Bölüm 1

ASPERGILLOMA

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Introduction

Aspergillosis is an infection caused by Aspergillus fungi, which are common in our environment (1,3). Recently, the increase in the quality and diversity of health care services, the increase in accessibility to health care services, and the developments in diagnostic methods and treatments have led to an increase in the number of people with chronic diseases or weakened immune systems. As a result, the incidence of aspergillosis infections has increased.

Aspergillosis has three main clinical conditions: allergic bronchopulmonary aspergillosis, pulmonary aspergilloma, and invasive aspergillosis. The most common form caused by Aspergillus is aspergilloma (4,5). The chapter focuses more on aspergillomas.

Etiology

Transmission of infection occurs by inhalation of spores in the air (6). They primarily cause disease in the respiratory system (1). Infection can occur in lung parenchyma as well as in the bronchial and pleural spaces (7). Low virulence of fungal spores (8) and mucociliary activity reduce transmission (9). Person-to-person transmission is not expected.

Although the most common infectious agent in aetiology is A. Fumigatus (2,9,10), types such as A.Niger, A. Flavus, A. Terreus are also encountered (6).

Especially patients are at risk for infection who have the low immune system (acquired or spontaneously immunosuppressed, low white blood cell level) or have underlying respiratory system disease (asthma, COPD, bronchiectasis, bullous emphysema or cystic fibrosis) or have an anatomical cavity in the lung (caused by tuberculosis, sarcoidosis, bronchogenic cyst, abscess, malignancy) (9,11,13). Other risk factors are to have a viral disease that damages the respiratory epithelium, such as influenza or Covid-19 infection or have systemic diseases such as diabetes or malignancy such as leukaemia-lymphoma, or using corticosteroids (9,11,13).

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The majority of Aspergillus species cannot easily infect people with a properly functioning immune system (7).

Diagnosis

Clinical symptoms are similar to many diseases. For this reason, diagnostic tests gain importance. Studies from blood, body fluids, sputum and bronchoscopic lavage samples and radiological imaging are important non-invasive methods in diagnosis (2). The most important guide is radiological (X-ray or CT) examinations (10). From time to time, histopathological samples can be taken from suspicious tissue by methods such as transthoracic biopsy to obtain a diagnosis. In fact, it has been reported in some studies that thoracotomy was performed for both diagnostic and therapeutic purposes since the diagnosis could not be made with these methods (14).

Aspergilloma has a typical appearance on radiological imaging; is observed as an oval radiopaque solid mass in the cavity of the lung parenchyma (13). (Figure 1)

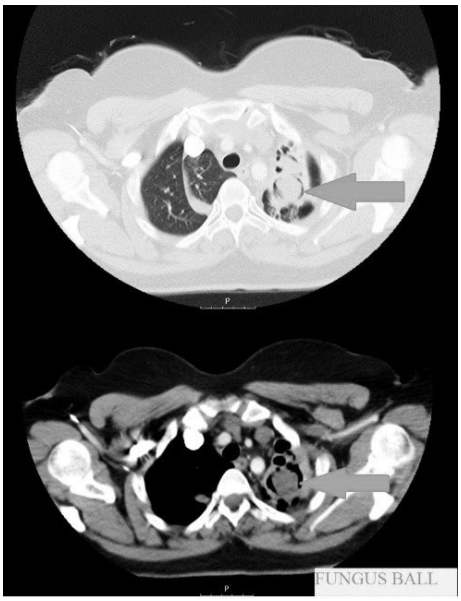

Figure 1. Aspergilloma

The air observed on the fungus ball in the cavity is called the 'air-crescent' sign. (9,13). Another feature of the fungus ball is displacement in the cavity with the change body position (9,13,15). Tuberculosis (Rasmussen aneurysm), echinococ, lung abscess should be kept in mind in the differential diagnosis of radiological imaging. In addition, the absence of a fungal ball in the cavity does not definitively exclude aspergillus infection, as it may not be visible in the early period (9,13).

