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Case Report

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Surgical Approach for The Diagnosis of Thoracic Tumors: A Series of Cases

(*Running Title:* *Surgical approach for the diagnosis of thoracic tumours*)

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Abstract

Background: *Lung parenchyma neoplasms account for the leading causes of death worldwide when associated with neoplasms, contributing to 18.4% of deaths worldwide. Most patients are detected in advanced stages and their diagnosis is difficult given the patient´s comorbidities mainly by the limited access to diagnostic tools and prolonged waiting times for a first-time consultation.*

Case Report: *We present a series of eight clinical and surgical cases from a second-level hospital where a multidisciplinary team was formed to address prolonged waiting time and treatment from the time of diagnosis, thus reducing complications, offering on-time treatment, and improving patient prognosis.*

Conclusion: *Tumor boards are essential for the comprehensive evaluation of a patient with oncological conditions, since a multidisciplinary approach has demonstrated better oncological outcomes.*

Keywords: *Neoplasms, thorax, thoracoscopy, thoracotomy, biopsy.*

1. Background

A neoplastic lesion is defined as the uncontrolled proliferation of cells in a tissue (tumor) which, due to its histological and even genetic characteristics, can be benign (non-cancerous tumors) or malignant (cancerous tumors/neoplasms). Benign tumors sometimes can grow in size but do not spread or invade nearby tissues or distant parts of the body, while malignant lesions invade nearby tissues and may spread to other parts through the blood and lymphatic system. Thoracic cavity neoplasms can be classified according to their location and the tissues in which they grow, as well as their pathological type; for that, lung parenchyma neoplasms account for one of the leading causes of death worldwide when associated with neoplasms [1]. In 2020, 1.8 million deaths were recorded worldwide according to the World Health Organization (WHO), contributing to 11.6% of total cancer diagnoses, and making up to 18.4% of total causes of death due to cancer [2].

Tumors of the thoracic cavity include those that are confined to the lung tissue (lung tumors), those located at the mediastinal compartments, and those that are attached to the lung pleurae; respectively, thoracic cavity tumors include pulmonary tumors which classified into epithelial tumors, neuroendocrine tumors, ectopic tumors, mesenchymal tumors and hemolymphatic tumors (according to the WHO (2021) [3]. Mediastinal tumors are divided according to the classification proposed by Shields into anterior, middle and posterior mediastinum, and the literature reports that 54% of the mediastinal tumors in adults develop in the anterior mediastinum, while 26% and 20% are reported in the posterior and middle compartments, respectively. Regarding pleural tumors, around 90% consist of malignant mesotheliomas with different histopathological variants, the main ones being the epitheloid (50-60%), followed by the bifasic or mixed variant (30%), and sarcomatoid (10-20%).

Due to the vast majority of patients with thoracic neoplasms are detected in advanced stages, screening with low dose computed axial tomography in patients with risk factors represents an efficient way to detect the disease at an early stage, which is why survival varies between 10 and 20% in most countries; despite the fact that some neoplasms have survival rates greater than 80% [4]. The diagnosis of thoracic tumors is sometimes difficult, given the comorbidities of patients, the access of the tumor for diagnosis and the need for a rapid diagnosis, which is why it is important to have a multidisciplinary team for decision making. For this reason, we present the following series of cases from a second-level hospital where a team was formed consisting of: oncological surgery, medical oncology, pulmonology, internal medicine, pathology, anesthesiology, psychology, pain medicine and palliative care. With this, timely diagnosis has been observed in the majority of patients, as well as the lowest rate of short-term complications, and sufficient tissue for histological and molecular evaluation of the tumor, which impacts in a proper treatment and therefore patient

prognosis. For the afore mentioned, we consider it important to share the experience in this care center.

To address them, in the present document we will divide them into pulmonary, mediastinal and pleural neoplasms. Lung neoplasms can be benign or malignant; likewise, the classification of this type of tumors has had multiple modifications, the last being that of the WHO in 2021, which is shown in figure 1.

