



E-QUID: ANSWER / ORL

Allergic fungal sinusitis. Answer to March e-quid[☆]

F. Desmots^{a,*}, C. Gabaudan^a, Y. Geffroy^a,
P. Cassagneau^b, A. Varoquaux^b

^a *Département de radiologie, hôpital d'Instruction des Armées Laveran, BP 60149, 13384 Marseille cedex 13, France*

^b *Medical Imaging Department, CHU la Timone, 264, rue Saint-Pierre, 13385 Marseille, France*

Case study

This was a 48-year-old woman referred by her ENT for assessment of nasal obstruction and frequent purulent nasal discharge, who had previously undergone surgery for sinonasal polyposis. In fact, the patient had a perfect example of chronic rhinosinusitis, resistant to the conventional antibiotics administered for infectious ENT conditions and short courses of corticosteroid therapy. The surgery consisted of a bilateral meatotomy, which provided partial but short-term regression of the symptoms. We also noted an atopic history with eczema that was well controlled by dermatological corticosteroids during flares.

An imaging workup was done consisting of a low dose (75 mGy.cm) CT scan of the sinuses without injection, with a hard- and soft-tissue reconstruction filter (Figs. 1–5). We decided to perform an MRI study as a second step (Figs. 6–9).

DOI of original article: [10.1016/j.diii.2012.01.009](https://doi.org/10.1016/j.diii.2012.01.009).

[☆] Here's the answer to the case previously published in the n° 03/2012. As a reminder we publish again the entire case with the response following.

* Corresponding author.

E-mail address: flo0162@yahoo.fr (F. Desmots).

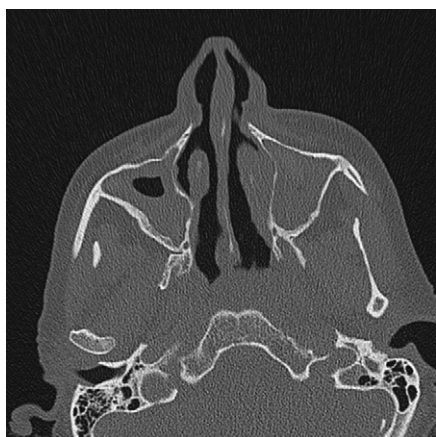


Figure 1. Axial CT scan with bone filter through the maxillary sinuses.



Figure 4. Axial CT scan with soft tissue filter centering on the sphenoid sinuses.



Figure 2. Axial CT scan with bone filter through the nasal fossae and sphenoid sinuses.



Figure 5. Axial CT scan with soft tissue filter through the ethmoid air cells.

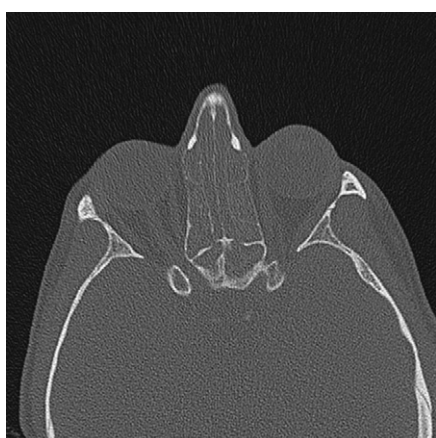


Figure 3. Axial CT scan with bone filter centering on ethmoid air cells.

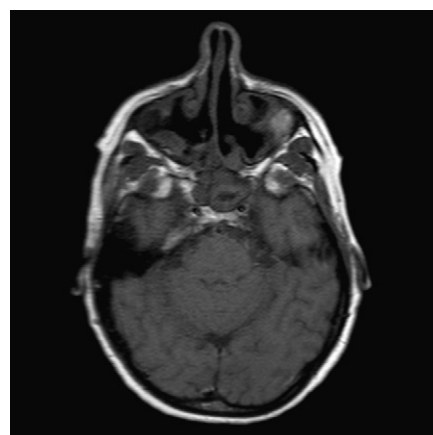


Figure 6. Axial T1-weighted SE MRI.