For diagnosis galactomannan, beta-D-glucan, IgG can be studied from blood serum samples, and special staining, culture, DNA detection of fungus (by PCR) can be done from bronchial lavage samples (1,9,16). Detection of aspergillus in sputum does not mean definitive diagnosis. Histopathological sampling is definitive diagnosis (17).

Clinic

The allergic type occurs due to the reaction to the fungus directly (Type 1 and Type 3 hypersensitivity) in people with underlying allergic respiratory disease (3). Those with asthma and cystic fibrosis are more affected (3). 1-2% of asthmatic patients are affected (9). While patients may be asymptomatic, symptomatic patients may have fever, cough, coughing up blood-mucus plugs, weight loss, night sweats, and exacerbated asthma (3,8,9). An increase in IgE antibody is observed in the blood serum. Central bronchiectasis and fibrosis secondary to infection may be observed over time (4). As can be seen, the symptoms of the disease are atypical, so the diagnosis can be easily missed.

The most complicated form of aspergillosis is invasive aspergillosis. It usually occurs in immunosuppressed individuals (16). In addition to the lungs, it can quickly affect many organs (eg brain, eye, bone) (6). Apart from main symptoms (dyspnea, fever, hemoptysis, headache), may also be seen depending on the condition of the organs involved such as joint pain, visual disturbances and skin lesions.

Aspergilloma is the seen of fungal balls, which consist of fungal fibres that colonize without invasion the cavities formed in the parenchyma, often in emphysematous lung diseases (5,10). Components of aspergillus are fungal fibres, inflammatory cells, fibrin, mucus and tissue debris (4,5). Some lesions may heal spontaneously, while others may heal by scarring (2). Aspergillomas may remain stable for a long time (3,5), may regress in 10% of cases (9,13), while some lesions may increase in size (5). The incidence is reported to be 1-17% in cavitary pulmonary lesions (2,10). It is most commonly observed in cavities caused by tuberculosis (2,10,14,17) In one study, aspergillomas were detected in 11% of tuberculosis cavities in radiological imaging (5). Because of the cavities are often in the upper lobes, they are usually observed in the upper lobes of the lungs (10). While it may not cause any symptoms (4,13), it may cause shortness of breath, wheezing, weakness, and hemoptysis. It is often asymptomatic (5), hemoptysis (50-83%) is the most common (15) and cough is the second most common symptom (3,10,14,17). Hemoptysis can be caused by the vascular invasion, toxin or mechanical irritation, and the risk of developing hemoptysis is higher in aspergillomas formed on the basis of tuberculosis (5). Hemoptysis is the most obvious influencing factor in the choice of treatment

method. It can cause hemoptysis with a high level of fatality (up to 25%) (7,8,14). 14-28% of deaths from aspergillus are due to hemoptysis (5,14).

Treatment

The main treatment strategies are prevention (avoiding exposure-prophylaxis), follow-up, medical treatment, vascular-intracavitary interventions (embolization, injection) or surgery.

It is recommended that risk groups stay away from places where the fungal load can be high, as it is almost impossible to prevent exposure. Prophylaxis can be applied in risky groups such as neutropenic patients (16). However, there are almost no studies demonstrating as the satisfactory efficacy of prophylaxis.

There is no definitive treatment algorithm in allergic bronchopulmonary aspergillosis. Treatment is basically medical. Antifungal therapy and steroid therapy are thought to be effective in acute attacks (1,3) In addition, symptomatic treatment can be applied for the symptoms encountered. In cases such as atelectasis, methods such as bronchoscopy can be used. Since the mortality of invasive aspergillosis is high, it is recommended to start treatment without waiting for the diagnosis, especially if there is clinical suspicion in immunosuppressive patients (1). Empirical treatment should be started as soon as possible. Although amphotericin B is a good initial option, itraconazole should be kept in mind as an alternative if there is a medical condition that may constitute a contraindication (1) Surgical intervention, frequent debridement, systemic antifungal and symptomatic treatment of the affected system should be performed.

