

Surgical Aspects of Pulmonary Aspergillosis: Personal Experience, Clinical Case

Opanasenko MS*, Konik BM, Shamrai MY, OV Tereshkovich, VI Lysenko, OD Shestakova, BN Konik, LI Levanda, MI Kalinichenko, SM Shalagai, OV SM Bilokon and AN Stepaniuk

State Institution "National Institute of Phthiology and Pulmonology Named After F. G. Yanovsky NAMS of Ukraine", Ukraine

***Corresponding Author:** Opanasenko MS, State Institution "National Institute of Phthiology and Pulmonology Named After F. G. Yanovsky NAMS of Ukraine", Ukraine.

Received: June 05, 2023; **Published:** July 20, 2023

Abstract

Aspergillosis is the second most common fungal infection after candidiasis. The causative agents of the infection (*Aspergillus*) are widely distributed worldwide and can be found everywhere in the environment. They can be constantly found in soil, grains, flour, hay (especially moldy), on building materials, in building ventilation systems, in indoor dust where skin, wool, and yarn are processed. *Aspergillus* can even be found in the dust of healthcare facilities, which can lead to nosocomial infection.

The main manifestation of aspergilloma is recurrent hemoptysis (diagnosed in 70 - 80% of cases). In 20 - 25% of cases, hemoptysis can be life-threatening due to the progression to massive pulmonary hemorrhage. The ability of *Aspergillus* to secrete toxins that cause erosion of the vessel wall and interfere with clot formation is the cause of hemoptysis. Even after radical removal of the aspergilloma, there is an increased risk of bleeding in the first 2 days postoperatively.

Over the past 15 years, 24 patients with pulmonary aspergillosis were treated in the Department of Thoracic Surgery and Invasive Diagnostic Methods at the National Institute of Phthiology and Pulmonology named after F.G. Yanovsky of the National Academy of Medical Sciences of Ukraine. In 18 (75.0%) cases, pulmonary aspergilloma was diagnosed; in 1 (4.2%) patient, aspergilloma of the residual pleural cavity developed, and in 5 (20.8%) patients, invasive aspergillosis was diagnosed after video-assisted thoracoscopic lung biopsy.

VATS lung biopsy was performed in 5 (20.8%) patients. Based on the results of histological and microbiological examinations, the diagnosis of invasive aspergillosis was established in 4 (16.7%) cases, and 1 (4.2%) patient was diagnosed with drug-resistant pulmonary tuberculosis in combination with invasive aspergillosis. The main indications for lung biopsy in these patients were atypical disease course with persistent resistance to conservative therapy, including antifungal agents for aspergillosis. The postoperative period was uneventful in 4 (16.7%) patients, while 1 (4.2%) patient died 2 weeks after the operation due to progressive invasive aspergillosis with the development of bronchopleural fistula and *Aspergillus* empyema of the pleura. The underlying condition for the development of aspergillosis in this patient was primary immunodeficiency.

Surgical treatment is the preferred method for managing pulmonary aspergilloma and achieves an overall treatment effectiveness of 93.3%. The administration of antifungal medications before and after surgery is a mandatory requirement for effective treatment of pulmonary aspergilloma. The issue of pulmonary aspergillosis is far from resolved, and therefore, effective communication among physicians of different specialties will contribute to its gradual resolution.

Keywords: *Pulmonary Aspergillosis; Video-Assisted Thoracoscopic Lung Biopsy; Hemoptysis*

Introduction

Aspergillosis is the second most common fungal infection after candidiasis. The causative agents of the infection (*Aspergillus*) are widely distributed worldwide and can be found everywhere in the environment. They can be constantly found in soil, grains, flour, hay (especially moldy), on building materials, in building ventilation systems, in indoor dust where skin, wool, and yarn are processed. *Aspergillus* can even be found in the dust of healthcare facilities, which can lead to nosocomial infection.

Pulmonary aspergillosis is a disease that occurs as a result of colonization of lung tissue by fungi of the genus *Aspergillus fumigatus*. The causative agents of the infection are widely distributed in the environment, and their spores can colonize the mucous membrane of the respiratory tract, paranasal sinuses, and, due to their small size (2.5 - 3.0 μm), reach the alveoli. Despite the ubiquitous presence of *Aspergillus*, immunocompetent individuals do not get sick. The development of the pathological process requires a combination of complex conditions and causes: a high infecting dose, asymptomatic carriage, decreased immunity due to antibacterial or immunosuppressive therapy, the presence of long-standing cavities in the lungs, etc. The main group of individuals affected by pulmonary aspergillosis consists of patients with pulmonary tuberculosis and individuals with compromised immune status.

