Case report

Aspergillus spondylodiscitis in an immunocompetent paraplegic patient

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A case of an immunocompetent 60 year old patient is reported, who suffered extensive thoracic spinal injury and paraplegia after polytrauma. In the course of rehabilitation he developed aspergillus spondylodiscitis in a part of the thoraco-lumbar spine which was primarily uninjured. The diagnostic assessment and therapeutic approach of this rare disorder is elucidated and discussed in the context of paraplegia and polytrauma. Possible mechanisms of inoculation and spreading of the moulds as well as predisposing factors of the disease are discussed in this paper and a review of the recent literature is provided.

Keywords: invasive aspergillosis; spondylodiscitis; polytrauma; paraplegia; immunocompetence

Introduction

Most commonly invasive aspergillosis develops as a result of an immunodeficiency¹ which may be due to one or a combination of the following causes: glucocorticoid, cytostatic, or antibiotic therapy; catabolism after transplantation or extensive surgery; chronic consumptive disease such as tuberculosis, neoplasma, or alcoholism with entailing cirrhosis of the liver.

Aspergillus species are ubiquitous moulds frequently isolated from air and environmental samples such as soil and decomposing organic materials. Only few of more than 200 known species can cause opportunistic infections, the most frequent being *A. fumigatus*, *A. flavus*, *A. terreus*, *A. nidulans* and *A. niger*.^{1–5} Inhalation of airborne conidia can lead to localized upper or lower respiratory infections, while rare cutaneous infections are caused by traumatic implantation of fungal spores. Invasive aspergillosis, uncommon in immunocompetent patients, may spread from respiratory infection to various tissues such as brain, kidneys, heart and bones, where the spine is a prime target.^{1–3,5}

Case report

The patient, who had no history of severe illness or injury was polytraumatised when falling off a tree in February 1994. He suffered dislocated fractures of thoracic vertebrae 7 and 8, several fractures of the ribs, contusion of the right lung and haematopneumothorax on both sides as well as a dislocated fracture of the left

olecranon. He had an incomplete paraplegia (sensory level Th6, incomplete; motor level Th6, complete, Frankel: B). After admission to the traumatologic center (University Hospital Zürich) he was treated with methylprednisolone, according to the NASCIS-II-scheme, within 8 h after the accident. He received a total dose of 9250 mg in 24 h. In order to minimize the risk of additional pulmonary complications and to allow for early mobilization it was decided in favour of an offensive therapeutic regimen. The spinal fractures were immediately stabilized by ventral and dorsal spondylodesis with internal fixation from Th6-9. However, the post-operative recovery was protracted and complicated by repeated thoracotomy, due to bleeding. Recurring pneumoniae, atelectasis and adult respiratory distress syndrome (ARDS) led to bronchial lavage which yielded growth of *Klebsiella*, *Pseudomonas* and moulds. Artificial respiration was stopped four weeks after the trauma and the patient was taken to the paraplegic center where he initially recovered well. Four weeks later, after the patient was already mobilized in a wheelchair, he started complaining about right-sided abdominal pain. Due to impaired sensory function he could not precisely localize or describe the pain. The development of neurogenic pain and of abdominal spasticity further confounded clinical judgement about the origin of the complaints. Clinical examination revealed no specific pathology. In particular, there was no local pain when tapping over the lumbar spine. The neurological examination was unchanged with respect to motor and sensory levels but spasticity of abdominal and lower extremity muscles

was increased. The patient developed chronic subfebrile temperatures. Blood sedimentation rate (BSR) was beyond 100 mm/h and the CRP was elevated to 50 mg/l. The blood cell count yielded a normocytic, orthochromatic anaemia. The level of ferritin was elevated (1684 $\mu\text{g/l}$; normal: 28–306 $\mu\text{g/l}$). The parameters for white blood cell (WBC) and platelet counts, differentiation of the WBC, and all other laboratory tests were normal. Control X-rays of the fractured thoracic vertebrae showed a sufficient consolidation of the fractures with no signs of infection or other pathology. Gastroenterologic diagnostics, including endoscopic examination and repeated CT-scans of the abdomen did not show any infectious or neoplastic focus. As the patient's condition continued to deteriorate, scintigraphic examination with ^{111}In -oxine marked autologous granulocytes was done in order to differentiate a putative inflammatory focus from increased metabolic turnover at the fracture site. A previously unknown infectious focus was found in the area of Th11/12. Corresponding X-rays (Figure 1b) could confirm the diagnosis of a spondylodiscitis of the intervertebral disc Th11/12 which was not visible in previous X-rays (Figure 1a). MRI-scans (T1-weighted sequence, Figure 2) of this region in addition revealed pannus-like paravertebral and epidural changes of the entouring soft tissue. The beginning of the development of a gibbus was due to erosion and instability of the infected vertebrae. CT-controlled needle biopsy only yielded coagulase-negative *Staphylococcus* in low concentration. Because of the destabilizing effect of destructive infection, hemilaminectomy and costo-transversectomy with debridement of the disc space and primary bone grafting were performed from a posterior approach. During ten weeks, the thoracic spine was stabilized externally from Th10 to L1.

Cultures of surgically removed tissue samples revealed no growth of bacteria, mycobacteria or fungi. However, histological sections allowed a preliminary diagnosis of invasive aspergillosis. The disc fragments contained faintly PAS-positive staining fungal elements consisting partly of uncharacteristic toruloid hyphae, but occasionally showing the typical aspect of dichotomously branched septated hyphae (Figure 3). The definite diagnosis could be established by seroconversion and reconversion during the course of disease. Immuno-electrophoretic analysis of a serum specimen from July 1994 showed precipitating antibodies to *Aspergillus fumigatus* (none to other *Aspergillus* sp.), while a prior specimen from February 1994 had been negative. Follow-up specimen from August 1994 (after one month of therapy) and from January 1995 showed a reduction of the number of precipitation lines and no precipitation lines, respectively.