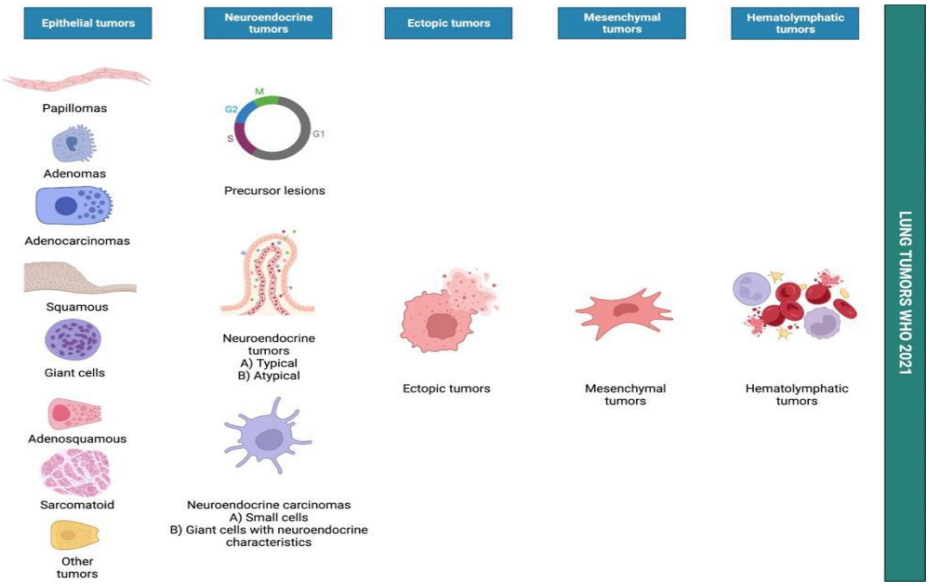


Figure 1: "Classification of pulmonary tumors according to WHO 2021". They are divided into epithelial tumors, neuroendocrine tumors, ectopic tumors, mesenchymal, and hemolymphatic tumors".

In relation to mediastinal tumors, 50% of these tumors in adult patients are thymomas, lymphomas and germ cell tumors, which are more frequent in the anterior and middle mediastinum. Computed axial tomography and magnetic resonance imaging are useful for the evaluation of homogeneous lesions, with well-defined borders to evaluate vascular involvement and diagnosis. Methods of choice for a definitive diagnosis consist of fine needle aspiration or Tru-cut biopsy guided by computed axial tomography, fluoroscopy or ultrasound and excisional biopsy [6]. (Figure 2).

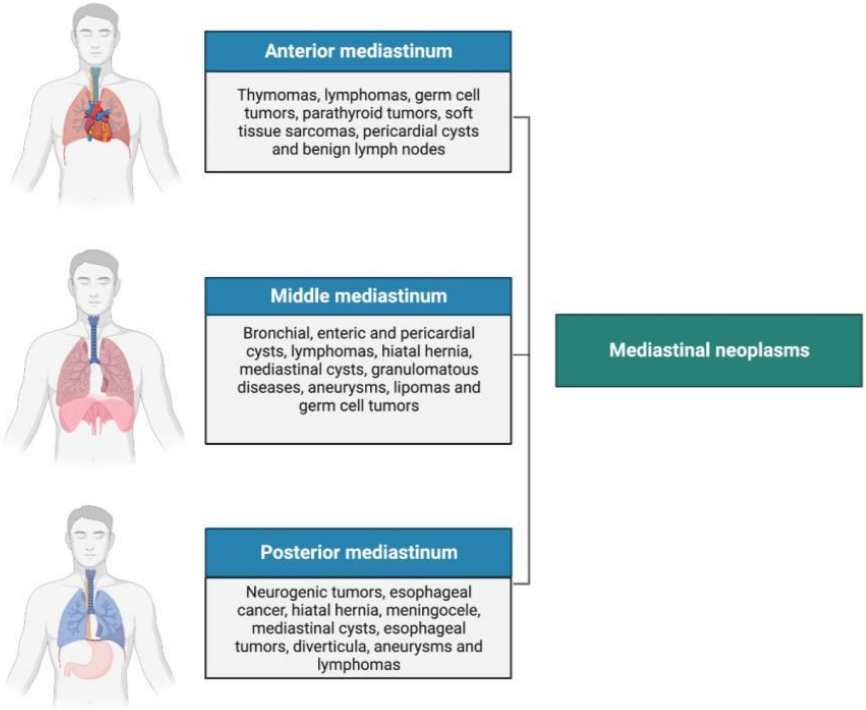


Figure 2: Mediastinal neoplasms. Lesions within the mediastinum are divided according to their compartmental localization: anterior, middle, and posterior.

