

# Isolated nasopharyngeal aspergillosis caused by *A flavus* and associated with oxalosis

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## Abstract

We report a case of isolated nasopharyngeal aspergillosis in a 52-year-old woman with Hashimoto's thyroiditis. We found the nasopharyngeal lesion incidentally while evaluating bilateral cervical lymphadenopathy, which we had discovered during a routine follow-up examination pursuant to the patient's thyroid problem. Biopsy analysis of the nasopharyngeal lesion revealed the presence of a mycelium made up of septate hyphae and associated oxalosis. Mycologic examination confirmed that *Aspergillus flavus* was the responsible pathogen. No systemic involvement or involvement of other head and neck sites was found. The patient had been exposed to a considerable amount of dust during the construction of her house, and this may have been the precipitating factor in the development of her infection. We treated the patient with a 4-week course of itraconazole. At the end of therapy, she exhibited no evidence of *A flavus* on physical and mycologic examinations.

## Introduction

The major manifestations of infection caused by species of the genus *Aspergillus* are allergic reactions, colonization, and fungal invasion. *Aspergillus* species reach the sinuses and lower respiratory tract via inhaled conidia.<sup>1</sup> In this article, we describe the case of a 52-year-old woman who acquired isolated nasopharyngeal aspergillosis that was caused by *Aspergillus flavus* and that was associated with

oxalosis. To the best of our knowledge, this is the first case of isolated nasopharyngeal aspergillosis without paranasal sinus or systemic involvement that has been reported in the English-language literature. Another interesting aspect of this case was the presence of oxalosis associated with *A flavus*; most cases of oxalosis occur in association with *Aspergillus niger*.

## Case report

A 52-year-old woman was referred to the Department of Otorhinolaryngology–Head and Neck Surgery for evaluation of bilateral cervical lymphadenopathy, which had been detected incidentally on neck ultrasonography during a follow-up examination for Hashimoto's thyroiditis. She had a history of hypertension, osteoporosis, total abdominal hysterectomy, and bilateral salpingo-oophorectomy for uterine leiomyoma, for which she took hormone replacement therapy. Her only complaint was postnasal discharge.

Findings on ENT examination were unremarkable except for the presence of a 2 × 3-cm lesion on the posterior wall of the nasopharynx; the lesion was covered with yellow-green crusts (figure 1). Computed tomography (CT) of the paranasal sinuses did not demonstrate any lesion, and the bony walls of the sinuses were intact.

A presumptive diagnosis of fungal infection was made, and biopsy specimens were obtained via nasopharyngeal endoscopy and submitted for both histopathologic and mycologic examination.

**Histopathologic examination.** Periodic acid-Schiff (PAS) staining revealed the presence of a mycelium on an inflammatory background that was made up of septate hyphae; no other diagnostic fungal structures were noted (figure 2, A). On hematoxylin and eosin (H&E) staining, numerous birefringent calcium oxalate crystals were identified by polarization (figure 2, B). The fungal morphology and the presence of associated oxalate crystals led to the diagnosis

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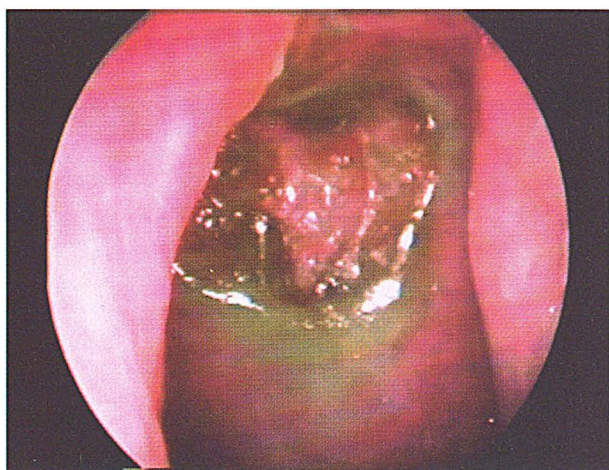


Figure 1. Endoscopic view of the posterior wall of the nasopharynx shows the 2 × 3-cm lesion, which is covered with yellow-green crusts. Other parts of the nasopharynx were intact.

of aspergillosis with oxalosis. The degree of fungal invasion could not be assessed because no recognizable mucosal tissue had been included with the specimen.

**Mycologic examination.** For mycologic analysis, the tissue was kept in sterile saline and specimens were cut into small pieces under sterile conditions. Gram's staining revealed branching hyphae at a 45° angle with parallel walls. Specimens were cultured in Sabouraud's dextrose agar and brain-heart infusion agar with blood, gentamicin, and chloramphenicol and incubated at 30°C. The culture plates were examined every 2 days. After 3 days, there was growth of white, feathery mold colonies that turned yellow-green by the end of the first week. Needle mounts in lactophenol cotton blue exhibited rough conidiophores with uniseriate and biseriate conidiogenous cells covering the entire vesicle. The mycologic analysis identified the pathogen as *A flavus*.

Subsequent to the histopathologic diagnosis of aspergillosis and the mycologic identification of *A flavus* as the responsible agent, a second nasopharyngeal biopsy was performed, and it ruled out an invasive mucosal infection. Systemic involvement was also excluded after a thorough examination of the patient. Findings on chest x-ray, blood culture, and urinalysis were within normal limits. Levels of total immunoglobulin (Ig) E, IgG, IgM, and IgA were also within normal ranges. The patient had no evidence of immunodeficiency and no predisposing factors for immunocompromise such as alcoholism, diabetes mellitus, or a hematologic disorder.