The patient was treated with a combination of Amphotericin B (60 mg intravenously per day, total dose of 1450 mg at a body weight of 70 kg) and 5-Fluocytosin (1000 mg orally per day in fractions of 250 mg every 6 h), according to the current litera-

Figure 1 Radiograph of the thoracic spine prior to (a) and after (b) diagnosis of spondylodiscitis Th11/12; internal fixation of the fractured 7th and 8th thoracic vertebrae was performed from Th6 to Th9; the destructive process in the intervertebral disc space Th11/12 can be seen two segments below the transpedicular fixation in Th9. The destructive infection is shown prior to surgical exploration and prior to secondary external stabilization

ture.²⁻⁵ This treatment was continued for 4 weeks. Antimycotic treatment was continued for another 4 weeks with Itraconazole (200 mg orally twice a day). After removal of the fixateur externe, a corset was applied for another 12 weeks. Radiologic controls showed satisfactory consolidation and recession of infectious signs, same as the laboratory markers. The patient recovered well without deterioration of the neurologic status and only with the residuum of a slight gibbus at Th11/12.

Vertebral osteomyelitis can follow hematogenous dissemination, develop by contiguity, (eg from a pulmonary aspergilloma), or occurs as an iatrogenic infection after surgery.¹⁻⁵ Laboratory data (elevated BSR and CRP, normal WBC) are consistent with a

chronic inflammatory process, but clinical and radiological findings do not help in differentiating bacterial spondylodiscitis. Diagnosis is achieved by isolation of the organism and/or by demonstration of characteristic hyphae in histological sections or specimen smears. A positive serology is a useful adjunct in determining the etiological role of *Aspergillus* sp. grown in culture.⁶

In our case the diagnosis of *Aspergillus* spondylodiscitis was ascertained by histology and by the development and disappearance of specific antibodies to *A. fumigatus*, respectively. To our knowledge fungal infection of the unimpaired spine in the setting of a pre-existing traumatic paraplegia has hitherto not been described. The combination of hypalgesia and hypaesthesia as well as neurogenic pain in the paralyzed areas tended to obfuscate complaints and symptoms. The delayed diagnosis was possible only

after an extended search using the sophisticated technique of autologous granulocyte scintigraphy.

Aspergillus infection of the intact vertebrae or discs is extremely rare in the absence of long-term immunosuppression. In the majority of similar cases, a preceding pulmonary aspergillosis could be documented.² In our patient repeated chest X-rays showed no pulmonary aspergilloma. In addition, clinical and laboratory data, including negative screening for HIV-1 and -2 antibodies, allowed us to consider our patient to be essentially immunocompetent. However, several factors are likely to have contributed to the establishment of the opportunistic mycosis:

- (1) There is evidence that high-dose steroid therapy can cause impairment of the conidiacidal function of human macrophages *in vitro*; furthermore, a single high dose of glucocorticosteroids leads to a substantial reduction of the LD₅₀ and decreased clearance of *A. fumigatus* from tissue in mice.⁷ The initial therapy with methylprednisolone (9250 mg/24 h) in our patient corresponds to a steroid concentration in the 10⁻⁴ M range, thus exceeding the concentrations used in these animal experiments.
- (2) A transient suppression of the immune system by repeated surgery, chronic bacterial pulmonary infection and by the protracted catabolic state including ARDS is conceivable.
- (3) During four weeks of artificial respiration and intermittent mandatory ventilation, cultures of bronchial aspirates repeatedly yielded growth of an unidentified mould. We hypothesize that referral of the isolate to the mycology laboratory would have allowed the identification of *A. fumigatus*. Retrospectively, the findings suggest that colonization with *A. fumigatus* and subsequent invasive disease occurred during that period.

It cannot be assessed retrospectively, to what extent thoracotomy and repeated surgery in the adjacent thoracic spine might have promoted a spreading of the infectious agent to the unimpaired spine, thus leading to invasive aspergillosis. Surgical intervention, however, was carried out at a large university center by an experienced team of specialists. The protracted recovery and necessity of repeated surgical revisions, particularly due to bleeding after primary haemato-pneumothorax, must therefore be seen as an inevitable complication. Postoperative intensive care could prohibit further deterioration of the patient's condi-

tion despite the serious complications. In this context, it should be critically mentioned, that complications might have been less severe in case of a less invasive surgical approach. However, invasive treatment was necessary because of intraspinal bone fragments and due to thoracic bleeding. This might have biased the decision towards a more aggressive surgical treatment next to an intention for early mobilization. This was particularly so, as there was extensive and multilevel spinal damage and it could not be expected that stability was to be attained with dorsal spondylodesis alone, neither in one operative session.

On the other hand, early impairment of alveolar macrophage function by the initial high-dose steroid therapy and unspecific immuno-compromizing factors were likely cofactors in the development of invasive aspergillosis. However, it remains surprising and unexplained why the infection was not localized in the fractured thoracic vertebrae, but affected unimpaired segments of the spine. Generally, development of neurogenic pain in combination with chronic inflammatory signs after SCI and polytrauma may indicate an infectious process. Opportunistic infections in unusual locations should be given consideration, as well. Serologic follow-up examination of our patient, and re-evaluation of earlier serologic specimen helped to ascertain the diagnosis.

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