There are four clinical forms of pulmonary aspergillosis: chronic necrotizing aspergillosis, allergic bronchopulmonary aspergillosis, invasive aspergillosis, and aspergilloma. Surgeons are particularly interested in the last two forms. Sometimes, the diagnosis of invasive aspergillosis is challenging for surgeons the necessary procedure for diagnosing pulmonary aspergillosis is lung biopsy. In cases of aspergilloma, radical treatment involves resectional interventions.

An aspergilloma develops as a result of colonization of the tuberculous cavity by spores of the fungus (most commonly *Aspergillus fumigatus*). It can also form in bronchiectatic changes of non-tuberculous etiology, chronic abscesses, cysts, bullae, within a necrotic tumor nodule, and even in the pleural cavity.

The diagnosis of aspergilloma includes the following aspects:

- Medical history
- Chest X-ray and computed tomography of the chest
- Serological testing (to determine galactomannan in bronchoalveolar lavage fluid and serum)
- Bronchoscopy
- Biopsy of the affected lesions
- Microscopy and culture of sputum, nasal secretions, and biopsy material.

The main manifestation of aspergilloma is recurrent hemoptysis (diagnosed in 70 - 80% of cases). In 20 - 25% of cases, hemoptysis can be life-threatening due to the progression to massive pulmonary hemorrhage. The ability of *Aspergillus* to secrete toxins that cause erosion of the vessel wall and interfere with clot formation is the cause of hemoptysis. Even after radical removal of the aspergilloma, there is an increased risk of bleeding in the first 2 days postoperatively.

On computed tomography of the chest, an aspergilloma appears as a round ball within the cavity. Since its main mass is often separated from the cavity contours by air space, the so-called "air crescent" sign (Monod sign) is formed (Figure 1).

Aspergillomas are classified into simple and complex forms. In complex aspergilloma, there is a pronounced clinical symptomatology, significant pericavitary infiltrates are detected on X-ray, and the development of new or enlargement of existing destructive cavities occurs. The course of aspergilloma can be complicated by the development of necrotizing aspergillosis (Figure 2). Simple aspergilloma is characterized by an asymptomatic course.

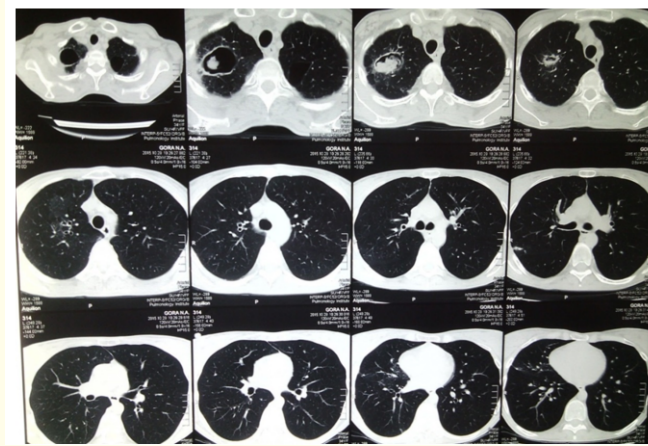


Figure 1: Radiological signs of pulmonary aspergilloma (Monod sign).

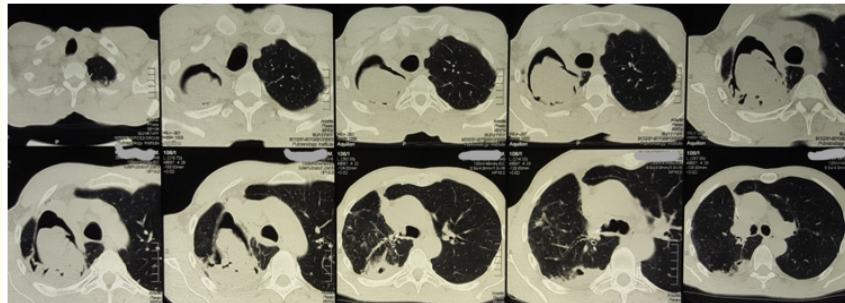


Figure 2: Radiological signs of aspergilloma complicated by necrotizing aspergillosis.