Likewise, within pleural tumors, malignant pleural mesothelioma represents more than 90% of cases of mesothelioma neoplasia. From 2004 to 2006 it represented 0.33% of malignant neoplasms. Malignant pleural mesothelioma has a 5-year survival rate of less than 10%, giving it a higher fatality rate than most neoplasms in general. It occurs in 80% of cases in men, with a mean age at diagnosis of 72 to 74 years, and is mainly due to occupational exposure to asbestos, with 5% of exposed workers developing the neoplasia. The latency time between exposure and the development of malignant pulmonary mesothelioma is long and highly variable, taking between 20 and 50 years for its appearance. The risk is proportional to the intensity and duration of exposure, but increases with early exposure [8]. The histological variants of pulmonary mesothelioma are represented in figure 3.

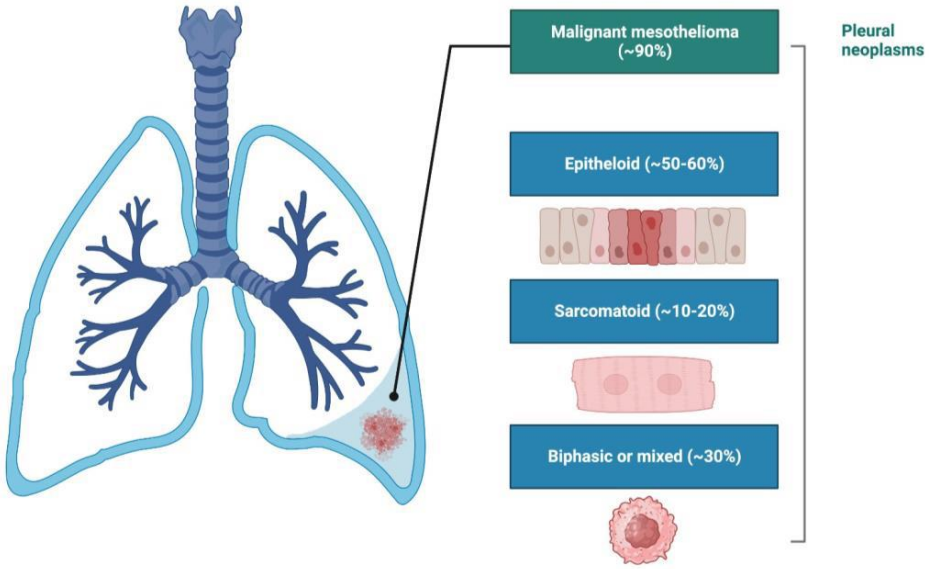


Figure 3: Pleural neoplasms: malignant mesothelioma. Histopathological variants of malignant mesothelioma are: epithelioid, sarcomatous and biphasic or mixed.

With the advent of new therapies targeting multiple genetic mutations and/or immunological targets, obtaining sufficient tissue for histopathological evaluation is extremely important; for example, in the case of associated pleural effusion, cytological analysis of pleural fluid has a sensitivity of 30 to 56%, like fine needle aspiration biopsy, so its usefulness is limited. Other alternatives are taking a percutaneous biopsy with a cutting needle (Tru-cut), image-guided cutting needle biopsy or biopsy with bronchoscopy techniques (Forceps or cryobiopsies); however, it is not always enough, so biopsy with video-assisted cutting needle (thoracoscopy) and thoracotomy may be necessary since their efficiency ranges from 80% to 90% [9]. Table 1 describes the characteristics, indications, contraindications, advantages and disadvantages of thoracotomy and video-assisted thoracoscopy (VATS).