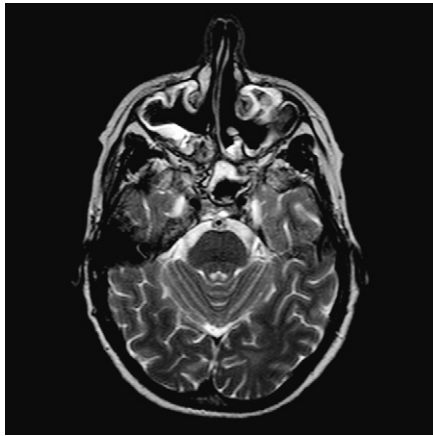


Figure 7. Axial T2-weighted SE MRI.

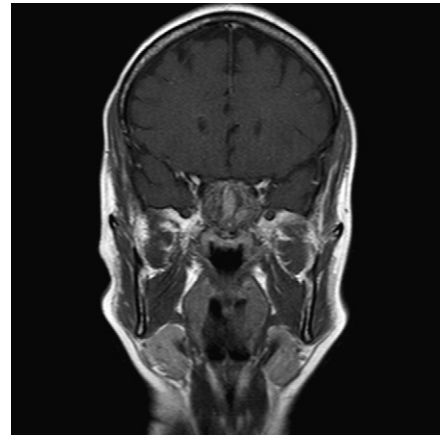


Figure 9. Coronal T1-weighted MRI after gadolinium injection.

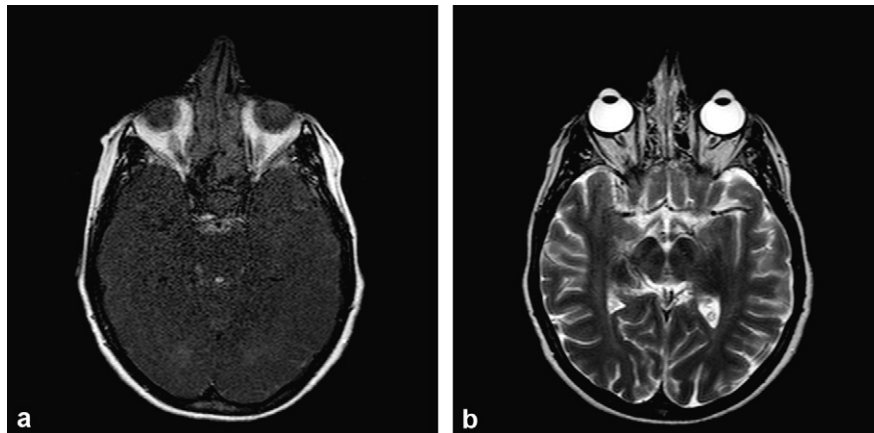


Figure 8. a: axial T1-weighted SE MRI; b: axial T2-weighted SE MRI (b).

What is your diagnosis?

Based on your reading of the case study, which of the following would be your diagnosis?

- spontaneous sinus bleeding;
- uncomplicated chronic sinusitis;
- chronic sinusitis with “fungus ball” type fungal process;
- allergic fungal sinusitis;
- invasive fungal sinusitis.

Diagnosis

Allergic fungal sinusitis.

Comments

First of all, the CT scan and MRI show postoperative scars from a bilateral middle meatotomy, well visualized on the axial CT scan sections (Fig. 10, red arrows). The purpose of this functional endonasal surgical procedure is to restore mucociliary drainage by anatomically freeing the ostial regions (ostioameatal complex) and eliminating the causal infectious agent.

The CT scan (Figs. 10–12, white arrows) shows nearly complete opacification of both maxillary sinuses, complete filling of the ethmoid air cells bilaterally and of both sphenoidal sinuses. This opacification, associated with a demineralized, sparse, and thin appearance of the bony ethmoid septa and internal orbital lamina papyracea (Fig. 12, white arrows) are suggestive of stage III sinonasal polyposis.

No other mucocoele-related change is seen (no intra-sinus distension). Furthermore, we see a thickening of the sphenoid and maxillary bone (Fig. 11, white arrow) due to a periosteal reaction (apposition) caused by chronic infectious stimuli. There are thus signs of chronic sinusitis.

