 1: Sagittal T2 weighted spine-echo image 1,700 milliseconds (ms)/90 ms/2 (TR/TE/excitations) demonstrates increased intramedullary signal intensity within the cervical cord, suggesting intramedullary edema.

Discussion

Aspergillus spp. are ubiquitous saprophytic fungi that rarely infect the human CNS. Invasion of the CNS most often occurs either by contiguous spread from a paranasal infected sinus or hematogeneously from a pulmonary focus [1]. Several distinct clinical entities may occur. Most commonly patients have signs and symptoms of single or multiple brain abscesses [1–8]. Meningitis due to *Aspergillus* is rare but has been described after drug abuse as well as transsphenoidal surgery [12]. Cerebral infarction may be caused by vasculitis or mycotic thrombosis [9,10].

Initial manifestation as spinal cord compression has been reported in a few cases only, based on an epidural mycotic abscess formation [11]. Direct invasion of the spinal cord by *Aspergillus* has been reported only once in an immunocompromised patient, where a direct extension from a primary pulmonary focus could be detected [13].

To the best of our knowledge this is the first report of an Aspergillus infection with symptoms and signs of an acute paraplegia only due to mycotic thrombosis of the anterior spinal artery in a non-immunocompromised patient.

None of the primary investigations, in particular of a normal CSF [15], suggested a fungal infection. No primary focus (neither pulmonary nor elsewhere) was evident. The tentative diagnosis of transverse myelitis, accentuated by the presence of intramedullary edema in MRI, prompted systemic corticosteroid therapy. Though no bacterial pathogens could be cultured, an antibiotic trial with ceftriaxone was started because of polymorphonuclear leucocytosis and raised body temperature.

Thus it is conceivable that both antibiotics and steroids [5,16] may have enhanced dissemination of fungal elements leading to *Aspergillus* induced sepsis syndrome and the terminally fatal multiorgan failure, accompanied by meningitis of the posterior fossa, multiple brain and organ abscesses. In conclusion, this case illustrates the extraordinary difficulties in diagnosing early aspergillosis when the

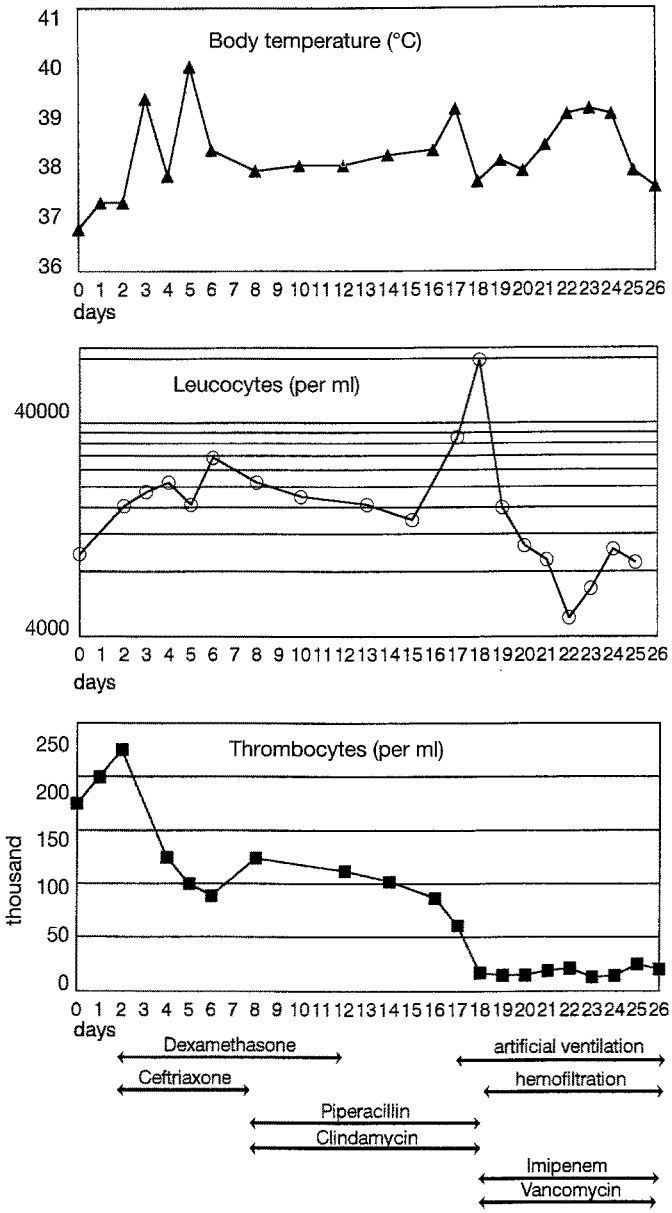

Figure 2: Body temperature, leucocytes and thrombocytes, antibiotic therapies and intensive care management throughout the course of disease.

