An autopsy case of disseminated angioinvasive aspergillosis

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Abstract Angioinvasive aspergillosis is a rare but potentially devastating disease especially in immunocompromised hosts. However diabetes mellitus is one of the chronic conditions that leads to immunosufficiency in patients, it is rarely reported in such cases. Here we aimed to present an autopsy case of disseminated angioinvasive aspergillosis with diabetes mellitus and discuss the other possible underlying reasons for this situation.

A 52 year old man with diabetes mellitus operated for the fracture of his L1 vertebra and tibia due to falling down from the third floor of a building. After his death on postoperative 34th day, histopathologic examination of the tissue samples presented multiple hyphae having dichotomous branching at 45-degree angles in infiltration areas.

In conclusion, in long-term hospitalized patients with diabetes mellitus, fungal infections should be taken into account and an empirical antifungal therapy is recommended. Besides, sterilization procedures should be obeyed in order to prevent infectious diseases.

1. Introduction

Suspicious deaths such as, suicide, falls, murder, accidents, poisoning are reported to judicial authorities. The patient had been recorded as a criminal case because of falling from a height. The patient was lost due to invasive aspergillosis.

Invasive aspergillosis (IA) is a potentially life-threatening infection, caused by an opportunistic fungi belonging to the genus Aspergillus. These fungi commonly exist in soil, on decaying plants and in the atmosphere. Recently they have become a health care problem for immunocompromised patients, such as those with hematological malignancies, solid organ transplantation, AIDS, chemotherapy or steroid use. However, IA is rarely reported with diabetes mellitus that leads to immunosufficiency in the host. Although the main entry of the mold into the human body generally occurs via the inhalation of the conidia, an inoculation of conidia through the damaged skin is not an infrequent way of gaining access to infection. Subsequently to the primer infection, a hematogenous dissemination may occur due to the several factors, especially the immunosuppression of the host and accompanying chronic diseases.
The diagnosis of IA is often made late in the course of the disease due to the lack of reliable and feasible diagnostic techniques. Therefore, early diagnosis is critical in order to commence an appropriate treatment and avoid potentially deleterious outcomes.  

Herein we presented the clinical importance and pathologic findings of disseminated angioinvasive aspergillosis originated from wound infection in postmortem examination of a patient with steroid dependent diabetes mellitus subsequent to an operation of tibia and L1 fracture owing to falling down from the third floor of a building.

2. Case report

A 52-year-old man recruited to the neurosurgery clinic with L1 fracture because of falling down from the third floor of a building. His physical examination was normal other than urinary and fecal incontinence. In the laboratory tests there were not any notable results of biochemical markers. He was operated of T10-L3 instrumentation. He also had an operation for tibia fracture in an orthopedic clinic. After the operation the patient had taken steroid therapy due to the findings consistent with subarachnoidal hemorrhage presumed to indicate the cerebral computed tomography findings of multiple hypodense areas. As the fasting glucose levels increased he was diagnosed as having diabetes mellitus. Thus he was commenced on parenteral insulin therapy.

Escherichia coli was isolated in the microbiological analyses of a culture taken from the wound. Piperacillin tazobactam was initiated, but due to the pancytopenia and elevated liver enzymes changed with meraopenem. After the isolation of Pseudomonas aeruginosa and Enterococcus spp. in the necrotic wound culture from the operation site on his back, teicoplanin was added to the treatment. As the patients clinical condition deteriorates he was shifted into the intensive care unit. Nevertheless, he got worse and died on the 34th day.

In the forensic postmortem pathologic examination, 10% formaldehyde fixed paraffin embedded samples (wound side, brain, lung, kidney and heart of the patient) were sectioned 5 μm, stained with Hematoxylin-eosin (H&E), periodic acid-Schiff (PAS) and Gomori methenamine silver (GMS) and examined under the light microscope. Microscopic examination of the lung samples patchy pneumatic infiltrations and thrombotic vessels were observed. There were multiple hyaline hyphae having dichotomous branching at 45-degree angles which are helpful in the differentiative diagnosis of other hyphae-producing fungi both in infiltration areas and vessels. Such findings were seen in the wound even more so in heart and kidneys’ samples. In heart samples especially in the myocardium it was evaluated as myocarditis with microabcesses including a large number of hyphae of the fungi (Figs. 1–3).