The following medications are used for the treatment of aspergillosis, including aspergilloma: itraconazole, voriconazole, amphotericin B, and caspofungin. Microbiological testing with sensitivity testing to the main antifungal agents is necessary for adequate therapy. In some cases, combination therapy with these medications may be necessary. As for aspergilloma, there are two radically different approaches to treatment: expectant management (no surgery is performed in asymptomatic cases) and active management (surgery is indicated for all patients diagnosed with aspergilloma in the absence of contraindications).

Aim of the Study

The aim of this study is to present our own experience in surgical treatment of aspergilloma due to the uncertainty regarding treatment methods and timing for patients with this condition.

Materials and Methods

Over the past 15 years, 24 patients with pulmonary aspergillosis were treated in the Department of Thoracic Surgery and Invasive Diagnostic Methods at the National Institute of Phthiology and Pulmonology named after F.G. Yanovsky of the National Academy of Medical Sciences of Ukraine. In 18 (75.0%) cases, pulmonary aspergilloma was diagnosed; in 1 (4.2%) patient, aspergilloma of the residual pleural cavity developed, and in 5 (20.8%) patients, invasive aspergillosis was diagnosed after video-assisted thoracoscopic lung biopsy.

The background for the development of aspergilloma was tuberculosis or post-tuberculosis changes in 14 (77.8%) cases, bronchiectasis in 2 (11.1%) patients (one of whom also had primary immunodeficiency), aspergilloma within a malignant tumor with necrosis in 1 (5.6%) case, bullous lung disease in 1 (5.6%) case, and aspergilloma in the residual pleural cavity after right upper lobectomy in 1 (5.6%) patient. The duration of the underlying disease before surgery ranged from 2 months to 16 years.

Different resectional procedures were performed in 14 (77.8%) patients with aspergilloma, while 4 (22.2%) patients were deemed unfit for surgery after further examination due to significant ventilation impairments (3 cases, 16.7%) or severe cardiovascular pathology (1 case, 5.6%). One (5.6%) patient with aspergilloma of the residual pleural cavity underwent primary extrapleural thoracoplasty as a second stage after video-assisted thoracoscopy.

The main characteristics of the patients who underwent surgical interventions for aspergilloma are presented in table 1. The number of male and female patients was approximately equal: 8 (52.8%) and 7 (46.2%) respectively. The mean age of the operated patients was (47.47 ± 13.94) years. Aspergilloma manifested as recurrent hemoptysis in 8 (52.8%) cases, which was the main reason for surgical treatment. The level of comorbidities was 80.0%.

No	Characteristics					
	Gender	Age,p	Hemoptysis	Background disease	Duration of background disease, months	Associated pathology
1	M	53	Yes	TB	108	Behcet’s disease
2	F	34	Yes	TB	2	Chronic pancreatitis
3	F	18	No	TB	4	-
4	M	59	Yes	RCPT	60	Hepatitis C
5	M	32	Yes	TB	48	COPD
6	M	62	Yes	RCPT	120	COPD
7	M	35	No	TB	36	Chronic alcoholism
8	M	57	Yes	TB	45	Hepatitis C
9	F	48	Yes	RCPT	24	COPD
10	M	56	No	TB	16	Hepatitis B
11	M	58	Yes	RPL	115	COPD
12	M	49	No	MT	2	COPD
13	F	61	Yes	BE	384	HD
14	F	63	Yes	BZD	24	-
15	F	33	No	BZD	24	Primary immunodeficiency

Table 1: Main characteristics of operated patients.

Notes: M: Male; F: Female; TB: Tuberculosis; RPTB: Residual Changes of Previous Tuberculosis; MP: Malignant Tumor; RPP: Residual Pleural Cavity; BE: Bronchiectasis; COPD: Chronic Obstructive Pulmonary Disease; HTN: Hypertension; BZD: Bullous Disease.

Results and Discussion

VATS lung biopsy was performed in 5 (20.8%) patients. Based on the results of histological and microbiological examinations, the diagnosis of invasive aspergillosis was established in 4 (16.7%) cases, and 1 (4.2%) patient was diagnosed with drug-resistant pulmonary tuberculosis in combination with invasive aspergillosis. The main indications for lung biopsy in these patients were atypical disease course with persistent resistance to conservative therapy, including antifungal agents for aspergillosis. The postoperative period was uneventful in 4 (16.7%) patients, while 1 (4.2%) patient died 2 weeks after the operation due to progressive invasive aspergillosis with the development of bronchopleural fistula and *Aspergillus* empyema of the pleura. The underlying condition for the development of aspergillosis in this patient was primary immunodeficiency.