Analysis of the contents of this diffuse opacification of the sinuses shows a spontaneously hyperdense mass with a tissue window (>100 HU) (Figs. 13 and 14, white arrows). The MRI study (Figs. 15–18, red arrows) finds opacification that is isointense on T1-weighted images and black (no

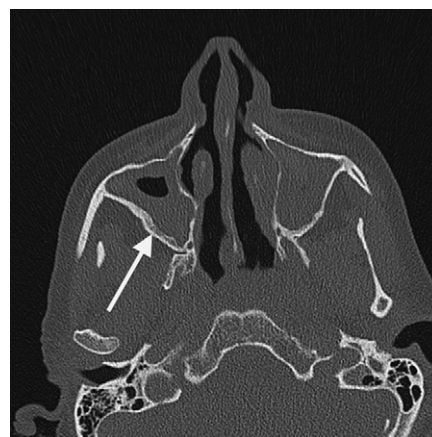


Figure 11. Axial CT scan through the maxillary sinuses showing mucosal thickening consistent with marked thickening of the bone walls. Aspect of chronic sinusitis with chronic periosteitis.



Figure 12. Axial CT scan through the ethmoid air cells showing complete opacification, a thinned and demineralized aspect of the lamina cribrosa and lamina papyracea of the ethmoid bone in connection with the existence of sinus polyps.

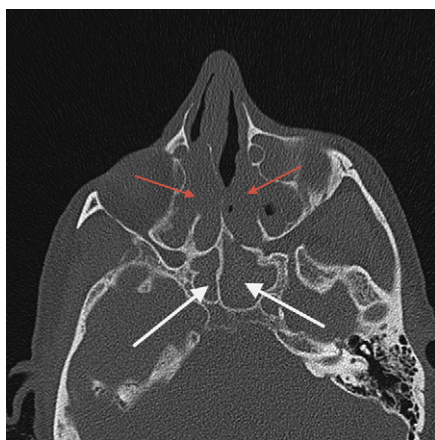


Figure 10. Axial CT scan through the nasal fossae and sphenoid sinuses showing complete intrasinus opacification with no spontaneously hyperdense mass on these hard tissue filter slices.



Figure 13. Spontaneously hyperdense left intra-sphenoid opacity (>100 HU) with soft tissue filter, evidence of fungal disease.



Figure 14. Spontaneously hyperdense and diffuse panethmoidal opacification with soft-tissue reconstruction filter, not visualized on hard-tissue filter slices. The diffuse nature is more suggestive of allergic fungal sinusitis than of a simple aspergillar “fungus ball” process.

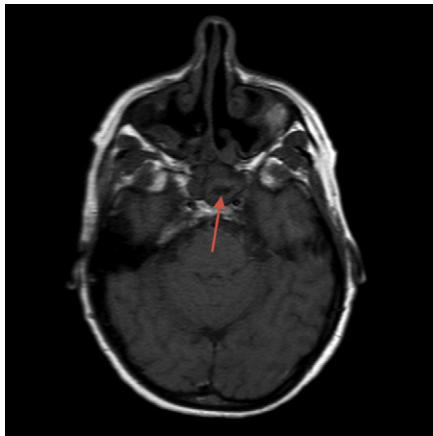


Figure 15. T1-weighted MRI showing a central low-intensity nodular lesion and a high-intensity peripheral corona (mucosal thickening with high protein content) within the left sphenoid sinus.

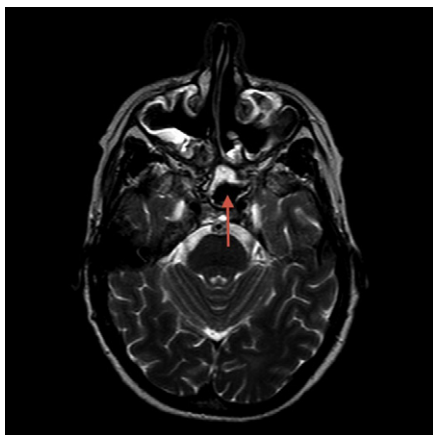


Figure 16. T2-weighted MRI with characteristic low-signal intensity clearly showing the presence of a fungal process.

signal) on T2-weighted images, not enhanced after injection of gadolinium chelates at the left sphenoid with a peripheral rim of high signal intensity on T1-weighted images and black (no signal) on T2-weighted images. The mucosa is thickened, enhanced by gadolinium, evidence of its inflammatory nature (Fig. 18, red arrow). It should be noted that there is no invasive aspect: no bone lysis or orbital or intracranial extension. The appearance is consistent with allergic fungal sinusitis based on the clinical context (atopic context) and the CT and MRI features of the sinus opacification (diffuse affected area, hyperdense mass, intrasinus low-intensity T2-weighted signal). The mycology and histopathology study confirmed the presence of *aspergillus* hyphae (fungal process, Fig. 19) and allergic mucin. The immuno-allergic mechanism was confirmed by the serum test for *Aspergillus fumigatus*-specific immunoglobulin E. The treatment was two-fold:

- medical with long-term administration of corticosteroid therapy and an oral antifungal agent;
- and surgical to decrease the local fungal antigen load and provide the best possible sinus drainage.