Aspergilloma does not have a clear treatment algorithm accepted by all authorities (2). The main treatment strategy should be to remove the fungus ball and to prevent complications that may occur whether it is removed or not, thus ensuring a better prognosis. For this purpose, follow-up, medical treatment, vascular-intracavitary interventions or surgery can be performed. While follow-up is recommended for single lesions that do not cause respiratory system symptoms and are stable in size for up to 2 years, resection is recommended for single lesions with symptoms such as hemoptysis (3,16). For asymptomatic cases, some authors suggest operation because of preventing future complications in the patient's medical condition and avoiding an operation to be performed in emergency conditions (14). Since the perfusion of the cavity is not good, efficacy should not be expected from medical treatment or intracavitary applications alone (1,15). In the control of hemoptysis, the success chance of embolization alone is not very high (40-50%), recurrence is expected in hemoptysis (8). But in massive hemoptysis, it can be beneficial in terms of reducing bleeding and gaining time until the operation (17). In addition, in mild

hemoptysis conditions, blood pressure control, review of the anticoagulant-aggregate order, tranexamic acid, bed head elevation, the sedative application can be applied if there is agitation, in order to save time until the operation. Surgical resection is the most effective treatment for aspergilloma cases (13,17,18). Surgical treatment is generally curative and provides nearly complete 5-year survival (3). Surgical treatment is most commonly performed for massive hemoptysis (14,17). The timing of the operation is important (7,8,15), but the progression is slow in patients with a single lesion, and therefore, there is no need to make a sudden surgical decision if there is no symptom such as hemoptysis (16). Although lobectomy is frequently preferred in surgical treatment (14), sublobar resections such as wedge resection or segmentectomy or cavernomyoplasty can be performed in patients with inadequate respiratory functions (7,8,17). The expected morbidity rate after surgery can be high (20-30%) (8). The main complications that can be encountered after surgery are bleeding, bronchopleural fistula, wound infection, empyema, prolonged air leakage, expansion defect, respiratory failure, massive hemorrhage (3,18). Complications rates are higher in those with multiple lesions.(18) Nutritional support and keeping the underlying lung disease under control before surgery can contribute positively to this situation (1,18). Mortality after surgical treatment is between 0-34% (8). The most common cause of mortality after surgery is underlying lung disease (5). If a single lesion is completely resected antifungal therapy is not required in the postoperative follow-up and follow-up is not recommended unless there is an underlying lung disease, but if complete resection has not been performed it should be followed closely for antifungal therapy at 3-month intervals (18). If the thorax is contaminated during the operation, using voriconazole or echinocandin is recommended for the prevention of empyema, and radiological follow-up and IgG follow-up are recommended for 3 years (16). If the person has 2 separate aspergillomas and the respiratory reserve is sufficient, it is recommended to remove both with anatomical resection (16). Although recurrence is expected at a low rate after surgery (3), there are also studies reporting a high relapse rate of up to 25% (16). Antifungal treatment is recommended in patients with multiple nodules if all of the nodules cannot be removed, and malignancy should not be overlooked if there is an increase in size in other nodules in the radiological follow-up (18).

Prognosis

The prognosis of aspergillus is closely related to the underlying lung disease, general medical condition and medical history (7,9). The mortality rate is high in neutropenic patients (40-80%), and relapse is reported at a rate of 14% after treatment (2,15). Mortality can reach 60% in patients with invasive aspergillosis with lung

transplantation (6). The expected 5-year mortality rate in patients with chronic aspergillosis is 50-60% (3). It has important effects on the prognosis in concomitant infections. For example, in a recent study, it was reported that a 19-44% increase in mortality was observed in the first 30 days in patients with covid-associated aspergillosis (12).

In aspergilloma, the number of lesions, increase in the size of the lesions, increased IgG levels are other important factors affecting the prognosis, apart from the course of hemoptysis and general medical condition (5). 10-year survival for single-lesion aspergilloma is 69-90%, while it is 63-80% for those with multiple-cavity lesions (18).

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