The main principles of surgical treatment for patients with aspergillosis were as follows:

- Performing anatomical lung resection (lobectomy or bilobectomy) or pneumonectomy (with the possibility of corrective thoracoplasty).
- Preoperative administration of antifungal agents (to achieve eradication of peri-cavitary invasive aspergillosis).
- Prolonged postoperative therapy using antifungal agents (3 - 6 months).
- Caution regarding the possibility of intraoperative and postoperative bleeding.

The main indicators of the performed surgical interventions and the postoperative period are presented in table 2.

No	Indicators					
	"Volume and side of resection	Duration, min	Blood loss, ml	Intraoperative complications	Postoperative complications	Duration of treatment, days
1	Left pleuropneumonectomy	320	1100	Damage to the left subclavian artery	Empyema of the pleura with bronchopleural fistula	36
2	Right lobectomy with thoracoplasty	240	310	-	-	30
3	VATS right pneumonectomy	300	150	-	Surgical wound infection	28
4	Left upper lobectomy	255	240	Cardiac arrest	Prolonged atelectasis of the operated lung	86
5	"Right pneumonectomy	320	340	-	-	30
6	Primary extrapleural 7 th rib thoracoplasty on the right side	200	600	-	-	45
7	Left-sided pleuropneumonectomy	180	200	-	Intrapleural hemorrhage	30
8	Primary extrapleural 7 th rib thoracoplasty on the left side	210	350	-	-	40
9	Upper lobectomy on the right side	120	130	-	-	18
10	Lower lobectomy on the right side	140	100	-	-	22
11	Primary thoracoplasty on the right side	220	600	-	-	103
12	Upper lobectomy on the right side with lymph node dissection	160	120	-	-	14
13	Resection of S6 on the right side	120	300	-	-	18
14	Upper lobectomy on the right side	120	50	-	-	14
15	Resection of the apex and S3 on the right side	170	200	-	Wound infection	25

Table 2: Indicators of surgical interventions and the postoperative period.

Analysis of table 2 allows us to conclude that the most common surgical procedure performed on patients with aspergillosis was lobectomy, accounting for 7 cases (46.2%). In one case, the resection was supplemented with corrective thoracoplasty, and in another case, it was combined with mediastinal lymph node dissection. Pneumonectomy was performed in 4 cases (26.4%) in the clinic for patients with aspergillosis. One patient (6.6%) underwent a video-assisted operation. Two patients (13.2%) underwent primary extrapleural 7-rib thoracoplasty (Figure 3). Additionally, one case each (6.7%) involved resection of the S3 pyramid on the right side and resection of S6 on the right side.

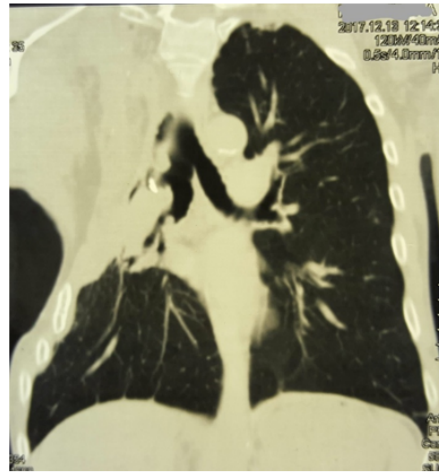


Figure 3: Shows the CT scan after primary extrapleural 7-rib thoracoplasty on the right side.

The average duration of the surgical intervention was (221.67 ± 62.201) minutes, and the average intraoperative blood loss was (318 ± 204.274) ml. The average duration of treatment in the postoperative period was (38.6 ± 20.899) days. The rate of intraoperative complications was 13.3%, while postoperative complications occurred in 33.3% of cases.

One patient (6.7%) was discharged with a drainage tube due to the development of chronic empyema of the left pleural cavity with bronchopleural fistula. The overall effectiveness of surgical treatment for patients with aspergillosis was 93.3%.