Clinical, laboratory, and CT follow-up was done every three to six months because of frequent recurrence.

Discussion

The real incidence of allergic fungal sinusitis is difficult to assess. It appears to represent up to 10% of surgical cases of chronic sinusitis [1,2]. The first cases were described in the early 1980s as a clinical and histopathological process similar to that of allergic bronchopulmonary aspergillosis based on retrospective studies [3]. While the diagnosis of fungus ball or fulminant invasive fungal sinusitis is standardized, allergic fungal rhinosinusitis (AFR) has been the subject of much discussion. The most likely physiopathologic hypothesis would be that of immune mechanisms. Chronic sinus inflammation, whether or not there is a predisposing anatomical factor, would lead to sinus blockage with allergic mucin formation and self-sustaining inflammation. The fungal agent plays an “antigenic” role with an IgE-dependent allergic reaction specific to the infectious agent, in this case *A. fumigatus*, a criterion necessary for making a diagnosis in our case. In fact, some authors [4] emphasize the doubt surrounding this AFR entity, which is increasingly reduced to cases of chronic rhinosinusitis with eosinophil-rich mucus in which there appears to be no specific interaction between the fungal agents present in the nasal mucus, but rather an undetermined inflammatory reaction. Other authors [5] rightly point out that the presence of multiple fungal agents is almost a constant in cases of chronic sinusitis, but also in healthy subjects, and that the presence of fungi in mucin does not necessarily mean they play a pathological role, even when associated with eosinophils.

The clinical presentation is generally of chronic sinusitis or rhinosinusitis, often with multiple surgeries, and in treatment failure. The most common clinical signs are nasal obstructions, purulent discharge, crust, presence of polyps, anosmia, and facial pain. Patients are generally young with no history of immunodeficiency, but most of them an atopic background with asthma, eczema, or allergic rhinitis.

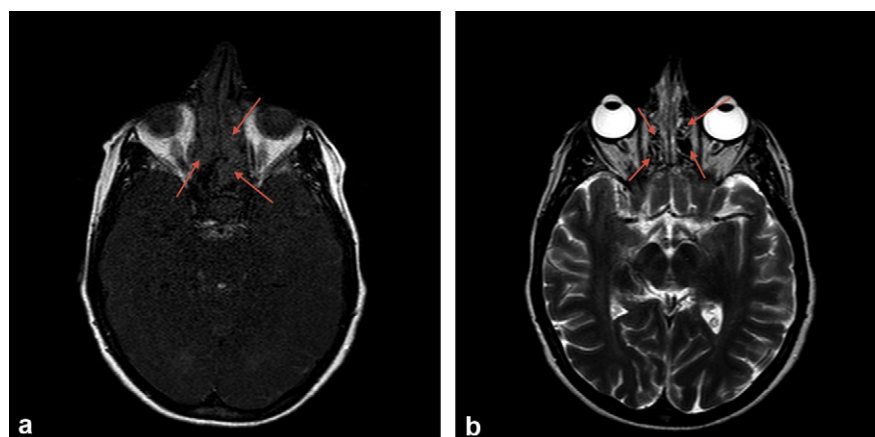


Figure 17. Diffuse ethmoid sinus opacification: a: high signal intensity in T1-weighted image and b: low signal intensity in T2-weighted image, confirming the diagnosis of allergic fungal sinusitis, suspected on the CT scan.