There were less hyphae in meningeal and intraparenchymal vessels of the brain. Histopathologically, it was diagnosed as invasive aspergillosis.

3. Discussion

Murder, suicide, poisoning, falls, electrical shock, deaths resulting from firearm injuries, suspicious deaths, and occupational accidents are related to medical jurisprudence. Such cases should be reported immediately to the related legal authorities. Our case was admitted to the emergency service because of falling from a height. The doctor who examined the patient was suspicious of this situation and had given notice to judicial authorities. The process of treatment and death of the case was evaluated as a criminal case, so that after the patient died, autopsy was performed. The results of histopathological examination of the tissue samples of the case showed that invasive aspergillosis.

Aspergillosis is an infrequent infectious disease that has a high mortality rate especially in immunosuppressive patients. The general risk factors are: hematological malignancies, neutropenia, corticosteroid usage, and organ transplantations. In recent years the cases of IA without common risk factors have been reported. These cases involve patients with chronic obstructive pulmonary disease and postoperative illness. Our patient was newly diagnosed to have steroid dependent diabetes mellitus postoperatively and had taken steroid therapy which may be the predisposing factors for IA. Aspergillus spp. are widespread saprophyte fungi found in nature. Although these molds are usually isolated from soil and plant debris they can also be isolated from air sampling of indoor buildings, including hospitals. In addition, a repairment in the hospital may increase the risk for mold infection by facilitating the spread of the conidia in the atmosphere. Nevertheless aspergillosis occurs frequently via the aeroziation of conidia produced by the mold, it is possible to occur it by direct inoculation of the conidia to the operation site. In the presented case, the patient had an operation for tibia and L1 fracture. The origin of the IA should be the wound infection of the mold that would probably gain access from the atmosphere during the operation. Therefore it is important to take attention during the disinfection of the material both in operation and in other parts in the hospital. Correspondingly environmental sealing, air sampling and air filtration are recommended in order to prevent hospital acquired fungal infections. The germination of the conidia that leads to invasion in immunocompromised patients plays an important role in the pathogenesis of the disease. The immunity of the host is necessary for combating with fungi dissemination. In our case, diabetes mellitus and steroid therapy are presumably the major culprits that delayed the healing of the infection which consequently lead to progression of the disease including lungs, brain, kidney and heart. Additionally, our patient had taken broad spectrum antibiotic therapy that may contribute to the invasive status of the mold. Thus, in such cases, even without any obvious immunosuppression, aspergillosis should come into mind in order to detect resistant infections in patients with diabetes mellitus.

The infection site of aspergillosis is as important as the host immunodeficiency state for the poor outcome of the disease. Patterson et al. evaluated the antifungal therapy in 595 patients with IA, nevertheless the response to the treatment in patients with severe immunosuppression was 28%, in less severe immunosuppressive groups it was 51%. The response to the treatment decreased from 40% to 9% in patients with pulmonary aspergillosis and cerebral IA, respectively. In the present case aspergillosis was disseminated to the brain that occurs in 10–15% of patients with disseminated aspergillosis in immunosuppressive patients. On this account, diabetes mellitus should be assumed as an immunocompromised situation.

Although aspergillosis could be treated with different kinds of antifungals like amphoteracin B and itraconazole, it can be
fatal in a high ratio in immunosuppressive patients.\textsuperscript{13} Hence an empirical antifungal treatment should be favorable for recovery of the patient in the presumption of aspergillosis.\textsuperscript{11}

In conclusion, in the long-term hospitalization patients with diabetes mellitus who have resistant infections despite extended spectrum antibiotic therapy, fungal infections especially aspergillosis should be taken into account even if the patient has no classical risk factors. Because IA usually confers no good clinical outcomes, the empirical antifungal therapy is recommended. In addition since the infectious diseases are mostly preventible by sanitation, it would be accomplished by obeying sterilization procedures.

Immunocompromised patients with comorbidities with long hospitalization should be evaluated for aspergillosis in order to provide rapid diagnoses and treatment. Also similar to the suspect and forensic cases, post-mortem pathological examination of tissues are quite helpful in determining the actual cause of death.

References