Table 1: Definition, Indications, Contraindications, Advantages and Disadvantages in Thoracotomy and Video-Assisted Thoracoscopy (Vats)*

	Thoracotomy	VATS
Definition	Procedure by which a wide incision is made in the thoracic region to gain access to the thoracic cavity	For its acronym in English, it is a technique that used a video camera and ports for entry and visualization of the thoracic cavity
Indications	Distal aortic disease • Aortic dissection • Aortic rupture • Aortic aneurism Heart disease • Congenital defects • Aortic, mitral or tricuspid valve disease • Pericardiac disease • Heart/ pericardiac tumor Lung disease • Advanced-stage lung cancer • Severe thoracic trauma • Lung transplant • Complicated empyema • Thoracic penetrating lesion	Diagnostic • Mediastinal lymph node biopsy • Pleural biopsy • Pulmonary parenchyma biopsy • Thoracic wall biopsy • Cancer staging Therapeutic • Lung resection (cancer) • Bulla resection • Pleural drainage (pneumothorax, hemothorax, empyema) • Mechanical/ chemical pleurodesis • Biopsy of mediastinal masses and nodules • Esophagectomy • Esophageal diverticulum excision

	• Unstable pneumothorax/ hemothorax • Complex diaphragmatic hernia repair Esophageal disease • Esophageal disease • Tracheoesophageal fistula	• Thoracic duct ligation • Sympathectomy • Thoracic wall tumor resection • Thoracoscopic laminectomy • Spinal abscess drainage
Contraindications	Coagulopathy Surgical site infection Cardiac ischemia	One-lung ventilation intolerance/ bilateral ventilation dependence Severe adhesions in pleural cavity/ pleural symphysis Intraluminal airway mass Coagulopathy Hemodynamic instability Severe hypoxia Severe pulmonary hypertension Absence of pleural space Inadequate visualization and instrumentation Nodular lesions less than 1 cm in depth Tumoral size greater than 5 cm
Advantages	Greater accessibility Greater visibility Flexibility Faster performance Adaptability	Minor invasion Minor bleeding Less surgical time Less systemic inflammatory response Less postoperative pain Less in-hospital stay Less intubation time
Disadvantages	Higher degree of invasion Higher probability of complications Greater postoperative pain Higher in-hospital stay	Technical limitations Surgeon experience Difficult access to profound lesions
*VATS: Video- Assisted Thoracoscopy		

Perioperative evaluation encompasses a complete and thorough clinical record. It includes laboratory and image studies, pulmonary function studies and echocardiogram (if the patient has a related symptom or sign or advanced age), airway assessment and difficult airway predictive factors [12].

Anesthetic procedure during surgery can be either local or with general anesthesia depending on the procedure, area extension, and other factors [13]. It is necessary to utilize lung isolation techniques to obtain a single-lung ventilation, protecting the lung from possible contamination of the contralateral lung, likewise in cases where there is bronchopulmonary fistula or hemorrhage and pulmonary lavage [14]. Lung isolation may be obtained by three ways: use of double-lumen tubes, bronchial blockers, or single lumen tubes [14]. General anesthesia with endotracheal intubation is considered the gold standard for thoracic surgeries in which single-lung ventilation is required; nonetheless, patients with high-risk intubation and general anesthesia are ideal candidates for the no-intubation technique. In the year 2004 Pompeo and colleagues proposed the use of VATS surgery without endotracheal intubation for the resection of pulmonary nodules to prevent complications related to endotracheal intubation [12]. Medications used for general anesthesia are listed in Table 2. [13].

Table 2: Medications utilized in general anesthesia.

Medication	Dose	Route	Function
Thiopental	3-5 mcg*/kg**	IV***	Induction
Propofol	1-2 mg/kg	IV	Induction
Fentanyl	2-3 mcg/kg	IV	Basal analgesia
Sufentanil	0.2-0.3 mcg/kg	IV	Basal analgesia
Rocuronium or Vecuronium	0.1 mg/kg	IV	Muscle relaxant
Sevoflurane or Desflurane 1%	MAC**** 2 a 3 vol.***** %	Inhaled	Maintainance
*mcg: micrograms, **kg: kilograms, ***IV: Intravenous, ****MAC: Minimal alveolar concentration, *****vol: volume			