On the basis of the histopathologic, mycologic, and clinical data, the patient was diagnosed with isolated nasopharyngeal aspergillosis. We initiated a 4-week course of antifungal treatment with 200 mg/day of oral itraconazole, which is a well tolerated and effective treatment for fungal infections.<sup>2</sup> Two weeks later, a nasopharyngeal examination

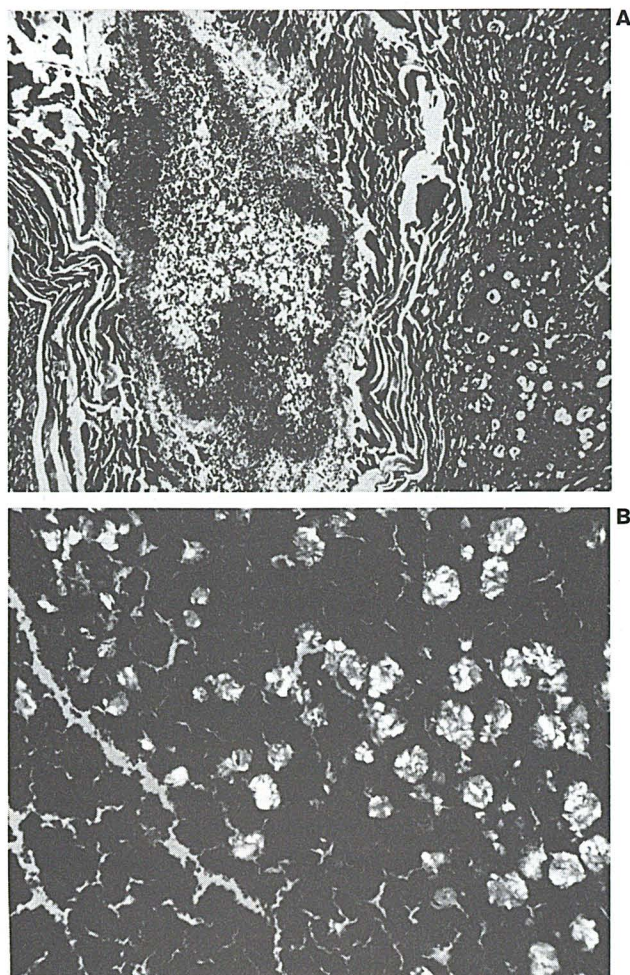


Figure 2. A: Histopathologic analysis reveals the *Aspergillus* mycelium with typical zonation on an inflammatory background (PAS, original magnification × 4). B: Strongly birefringent calcium oxalate crystals are visible under polarized light (H&E, original magnification × 40).

revealed a reduction of the size of the lesion. At the end of itraconazole therapy, we found no evidence of *A flavus* on physical and mycologic examinations.

## Discussion

Although aspergilli are ubiquitous in the environment, only eight species are known to have been involved in human infections.<sup>1,3</sup> *Aspergillus fumigatus* is the most frequently encountered fungus in humans.<sup>3,4</sup> The association of aspergillosis and oxalosis was first reported by Nime and Hutchins in 1973.<sup>5</sup> Oxalic acid is a mycotoxin produced by *A niger* and occasionally by other *Aspergillus* species, including *A flavus* and *A fumigatus*.<sup>6</sup> Oxalic acid reacts with tissue and blood calcium to precipitate as calcium oxalate.<sup>7</sup> Oxalate crystals are strongly birefringent, they form in various shapes (e.g., rosette, needle, dumbbell, and ellipsoid), and they exhibit sheaf-like groupings.<sup>8,9</sup>

These crystals can be seen in cytologic specimens as well as in tissues.<sup>8-10</sup> In most of the reported cases of oxalosis associated with aspergillosis, the etiologic agent was *A niger*.<sup>5-7,9-12</sup> The presence of calcium oxalate crystals associated with a fungal infection serves as a diagnostic clue for aspergillosis.<sup>1</sup>

In the head and neck, *Aspergillus* species can cause otomycosis, allergic paranasal sinusitis, invasive paranasal sinusitis, and aspergilloma of the paranasal sinuses.<sup>13,14</sup> In our patient, findings on paranasal sinus CT and endoscopic examination of the nasal cavity were normal. Likewise, the total IgE level was normal, and hematologic examination revealed a normal eosinophil leukocyte population. Based on these findings, we concluded that she had no evidence of fungal rhinosinusitis.

*A flavus* has a worldwide distribution, and it normally exists as a saprophyte in soil and on many types of decaying organic matter.<sup>1</sup> Our patient was exposed to a dusty environment for a considerable period of time during the construction of her house, and this exposure may have been the source of infection. She was postmenopausal and she had Hashimoto's thyroiditis, and she was taking estrogen and thyroid hormone therapy. These alterations of her hormonal status might have been a predisposing factor for her infection; it has been suggested that such alterations play a role in isolated sphenoid sinus aspergillosis, which is predominantly seen in elderly women.<sup>13</sup> According to the literature, there is no uniform body of information regarding the relationship between Hashimoto's thyroiditis and natural killer-cell activity.<sup>15-17</sup> Whatever the reason, we are not able to explain why the nasopharynx was the only affected site in our patient.

This case illustrates the fact that *A flavus* can colonize nasopharyngeal tissue in the absence of immunocompromise or allergic fungal sinusitis and that it can be associated with oxalosis.

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