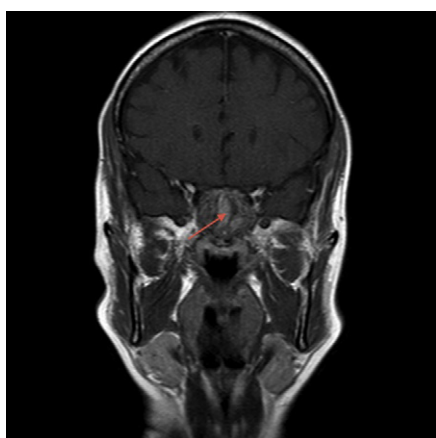


Figure 18. Coronal CT scan through the sphenoid sinuses, showing mucosal enhancement after injection of gadolinium, confirming the presence of sinusitis.

The diagnostic criteria for allergic fungal sinusitis (AFS) are still debated and often vary from author to author. In the reported case, we recognized the need for clinical, CT, histological, laboratory, immuno-allergic, and mycologic criteria in order to make sense of the terms “fungal *and* allergic” in agreement with the study by Braun JJ (2004) [6]. The main clinical criteria have been described above.

According to Manning [7], the CT scan and MRI are highly specific for AFS: somewhat hyperdense, heterogeneous sinus opacity, low intensity signal on T1-weighted images and very marked low intensity signal on T2-weighted images. According to Mukherji [8], the CT is suggestive but not specific. It should be noted that these old retrospective studies did not include immuno-allergic diagnostic criteria. The imaging turns out to be non-specific and may suggest the diagnosis depending on the clinical context: pansinusitis or polysinusitis, whether unilateral or bilateral, symmetrical or otherwise, sometimes with a pseudo-tumoral aspect, heterogeneous opacities with bone changes (rich in iron or calcium, high in protein, dehydrated) [9]. In other cases, the symptoms are more uncouth, with a fine fungal layer over

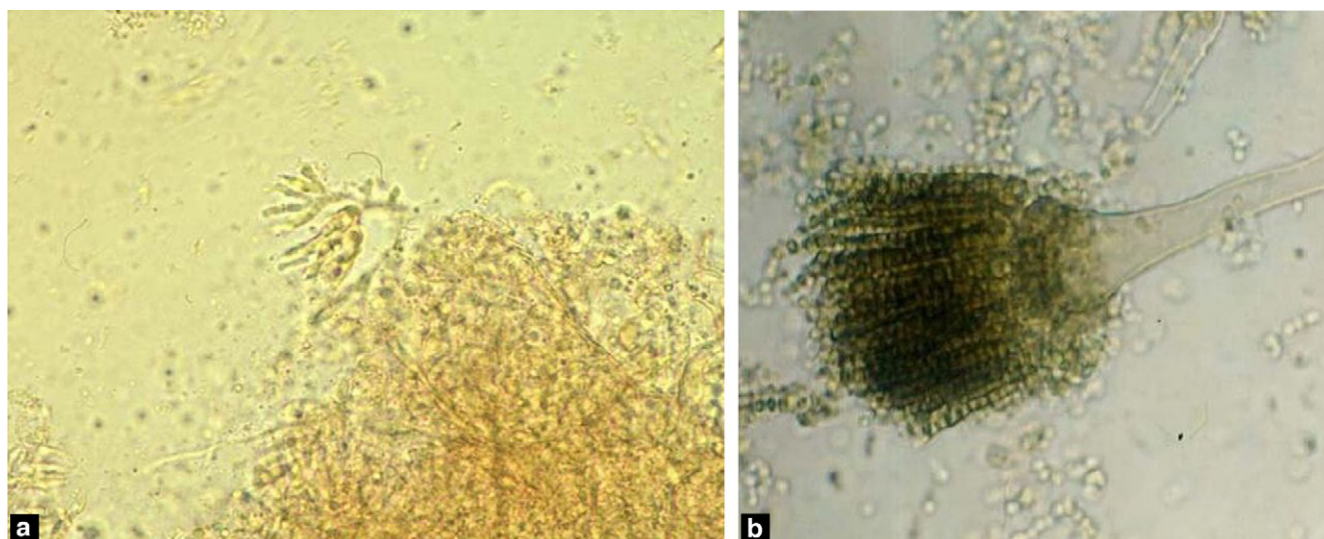


Figure 19. a and b: aspergillus mycelial filaments.

a hyperplastic mucosa not visualized on the CT scan. Some authors consider heterogeneous opacification of the sinuses a pathognomonic sign [10]. Bone changes are non-specific and more suggestive of the chronicity of the infectious process.