Double lumen intubation is performed by verifying with physical examination and bronchoscope (gold standard). With this technique the lung that will be operated on is allowed to collapse and the ventilated lung is managed with tidal volumes of 6 to 8 ml/kg, respiratory rate from 10 to 16 breathing per minute (bpm), positive end-expiratory pressure (PEEP) from 5 to 6 mmHg and a relation of 1:2 with the purpose of maintaining carbon dioxide (CO2) in values from 35 to 45 mmHg and a maximum concentration of exhaled carbon dioxide (ETCO2) from 30 to 35 mmHg (keeping into account the patient´s underlying pathology) [13]. In regards to postoperative analgesia, multimodal analgesia is recommended. It is described as a procedure that combines systemic pharmacological therapies such as non-steroid anti-inflammatory drugs, alpha-adrenergic agonists, n-methyl-d-aspartate receptor antagonists, opioids and regional analgesia [14]. Regarding regional analgesia intercostal blockage may be used, intrapleural analgesia, paravertebral blockage and/or epidural thoracic catheter. Table 3 shows sensory afferents for nociceptive stimuli in thoracotomy [14].

Table 3: Sensory afferents for nociceptive stimuli in thoracotomy.

Surgical incision	Intercostal nerves T4-T6
Thoracic dreins	Nerves T7-T8
Mediastinal pleura	Vagus nerve, X cranial pair
Diaphragm pleura	Phrenic nerve C3-C5
Ipsilateral shoulder	Brachial plexus

It is suggested that post- thoracic surgery patients be admitted to the intensive care unit (ICU), especially in the first 24 to 72 hours of the immediate postoperative period and in particular patients with previous comorbidities, diminished cardiopulmonary reserve, broad lung resections or those who require advanced support due to failure of a vital organ [15]. Likewise, intensive cardiorespiratory monitorization, proper drainage management, optimal control of analgesia and rehabilitation must be carried out to avoid adverse effects [15].

2. Multiple Case Report

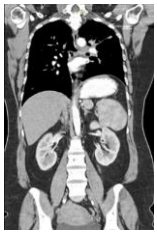
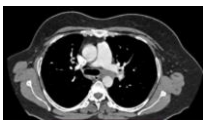
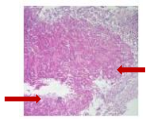
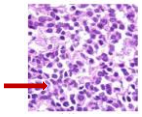
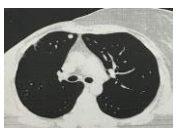
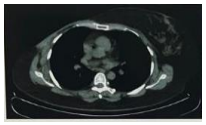
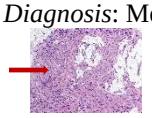
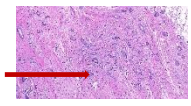
Eight clinical cases are described, four of which had a previous neoplastic diagnosis (3 with breast cancer and 1 patient with a colorectal cancer diagnosis), for which initial surgical procedures were metastatic resection. This was achieved in three cases given that the patient with colorectal cancer background presented a hamartoma (benign tumor in thorax) after resection of the lesion. Likewise, two patients with initial diagnosis made through bronchoscopy of a typical carcinoid and a hamartoma, respectively, taken to surgery for tumor resection. Also, a case of a fibrous pleural tumor, initially diagnosed through CT-guided biopsy with posterior total resection of the tumor and lastly, a case of a patient in whom, due to the difficult access of the tumor, had to undergo surgery to obtain the initial diagnosis (epidermoid tumor). Tables 4 and 5 show the clinical, diagnostic, histopathological and therapeutic characteristics of every patient.

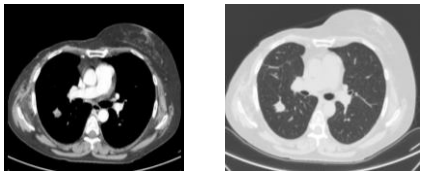
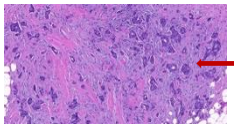
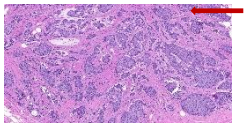
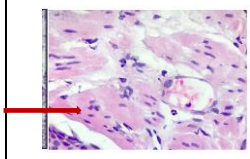
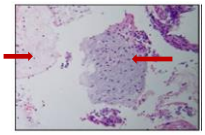
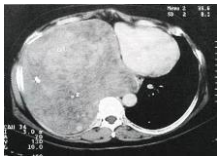
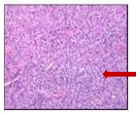
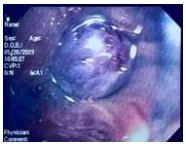
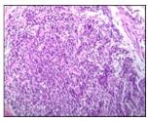
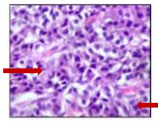
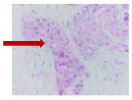
Table 4: Description of The Clinical, Surgical, Anesthetic and Therapeutic Characteristics.

