

## Brief Reports

### A Case of Disseminated Aspergillosis with Thyroid Involvement

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Invasive aspergillosis has become the most prevalent life-threatening mold infection. It remains a common opportunistic infection, complicating the clinical course of illness in patients who are severely immunodeficient due to conditions such as hematological malignancy, bone marrow or solid organ transplantation, AIDS or steroid therapy. Invasive pulmonary aspergillosis with respiratory symptoms is the predominant form of the disease [1]. Although thyroid involvement is found frequently at necropsy, it is rarely suspected antemortem [2]. Reported here is a case of disseminated aspergillosis that occurred in a patient with myelodysplasia, who demonstrated symptoms of both thyroid and pulmonary involvement. The literature about this unusual presentation is also reviewed.

A 78-year-old woman with a 4-year-history of myelodysplasia, type refractory anemia with excess blast, was admitted to our hematology department in July 1999. She had been severely immunocompromised for 5 months with profound neutropenia ( $<0.1 \times 10^9/l$ ). During this period she experienced two episodes of *Escherichia coli* septicemia, which were treated with piperacillin-tazobactam plus tobramycin. Her therapy for myelodysplasia was limited to a palliative regimen with low-dose aracytin and transfusions.

She presented with fever, right-sided lower thoracic pain and mucopurulent sputum. Cefixim and ciprofloxacin therapy had been unsuccessful in treating the pulmonary symptoms. At admission, a chest radiograph showed consolidation of the right lower lobe with

pulmonary atelectasis. Culture of the sputum yielded a few colonies of *Candida albicans*. No symptom indicating focal infection of the sinuses was present. Since the prognosis of the patient's myelodysplasia was poor, no other pulmonary investigation was performed. Five days after admission, a dramatic enlargement of the neck with erythema and local warmth was noted. A computed tomographic scan of the cervical region showed a mass suggestive of a thyroidal edema predominant on the right lobe. No symptom of thyroid dysfunction was noted. The thyroid mass progressed rapidly and resulted in airway compromise. The patient's condition worsened, and she died within 3 days.

An autopsy was performed. The thyroid gland was asymmetric with an enlarged right lobe measuring  $5 \times 5 \times 3$  cm and a normal left lobe measuring  $3 \times 1 \times 1.5$  cm. An edema with few hemorrhages was present in the cervical area around the thyroid parenchyma. The other major macroscopical lesions were in the lung, with an hemorrhagic infarct of the right lower lobe measuring  $5 \times 5 \times 3$  cm and a localized area of necrosis measuring 2 cm in the left lower lobe. Histological analysis of the right lobe of the thyroid and of the two lung lesions revealed numerous septate hyphae with acute-angle branching consistent with *Aspergillus* spp. These hyphae were present in areas of ischemic necrosis in both the thyroid and the lung; they were also found in the vascular walls, and some hyphae were present in the cervical area surrounding the thyroid gland. No other localization of the disease was found in the thoracic, abdominal or pelvic organs. The sinuses and the brain were not analyzed.

In this case the histopathological findings were highly suggestive of invasive aspergillosis of the lungs with secondary spread to the thyroid. However, this diagnosis was not confirmed by culture, since the procedure was not performed. It should also be noted that infections with other filamentous fungi (i.e., *Fusarium* spp. and *Pseudallescheria* spp.) may histologically and clinically resemble infection with *Aspergillus* spp. [1].

Although thyroid invasion by *Aspergillus* hyphae is frequently seen at necropsy and has been reported in up to 35% of autopsied patients with disseminated aspergillosis, thyroid involvement is rarely suspected antemortem [2]. In a search of the English-language medical literature since 1960 (databases: Medline, Aidsline, Cancerlit and EBM reviews), only seven reports of symptomatic thyroid involvement in cases of invasive aspergillosis were found. In four cases the major symptoms were local pain, tenderness and enlargement without clinical or biological signs of gland dysfunction [3–6]. In two other cases the predominant feature was clinical thyrotoxicosis, which was confirmed by biological tests [7, 8]. In the remaining case the

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patient experienced a multinodular goiter and biological thyrotoxicosis [9]. Rapid enlargement of the thyroid gland with airway compromise, as seen in our patient, has not been described previously. None of the reported cases, including our case, had a history of thyroid disease.

All but one of the patients with symptomatic thyroid involvement in disseminated aspergillosis died. The patient who survived was a child with chronic granulomatous disease, who presented with thyrotoxicosis and acute thyroiditis. He had no evidence of dissemination and recovered from thyroiditis due to *Aspergillus* sp. after surgical treatment and intravenous therapy with amphotericin B [8]. The lesions seen in cases of *Aspergillus* thyroiditis are mostly described as focal abscesses, hemorrhagic lesions with fungal vascular invasion or diffuse necrotizing thyroiditis; these forms are consistent with the hematogenous route of gland invasion [10]. In contrast with bacterial infections of the gland, aspergillosis infections do not appear to be facilitated by pre-existing thyroid illness. Aspergillosis thyroiditis is more likely to be associated with immunodeficiency and disseminated disease rather than local thyroid illness [10]. Risk factors for disseminated aspergillosis with thyroid invasion are hematological malignancies, bone marrow or solid organ transplantations, steroid therapy and AIDS, as in other forms of disseminated aspergillosis [1].

The case described here emphasizes the significance of symptoms localized in the thyroid region in patients at risk for aspergillosis. Such clinical findings or signs of thyroid dysfunction should lead to additional investigations in order to either establish or rule out the diagnosis of disseminated aspergillosis. Histological examination and culture of a specimen obtained by fine-needle aspiration or biopsy of the thyroid may confirm the diagnosis.

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## Salmonella Lymphadenitis Associated with Undiagnosed Lymphoma

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Lymphadenitis as an extraintestinal manifestation of *Salmonella* infection is rare [1]. A case of *Salmonella braenderup* lymphadenitis is described here that was associated with unrecognized lymphoma.

A previously healthy 38-year-old female nurse noted that she had left-sided nontender cervical lymphadenopathy. Other than two soft contiguous lymph nodes measuring 2×2 cm in diameter lateral to the anterior sternocleidomastoid muscle, her physical examination was entirely normal. She soon developed pleurisy with a friction rub. A 5-day course of prednisone was prescribed that resulted in resolution of the rub and discomfort and a decrease in the size of the nodes. A complete blood count and liver chemistries were normal. An anti-streptolysin O titer and serology for *Borrelia burgdorferi*, *Toxoplasma gondii*, coxsackie virus, HIV and cytomegalovirus were negative. Epstein Barr virus (EBV) serology revealed an elevated viral capsid antigen IgG antibody but negative IgM antibody. A chest radiograph, mammogram and a PPD were negative.

The patient was well for the next 5 months, until she developed pain, swelling and erythema of the same

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