

showed an increased bilateral latency time of wave V and increased I-V interval. Except for the abnormal audition, the rest of the neurological examination was normal. Didanosine therapy was discontinued, but the azithromycin and myambutol were continued. Clarithromycin treatment was started again in June 1996. As antiviral treatment the patient received zalcitabin, followed by ritonavir, followed by indinavir. All of these antiviral agents were discontinued after a few weeks because of side effects. The patient's audition improved progressively and returned to normal by August 1996. He improved immunologically and virologically after a combination treatment that included a high dose of saquinavir, lamivudine, and stavudine was started. The patient was still in relatively good health in October 1997. Stavudine was stopped after he developed polyneuritis and slightly diminished audition again. His CD4+ lymphocyte count had increased to 237/mm<sup>3</sup> and his viral load was low: 4714 copies per milliliter of plasma.

We do not have proof that our patient's deafness was caused by didanosine because he has not been rechallenged with the drug. However, because didanosine is known to cause neuritis and because the deafness disappeared after stopping the didanosine, it is likely that this drug was the cause of the hearing deficit. Because the hearing deficit occurred at a moment the patient was treated with didanosine and clarithromycin, it may be that this deficit was caused by the prolonged association of these two drugs. Hearing loss has been described previously in AIDS patients treated with clarithromycin for a *Mycobacterium avium* complex infection [2-4]. However, this always occurred in patients who were receiving several other medications, and therefore the effect of clarithromycin on hearing loss remains unclear. It seems prudent to monitor hearing in patients receiving long-term clarithromycin-didanosine treatment.

## References

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## Steroid-Induced Invasive Aspergillosis with Thyroid Gland Abscess and Positive Blood Cultures

Leukopenia is the most important risk factor for invasive aspergillosis, but steroid therapy is a recognized predisposing condition as well [1, 2]. We report a case of steroid-induced fatal aspergillosis with an atypical presentation and an uncommon feature of premonitory diagnosis.

On 19 October 1993 a 74-year-old male patient was admitted for malaise and persistent pain in the neck and shoulders. Laboratory tests showed evidence of inflammation (erythrocyte sedimentation rate 126/148, C-reactive protein 2.97 mg/dl). Serological tests for autoimmune diseases were negative and a biopsy of the arteria temporalis was nondiagnostic; thus, autoimmune disease could be neither proven nor excluded. Cultures and serological tests for infectious agents, including mycobacteria and fungi, were negative. Extensive diagnostic tests were performed, but no infection or neoplasm was found; the patient was diagnosed with polymyalgia rheumatica. Treatment with prednisolone was begun (tapered from 60 to 40 mg/day), and symptoms improved and signs of inflammation declined.

After three months of steroid therapy the patient's condition worsened again and he was readmitted to the hospital (1 May 1994). The leukocyte count (under steroid treatment) was  $28.4 \times 10^9/l$ ; an intensive search for a possible infectious or neoplastic cause of the patient's complaints was repeated. An examination of the bone marrow showed locally increased granulopoiesis. Chronic myelogenous leukemia could not be ruled out morphologically, but the Philadelphia chromosome was not present, and no rearrangement in the *bcr* gene was found. A computed tomographic (CT) scan of the thorax (11 May 1994) showed no pulmonary infiltrations but revealed a hypodense node 1.5 cm in diameter in the left caudal thyroid lobe that had not been present seven months earlier; a fine-needle puncture of the focus (18 May 1994) yielded 5 ml of fluid that was almost free of cells.

Two days later (20 May 1994) the patient became febrile (39.5°C), and a urinary tract infection due to *Escherichia coli* was diagnosed and treated with ciprofloxacin. The patient's condition improved initially, but

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after five days his temperature rose again to 39.5°C. Cefotaxime, gentamicin, and erythromycin were added, but septicemia persisted and the leukocyte count rose to  $70 \times 10^9/l$ . No infectious focus was found, and broad surveillance cultures revealed only a few *Candida albicans* in the sputum. Two blood cultures were taken on 5 June 1994 and three on 6 June 1994. Cytological examination of the urine revealed abundant inflammatory cells but also suspicious urothelial cell clusters and branched hyphae that were considered probable contaminants; the urine culture was negative.

On 8 June 1994 a lumbar puncture was performed; the CSF culture was negative, and the liquor was found almost free of cells. One day later a tender swelling of 4 cm in diameter was noted in the left lobe of the thyroid; the CT scan showed a cystic formation in the caudal region that was promptly punctured again. Cytological examination of the fluid showed mycelial structures that could not be classified because of autolytic alterations. Therapy with fluconazole was started, and the other antibiotics were discontinued. On the same day right-sided hemiparesis developed with progressive loss of consciousness. The CT scan of the brain showed diffuse hypodensities of the basal ganglia on both sides. A central venous catheter was inserted for the first time.

On 11 June 1994 *Aspergillus fumigatus* was grown from one of the two blood cultures taken on 5 June 1994 and from two of the three blood cultures taken on 6 June 1994. Treatment with amphotericin B was started, but the patient died of circulatory failure one day later.

The necropsy revealed disseminated invasive aspergillosis with multiple abscesses in the left ventricular myocardium and both kidneys, a fungal thrombus in the left renal artery, abscesses in both lobes of the thyroid, cerebral aspergillosis of the basal ganglia, and septic dissemination into both lungs; a tumor or a hematological malignancy was not detected.

In the case presented the entry of *Aspergillus* infection and the precise time course of the dissemination remain unknown; the pulmonary abscesses that were detected by necropsy and yet invisible on the CT scans may have developed by dissemination into the lungs. Invasive aspergillosis without prominent involvement of the lungs is not frequent, and most cases are discovered unexpectedly by necropsy. Of 28 cases of fatal invasive aspergillosis, we found only four patients without primary infection of the lungs [3].

Three of the five blood cultures taken during dissemination were positive, resulting in good sensitivity in this individual case; however, the positive results were obtained only after six days of cultivation. Growth of *Aspergillus* in blood cultures is found extremely rarely [4], but it is highly specific for disseminated aspergillosis, especially if no central venous catheter is used. The present case is the only one we observed over a five-

year period; thus, using closed blood culture systems (Bactec 860, Becton Dickinson), contamination of blood samples by *Aspergillus* obviously occurs very rarely. In contrast, false-positive results have been reported for systems that require opening [5].

The organ that first led to the diagnosis of disseminated fungal infection was the thyroid gland. A suspicious node in the left caudal lobe was found 26 days antemortem and was examined aggressively by puncture, but without a conclusive result. There are three possible explanations for this. Dissemination could already have occurred, and the negative finding may represent a sampling error; this case would thus represent a slow course of invasive aspergillosis, with extreme leukocytosis mimicking hematological disease. It is also possible that the thyroid cyst was an "innocent bystander" that later became a site of dissemination. Finally, the fine needle puncture itself must be considered as the possible portal of entry for *Aspergillus*.

Thyroid abscesses were present in three of 28 cases of fatal aspergillosis in our institution [3]. Boon et al. [6] reported eight cases of thyroid abscesses among 32 patients with fatal aspergillosis. The thyroid is thus a relatively frequent site of dissemination in aspergillosis. In patients at risk for fungal infection, local findings in the thyroid region may therefore arouse suspicion of aspergillosis.

Retrospective correlation of the CT and the necropsy results leads us to assume that cerebral aspergillosis was present at the time when culture and cytological examination of the CSF were negative; this further suggests that the sensitivity of CSF cultures in the diagnosis of cerebral aspergillosis is rather poor [7].

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