It is considered that the risk of postoperative complications in aspergillosis is very high, ranging from 25% to 56.7%. Typical postoperative complications include intrapleural bleeding, prolonged air leak, residual empyema of the pleural cavity with bronchopleural fistula, and frequently observed cardiogenic disorders in the postoperative period. The postoperative mortality rate reaches 23%.

C. Jiang reports on 100 cases of pulmonary aspergillosis, where 60.2% of patients had a complicated course of the disease, and 72% experienced hemoptysis. Thoracotomy was performed for resection in 75 (75.0%) patients. The most common postoperative complication was prolonged incomplete lung expansion (10.2%), and bronchopleural fistula developed in 1 patient (0.6%). One patient (0.6%) died 30 days after the operation due to progressive respiratory failure. The overall effectiveness of surgical treatment for pulmonary aspergillosis patients was 87.7%.

Young Tea Kim., *et al.* describe 24 postoperative complications in patients with pulmonary aspergillosis, accounting for 27.0% of all operated patients. Prolonged incomplete lung expansion was most frequently diagnosed (11 cases, 45.8%), residual pleural cavity was identified in 7 patients (29.2%), postoperative bleeding occurred in 3 patients (12.3%), empyema of the pleura developed in 2 cases (8.3%), and wound infection occurred in 1 patient (4.2%). The overall treatment effectiveness for this group of patients was 80.0%.

Mariusz Kasprzyk, *et al.* report the results of surgical treatment in 49 patients with aspergillosis, stating that the rate of postoperative complications was 63.3%, while postoperative mortality reached 4.1%. No disease recurrence was observed within a follow-up period of up to 5 years.

E. Hammoumi reports on 61 cases of complex and 54 cases of simple pulmonary aspergillosis. Postoperative complications were observed in 16.0% and 9.0% of patients, respectively.

K. Aydoğdu, *et al.* describe 77 patients with pulmonary aspergillosis, where 52 cases (67.5%) had recurrent hemoptysis as an indication for surgery. The rate of postoperative complications was 23.4%, and postoperative mortality was 3.9%.

Clinical Case

Patient P, 63 years old, was admitted to the clinic with complaints of recurrent massive hemoptysis. From the medical history, it was learned that she underwent right upper lobectomy 16 years ago due to pulmonary tuberculosis. No X-ray images were provided, but the patient recalled that after the operation, the doctor informed her that a cyst measuring approximately 5 cm remained in the right S6 area.

Upon admission to the clinic, a CT scan of the chest (Figure 4 and 5) revealed a right S6 aspergilloma.

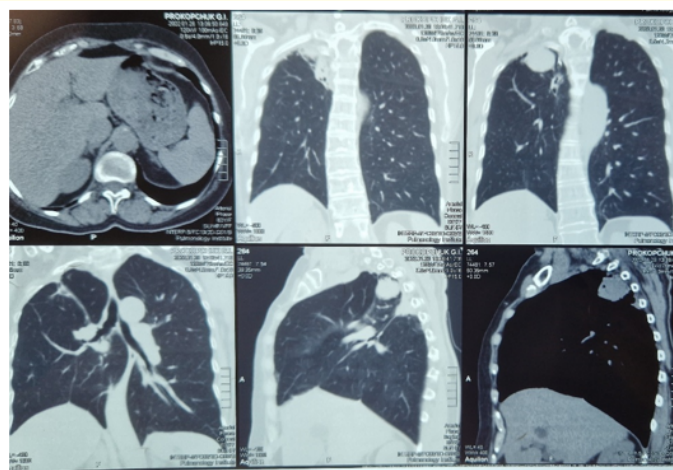


Figure 4: CT scan on admission, sagittal sections (a - aspergilloma).

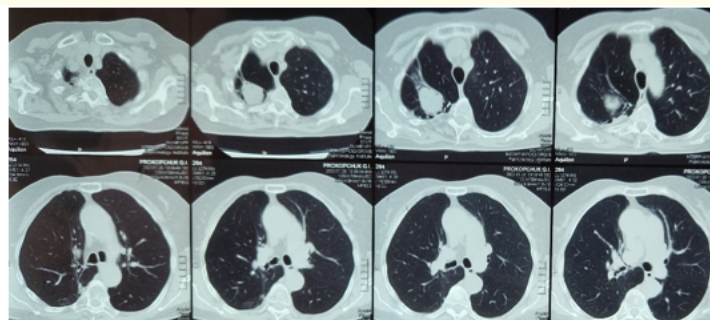


Figure 5: CT scan on admission, transverse sections (a - aspergilloma).