The histopathology criteria [6] are based on finding allergic mucin with eosinophils, Charcot-Leyden crystals and hyphae, and absence of tissue invasion.

The immuno-allergic workup [6] shows serum hyper-eosinophilia (to be interpreted relative to intercurrent corticosteroid therapy), an elevated total serum IgE level, positivity for specific IgE, and positive skin tests for the offending fungal agents.

Mycological testing of the mucin, with cultures (Sabouraud agar, Malt extract agar) and direct examination is also beneficial but should be compared with the clinical picture [6].

According to many authors, it is the weight of all of these criteria that make it possible to reach a diagnosis of AFS, but their validation requires large-scale studies in order to clarify and differentiate the many sinonasal conditions grouped under the umbrella term of AFR (eosinophilic fungal rhinosinusitis? eosinophilic mucin rhinosinusitis? mucoid fungal rhinosinusitis without allergy?).

The treatment, monitoring procedures, and expected results have not been clearly established for this disease. Treatment is essentially medical and surgical with the objective of endoscopically restoring mucociliary drainage, correcting the predisposing anatomical variations, and decreasing the fungal antigen load (allergic mucin) with oral corticosteroid therapy [1]. The order of the treatments remains to be determined, along with the routine use of a local or systemic antifungal (e.g., Amphotericin B, itraconazole, ketoconazole) [11]. Immunotherapy is also very much a matter of debate.

Since recurrences are common, there is a definite benefit to monitoring patients clinically, as well as with laboratory tests (specific IgE, aspergillosis serology), and even CT scans. But there is no clear consensus in the literature.

In conclusion, an article by Braun JJ (2007) [10] showed that, while nosological individualization of AFS is recent and has not been well standardized, that of allergic bronchopulmonary aspergillosis has been clearly defined; in light of the physiopathological relationship between these two

entities and the oneness of the respiratory tract, it is advantageous to systematically look for dual (both sinus and bronchopulmonary) involvement, which may be underestimated.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

- [1] Marple FM. Allergic fungal rhinosinusitis: current theories and management strategies. *Laryngoscope* 2001;111:1006–19.
- [2] Corey JP, Delsupehe KG, Ferguson BJ. Allergic fungal sinusitis: allergic, infectious, or both? *Otolaryngol Head Neck Surg* 1995;113(1):110–9.
- [3] Katzenstein AL, Sale SR, Greenberger PA. Allergic Aspergillus sinusitis: a newly recognized form of sinusitis. *J Allergy Clin Immunol* 1983;72:89–93.
- [4] Klossek JM, Dufour X, Rodier MH, Kauffman-Lacroix C. Est-ce que l'allergie rhinosinusienne fongique existe? *Rev Fr Allergol Immunol Clin* 2003;22:240–5.
- [5] Braun H, Buzina W, Freundenschuss K, Beham A, Stammberger H. Eosinophilic fungal rhino sinusitis: a common disorder in Europe? *Laryngoscope* 2003;113:264–9.
- [6] Braun JJ, Letscher-Bru, Gasser B, Gentine A. La sinusite fongique allergique (SFA). *Ann Otolaryngol Chir Cervicofac* 2004;121:167–74.
- [7] Manning SC, Merkel M, Kriesel K, Vuitch F, Marple B. Computed tomography and magnetic resonance diagnosis of allergic fungal Sinusitis. *Laryngoscope* 1997;107:170–6.
- [8] Mukherji SK, Figueroa RE, Ginsberg LE, Zeifer BA, Marple BF, Alley JG, et al. Allergic fungal sinusitis: CT findings. *Radiology* 1998;207:417–22.
- [9] Braun JJ, Riehm S, Veillon F. Intérêt de la tomodensitométrie dans la sinusite fongique allergique. *J Radiol* 2008;89:480–6.
- [10] Braun JJ, Pauli G, Schultz P, Gentine A, Ebbo D, de Blay F. Allergic fungal sinusitis associated with allergic bronchopulmonary aspergillosis: an uncommon sinobronchial allergic mycosis. *Am J Rhinol* 2007;21:412–6.
- [11] Ferguson BJ. What role do systemic corticosteroids, immunotherapy and antifungal drugs play in the therapy of allergic fungal rhinosinusitis? *Arch Otolaryngol Head Neck Surg* 1998;124:1174–7.