

The Different Clinical Expressions of the Aspergillus/Host Interactions in Humans

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Abstract

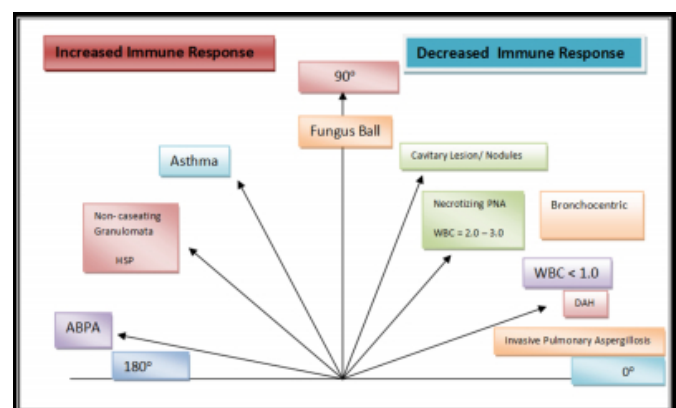
Aspergillus is very ubiquitous. It is a highly aerobic fungus and found as mold on surfaces. It spreads most commonly through spores in the air that are not detected with the naked eye. These spores get into the respiratory tract where they colonize and often cause different kinds of reactions. Human beings respond to these inhalations in several ways depending upon the status of one's immune system. In fact some of these responses are diametrically opposed from each other to the point that we decided to report our experience of the different expressions of the Aspergillus/human interaction in a spectral fashion. We have represented these findings in a parabola pictured below where to the right of the parabola from 0° to 90°, we included the interactions of Aspergillus with an immune deficient host, and to the left of the parabola from 90° to 180°, we considered the interactions of Aspergillus with a host of a hyperergic immune system.

INTRODUCTION

Aspergillus is very ubiquitous. It is a highly aerobic fungus and found as mold on surfaces. It spreads most commonly through spores in the air that are not detected with the naked eye. These spores get into the respiratory tract where they colonize and often cause different kinds of reactions. Human beings respond to these inhalations in several ways depending upon the status of one's immune system. In fact some of these responses are diametrically opposed from each other to the point that we decided to report our experience of the different expressions of the Aspergillus/human interaction in a spectral fashion. We have represented these findings in a parabola pictured below where to the right of the parabola from 0° to 90°, we included the interactions of Aspergillus with an immune deficient host, and to the left of the parabola from 90° to 180°, we considered the interactions of Aspergillus with a host of a hyperergic immune system.

Parabola:

Figure 1



COMMENTARY

Starting at the 0° line, patients who are severely neutropenic develop invasive pulmonary aspergillosis sometimes expressed as diffuse alveolar hemorrhage (DAH) and causing widespread hematogenous dissemination involving the heart valves, brain, and kidneys (1). These patients are usually neutropenic with an absolute neutrophilic count of 100 or less. A patient who remains neutropenic at this level for one week, has a 50% chance to develop aspergillosis (2,5,6,9). Once the immune system is partially reconstituted and the absolute neutrophil count is around 1,000, we tend to see necrotizing pneumonias (PNA) and/or bronchocentric implantations as reactions to the inhalation of aspergillus (7). By the time the absolute neutrophil count is around 2-3,000

we see cavitating nodules as a result of better confinement of the infection but with preservation of destructive properties of the aspergillus causing these lesions. In this side of the spectrum, we also find the patients who had undergone bone marrow transplantation, more so if they have graft vs. host disease and require immunosuppressant therapy. The therapeutic options include intravenous voriconazole 6mg/kg every 12 hours for 1 day, followed by 4 mg/kg every 12 hours until improvement, followed by oral voriconazole 200 mg every 12 hours or oral itraconazole 400-600 mg/day until resolution or stabilization of all clinical and radiographic manifestations or intravenous liposomal amphotericin B 3-5 mg/kg/day until improvement, followed by oral voriconazole 200 mg every 12 hours or itraconazole 400-600 mg/day until resolution or stabilization of all clinical and radiographic manifestation (7).

At the straight 90 ° angle is where we see the classic fungus ball pattern of Aspergillosis or Aspergilloma trying to live in a symbiotic environment not causing further destruction but living in previously formed cavities. However aspergillus occasionally may cause erosions and bleeding in these cavitary lesions. Consequently, patients then present with hemoptysis which might be massive in which case bronchial artery embolization and even surgical resection may be considered. The cavities usually result from preexisting tuberculosis, bronchiectasis, old infarcts or abscesses (5).

Moving counterclockwise to the left from 90 ° we enter the zone of increased immune response to the Aspergillosis inhalation. When the host is immunocompetent, the inhalation of Aspergillus could cause bronchitis with consequent bronchospasm and eventually leading to the development of asthma. Patients develop an allergic or hypersensitivity reaction to the spores of Aspergillus due to the antibodies producing a type I acute hypersensitivity reaction with the release of immunoglobulin E (IgE). Immune complexes and inflammatory cells are then deposited within the bronchial mucosa. This deposition produces tissue necrosis and eosinophilic infiltrate, a type III reaction, and results in damage to the bronchial wall (3). The body's reaction to this is to mount an immune response towards the Aspergillus species. The following inhalations provoke an asthmatic response with bronchospasm and airway inflammation.

When the inhalation is chronic and in small loads, the lymphocytic response that it triggers will eventually chemoattract macrophages that will lead to the formation of non-caseating granulomata, a phenomena which is the

pathological expression of hypersensitivity pneumonitis (HSP), also called extrinsic allergic alveolitis. This may be treated with simple avoidance of exposure and there is no need of antifungal therapy.

The most exaggerated response is seen when the inhalation of aspergillus triggers a major eosinophilic response with the development of bronchoconstriction, mucus plugging, severe inflammation that leads to bronchitis and bronchiectasis. This is known as Allergic Bronchopulmonary Aspergillosis (ABPA) in whom there is significant peripheral eosinophilia and elevated IgE and only responds to high dose corticosteroids (4).

In addition to all aforementioned, it is possible to find a combination of these different clinical expressions, such as a Bronchocentric Aspergillosis in the immunosuppressed side of the spectrum having an asthmatic response, and the reverse case, an ABPA patient in the hyperergic immune response side of the spectrum having a Necrotizing pneumonia or Bronchocentric Aspergillosis.

CONCLUSIONS

In order to understand what is happening in an aspergillus/human being interaction, it is imperative to know the absolute neutrophil count and the bone marrow function, the preexisting structural and functional abnormalities of the lung, the status of the immunoreactivity before the interaction (bronchial hyperreactivity, eosinophilia, Ig E levels) and during the interaction: B-cell immunity (antibodies, other gammaglobulin levels, corticosteroid use, etc.) and T-cell immunity (HIV status, CD4 count, skin tests, etc.), and the history and stage of the bone marrow transplantation.

Finally, another important message is that aspergillus is very difficult to retrieve from sputum, tracheal aspirates, bronchial washings, bronchial washings, bronchial biopsies, or bronchoalveolar lavage (5,6), consequently it is of utmost important to keep a high index suspicion and use all the technology (11) you have available to identify its presence as early as possible because when advanced it is very difficult to eradicate.

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