Considering the recurrent hemoptysis and the absence of radiological evidence for invasive aspergillosis, surgical intervention was proposed for the patient, with the specific extent to be determined intraoperatively. Therefore, after a brief preoperative preparation period of 5 days, the patient underwent a standard resection of S6 with phrenic stripping. It should be noted that the adhesion process in the pleural cavity was moderately expressed, and pneumolysis did not cause significant damage to the lung parenchyma.

The postoperative period was uneventful. Figure 6 shows the postoperative chest X-ray taken 6 days after the surgery, demonstrating expanded operated lung, elevated right diaphragmatic dome, and no infiltrative lesions in the lung fields. The patient was discharged from the hospital in a satisfactory condition after 18 days.

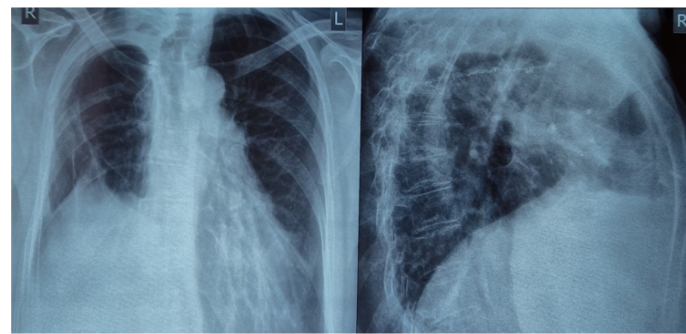


Figure 6: Postoperative chest X-ray at 6 days after the surgery.

Conclusion

1. Surgical treatment is the preferred method for managing pulmonary aspergilloma and achieves an overall treatment effectiveness of 93.3%.
2. The administration of antifungal medications before and after surgery is a mandatory requirement for effective treatment of pulmonary aspergilloma.
3. The issue of pulmonary aspergillosis is far from resolved, and therefore, effective communication among physicians of different specialties will contribute to its gradual resolution.

Bibliography

1. Izumikawa K, *et al.* "Bronchoalveolar lavage galactomannan for the diagnosis of chronic pulmonary aspergillosis". *Medical Mycology* 50 (2012): 811-817.
2. Shin B, *et al.* "Serum galactomannan antigen test for the diagnosis of chronic pulmonary aspergillosis". *Journal of Infection* 68 (2014): 494-499.
3. Franquet T, *et al.* "Spectrum of pulmonary aspergillosis: histologic, clinical, and radiologic findings". *Radiographics* 21 (2001): 8258-8237.
4. Tashiro T, *et al.* "A case series of chronic necrotizing pulmonary aspergillosis and a new proposal". *Japanese Journal of Infectious Diseases* 66 (2013): 312-316.
5. Van Toorenbergen AW. "Between laboratory quality control of automated analysis of IgG antibodies against *Aspergillus fumigatus*". *Diagnostic Microbiology and Infectious Disease* 74 (2012): 278-281.

6. Baxter CG., *et al.* "Performance of two *Aspergillus* IgG EIA assays compared with the precipitin test in chronic and allergic aspergillosis". *Clinical Microbiology and Infection* 19 (2013): E197-E204.
7. Jiang C., *et al.* "Review. Surgical Treatment of Pulmonary Aspergilloma: A 13-year Experience From a Single Clinical Center". *The Annals of Thoracic Surgery* 114.1 (2022): 311-318.
8. Kim YT., *et al.* "Good long-term outcomes after surgical treatment of simple and complex pulmonary aspergilloma". *The Annals of Thoracic Surgery* 79.1 (2005): 294-298.
9. Kasprzyk M., *et al.* "Surgical treatment for pulmonary aspergilloma - early and long-term results". *Kardiochirurgia i Torakochirurgia Polska* 14.2 (2017): 99-103.
10. El Hammoumi MM., *et al.* "Lung resection in pulmonary aspergilloma: experience of a Moroccan center". *BMC Surgery* 15 (2015): 114.
11. Aydoğdu K., *et al.* "Surgical management of pulmonary aspergilloma: clinical experience with 77 cases". *Turkish Journal of Medical Sciences* 45.2 (2015): 431-437.

Volume 12 Issue 6 June 2023

©All rights reserved by Opanasenko MS., *et al.*