primary presentation is so untypical (acute paraplegia) and no known immunosuppression is an indicator. Contrast enhanced MRI helped to exclude extra- and intramedullary tumor or abscess formation but could not differentiate between transverse myelitis and infarction. Since it is more likely to occur in a young person, transverse myelitis was assumed to be the cause of the disease, in spite of repeated normal CSFs and the absence of intrathecal IgG production as well as oligoclonal bands. As pointed out above, this diagnostic consideration indirectly may have been the reason for the dissemination of the initially most unlikely causative agent, *Aspergillus* spp. The final diagnosis was established only post mortem precluding any specific therapeutic trials [6,16,17].

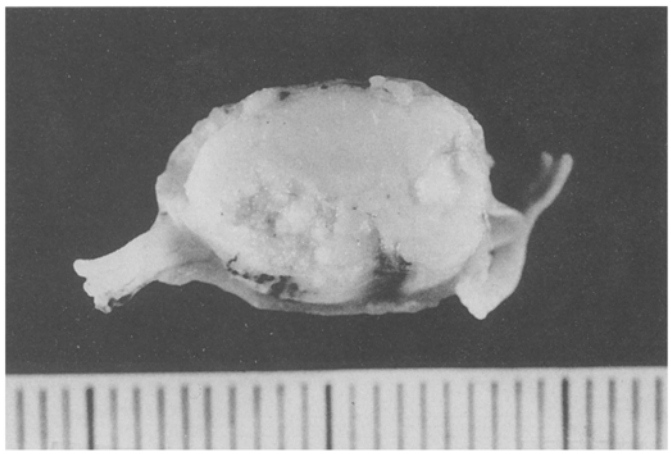

Figure 3: Cross section of the cervical cord at the C5 level revealing necrosis in both lateral columns and right-sided grey column.

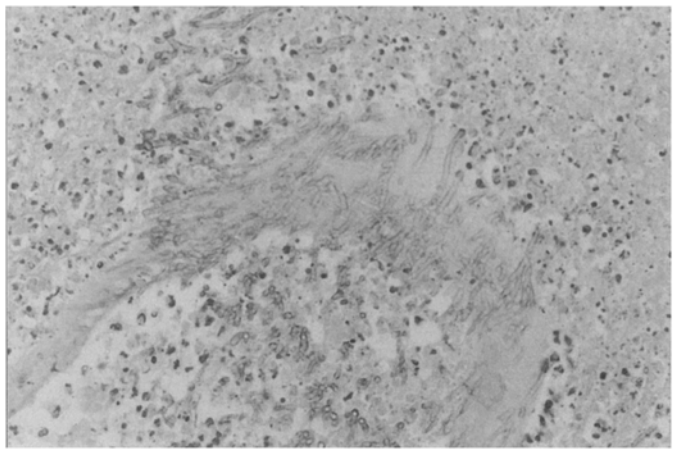

Figure 4: Anterior spinal artery showing diffuse invasion of the vessel wall by septate fungal hyphae with secondary thrombosis of the vessel lumen (PAS stain, original magnification x 100).

Zusammenfassung: Aspergillus spinalis anterior-Syndrom als Erstmanifestation einer Aspergillose. Eine Aspergillose des zentralen Nervensystems (vorwiegend cerebrum) ist eine ungewöhnliche Infektion, die hauptsächlich bei immunkompromittierten Patienten vorkommt. Eine Aspergillose, die sich initial als akutes A. spinalis anterior Syndrom präsentiert – bei mykotischer Thrombose – wurde bis jetzt noch nicht mitgeteilt. In diesem sonst gesunden Patienten war kein Fokus gefunden worden.

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