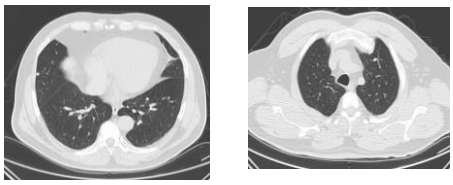
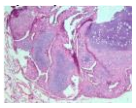
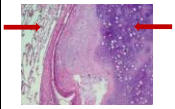
Clinical presentation	Surgical/ anesthetic procedure	Treatment
1. 42-year-old feminine *Background*: Poorly differentiated infiltrating ductal carcinoma, grade II, estrogen receptor, progesterone, Ki-67* >20, Luminal B *Symptoms*: Dry cough, dysphagia, medium-effort dyspnea, dysphonia	*Surgical procedure:* Thoracotomy with tumor biopsy *Anesthetic technique*: Balanced general anesthesia with selective intubation	Second-line endocrine treatment: Abemaciclib, Fulvestrant, Goserelin
2. 60-year-old feminine *Background:* Breast cancer 2-year remission prior to onset of symptoms *Symptoms*: Dry cough, medium-effort dyspnea	*Surgical procedure:* Thoracotomy with metastasectomy *Anesthetic technique*: Balanced general anesthesia with selective intubation	Second-line endocrine treatment: Palbociclib, Fulvestrant
3. 58-year-old feminine *Background:* Breast cancer 6-year remission prior to onset of symptoms *Symptoms*: Dry cough, medium-effort dyspnea	*Surgical procedure:* Thoracotomy with right inferior lobe metastasectomy *Anesthetic technique*: Balanced general anesthesia with selective intubation	Second-line therapy: Research protocol VIKTORIA-1 (Gedatolisib, Palbociclib and Fulvestrant)
4. 24-year-old masculine *Background:* Gastroesophageal reflux disease *Symptoms*: Cough with white expectoration, exacerbated by talking and exercise	*Surgical procedure:* Thoracotomy with middle lobe lobectomy *Anesthetic technique*: Balanced general anesthesia with selective intubation	Surveillance
5. 66-year-old masculine *Background:* None	*Surgical procedure:* Thoracotomy with tumoral resection	Surveillance

Symptoms: Dry cough, low-effort dyspnea, thoracic pain.	*Anesthetic technique*: Balanced general anesthesia with selective intubation	
6. 81-year-old masculine *Background:* None *Symptoms*: Dry cough, dyspnea, wight-loss	*Surgical procedure:* Thoracotomy with right-upper lobe lobectomy con *Anesthetic technique*: Balanced general anesthesia with selective intubation	Surveillance
7. 60-year-old masculine *Background:* None *Symptoms*: Dry cough, dyspnea, dysphonia	*Surgical procedure:* Thoracoscopy with biopsy *Anesthetic technique*: Balanced general anesthesia with selective intubation	Carboplatin + Paclitaxel + Concomitant radiotherapy
8. 62-year-old masculine *Background:* Right hemicolectomy secondary to ulcerated, invasive, well-differentiated adenocarcinoma *Symptoms*: Dry cough, low-effort dyspnea, weight-loss	*Surgical procedure:* Left thoracotomy with upper-lobe metastasectomy *Anesthetic technique*: Balanced general anesthesia with selective intubation	Surveillance
*Ki-67: Antigen Kiel 67		

Table 5: Description of The Diagnostic Method and Histopathology Characteristics.

