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Reply to "Thoracic conidiobolomycosis: Invasive or allergic?"



To the Editor:

We thank Muthu and Agarwal¹ for their interest in our report.² In our view, the report illustrates the blurred boundaries between infection and allergic responses to fungal pathogens and a potential role for adjunctive targeted immunotherapy in the multimodal management of complicated cases refractory to conventional approaches.

Muthu and Agarwal question whether the primary pathologic process was an allergic reaction with bronchocentric granulomatosis rather than invasive fungal infection. In our patient, baseline computerized tomography imaging of the chest showed a mediastinal mass encasing the pulmonary vessels and causing extrinsic compression of the right main bronchus (Figure 1). The location and scale of the lesion can also be appreciated from the initial fluorodeoxyglucose positron emission tomography/magnetic resonance imaging panel in our report. Fungal hyphae with surrounding eosinophilic inflammatory material (Splendore-Hoeppli phenomena) were apparent on histopathological examination of a biopsy sample, and *Conidiobolus incongruus* was identified by culture. Fluid collected at the same time by bronchoalveolar lavage was culture negative. These features match previously reported cases of invasive mediastinal conidiobolomycosis.^{3,4}

Muthu and Agarwal also highlight that glucocorticoids may be detrimental in the setting of invasive fungal infection. Corticosteroid use is indeed associated with increased susceptibility to fungal and other infections.⁵ However, there are a myriad of examples for the use of corticosteroids in an attempt to control a disproportionate and dangerous inflammatory response to invasive infection, including with fungi. Steroids are routinely used for *Pneumocystis jiroveci* pneumonia in patients with HIV⁶ and



FIGURE 1. Computed tomography of the chest at baseline showing a right-sided mediastinal mass with compression of right main bronchus and branches.

for cryptococcal meningitis complicated by immune reconstitution inflammatory syndrome.⁷ For conidiobolomycosis specifically, proliferation of Th2 lymphocyte subsets during invasive infection is well described and may be a pathogen-directed survival mechanism.⁴ In a previous case of an adolescent with disseminated conidiobolomycosis, also associated with characteristic histopathological eosinophilic inflammation, clinical and radiological response occurred after administration of corticosteroids.³

In our report, we postulated that the benefits of corticosteroid therapy were counterbalanced by suppression of Th1, Th17, and innate immune responses, preventing clearance of the fungal infection. Cure coincided with initiation of more selective immunotherapy (mepolizumab) and gradual withdrawal of steroid therapy. A recently reported case of dupilumab immunotherapy in the successful treatment of a child with refractory disseminated coccidioidomycosis adds further weight to our position that targeted immunotherapy may be beneficial in selected cases of invasive fungal infection.⁸

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Current approach to the diagnosis of allergic bronchopulmonary aspergillosis



To the Editor:

We read the work of Saxena et al¹ with great interest. In this study, the authors aimed to compare the diagnostic performance of various criteria used for evaluating allergic bronchopulmonary aspergillosis (ABPA) and found that the International Society for Human and Animal Mycology (ISHAM) criteria were only marginally better than the Rosenberg-Patterson criteria to identify ABPA in patients diagnosed with asthma. They also improved the sensitivity of the ISHAM criteria by modifying it. We thank the authors for working on a subject for which data are lacking in the literature.

In this study, the authors reported that, of the 543 subjects, 338 (62.2%) were mild-to-moderate asthma and 205 (37.8%) were severe asthma cases. However, the data regarding the percentage of the severe asthma cases in patients with ABPA, diagnosed separately with the ISHAM and Rosenberg criteria, were missing. We believe that this information is important to answer the questions: (1) Is ABPA only seen in severe asthmatics? (2) In what proportion of patients with mild-to-moderate asthma should we expect ABPA? Providing the percentage of severe asthma cases in both diagnostic criteria separately might guide and alert clinicians to diagnose ABPA in their daily clinical practice.

Another important point we want to draw attention is that the low sensitivity of the ELISA method used to detect *Aspergillus fumigatus*-specific IgG and the lack of a consensus on the definite cutoff value lead to a discussion on the need for this parameter in ABPA diagnosis.² This is also valid for *Aspergillus* precipitating antibody tests. In-house precipitin assays with poorly defined antigens have been prepared by various specialist laboratories for this purpose, but their replication in other laboratories is inconsistent.³ It is therefore not possible to use them in resource-poor facilities, and specialist mycology laboratories are few.⁴ The results with precipitins were deficient in this study, similar to an earlier one.⁵ The technique is also manual

and time-consuming, the results are subjective, and reliable replication is difficult.⁶

We believe that it is necessary to discuss and re-evaluate the necessity of *A. fumigatus* precipitating antibodies and specific IgG positivity and be flexible with the current diagnostic criteria, especially in patients with radiological findings that are consistent with ABPA with elevated total IgE levels.

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Reply to "Current approach to the diagnosis of allergic bronchopulmonary aspergillosis"



To the Editor:

We thank Türk et al¹ for the interest shown in our article.² Regarding their first question, the prevalence of allergic bronchopulmonary aspergillosis (ABPA) in our study was 19.6% (106 of 542) as assessed by a multidisciplinary team (MDT). We classified our asthmatic subjects as mild-to-moderate (mild intermittent, mild persistent, and moderate persistent) and severe (comprising severe persistent), according to the 2004 Global Initiative for Asthma guidelines.³ The prevalence of ABPA was not statistically different in the 2 categories of asthma with either the Rosenberg-Patterson, International Society for Human and Animal Mycology (ISHAM) ABPA working group, modified ISHAM ABPA working group criteria, or ABPA diagnosed by an MDT evaluation (Table I). We have also previously shown