Diagnostic method	Histophatology
1. *Tomography* Lymph node tin the aortopulmonary window measuring 29x32x17 mm* that caused a decrease in the caliber of the caliber of the left main bronchus Left parahiliar tumor towards the eft upper lobe of 22 mm in diameter that is associated with ipsilateral apical subsegmental atelectasis  	Metastatic lobular breast carcinoma. Lymph node with grade 3 infiltrating lobular carcinoma, GATA** 3+, RE*** 2+, RP****-, Her***** 2 low +, Ki67****** 20%  Transition zone between tumor (pink zone) and lymphoid tissue (clear zone)  Small neoplasm of nests and cords with plasmacytoid appearance
2. *Tomography* 8 mm solid nodule with lobulated edges located in the apical segment of the left upper lobe  	Metastatic infiltrating ductal carcinoma in lung RE 90%, Negative Her 2 *Diagnosis*: Metastatic breast cancer  Neoplasm with parenchymal infiltration (pink zone)  Neoplasm that forms ducts and tubes in a dispersed manner

3. *Tomography* Right subpleural spiculated solid nodule within the upper segment of the right lower lobe of 18 mm 	Classical type infiltrating ductal carcinoma, grade II, lymphatic permeation. RE 80%, RP negative, Her 2 negative *Diagnosis*: Metastatic breast cancer  Neoplasm that forms tubules with infiltration to the stroma  Neoplasm that infiltrates stroma with a solid pattern
4. *Tomography* Atelectasis of the medial segment of the middle lobe 	Epithelium with areas of squamous metaplasia, acute and chronic inflammatory infiltrate. Fragments of hyaline cartilage with areas of myxoid appearance and foci of smooth muscle  *Diagnosis*: Pulmonary hamartoma Myxoid component and spindle cells with smooth muscle fibers (pink)  Myxoid component (light pink), cartilage (center)
5. *Tomography* Tumoral lesion that covers the entire hemithorax with well-defined edges, heterogeneous. 	Malignant solitary fibrous tumor measuring 20x15 cm*******, 8 mitoses in 10 fields of 40x, 20% necrosis. Negative for perineural infiltration, lymphovascular permeation  Spindle cell neoplasm with storiform component, irregular vessels in deer antlers  Lobulated tumor of fleshy appearance with multinodular hemorrhagic areas
6. *Bronchoscopy* Tumor in the right upper lobe that obstructs 100% of the lumen with pearly characteristics 	Grade 1 neuroendocrine tumor (typical carcinoid tumor). Positive chromogranin, CD56******** positive, positive Ki67 in 2% Small round cell solid nest neoplasms   Cells forming acinar and solid pattern
7. *Tomography* Tumor in the middle mediastinum of approximately 4x3 cm in the territory of the left recurrent laryngeal nerve, with runs parallel to the main carina 	Moderately differentiated keratinizing invasive squamous cell carcinoma  Solid nests of neoplastic cells with malignant epithelioid appearance (purple)

8. *Tomography* Two pulmonary nodules: apical in the left hemithorax of 9 mm and anterior basal in the right hemithorax of 7 mm 	Encapsulated, well-defined nodule, built by collapsed and irregular cavities lined by respiratory epithelium and fibrosis with nodules of mature, hyaline cartilage, without nuclear alterations  *Diagnosis*: Pulmonary hamartoma Hamartomatous nodules  Hyaline cartilage (purple), collapsed alveolus (white)
*mm: milimeters, **GATA: Erythroid transcription factor, ***RE:, ****RP:, *****Her2: Human epidermal growth factor receptor 2, ******Ki67: Antigen Kiel 67, *******cm: centimeter, ********CD56: Neural cell adhesion molecule 56.	

3. Discussion

As part of the detection of lung cancer, NCCN guidelines (National Comprehensive Cancer Network) provide information on the following risk factors: history of passive or active smoking, exposure to radon, occupational exposure, family history, chronic obstructive pulmonary disease, diffuse interstitial lung disease, etc. A high-risk patient is defined as someone who is 50 years or older, consumes 20 packs of cigarettes a year or more, has stopped smoking for less than 15 years; which must be referred with a simple chest tomography to pulmonology, internal medicine or oncology for follow-up. At the moment, minimally invasive techniques represent the first option for the approach and resection of tumors at thoracic level due to the multiple advantages they have over open techniques, among which are shorter surgical time, less bleeding, less post-surgical pain and, above all, the shorter hospital stay. However, one of its main disadvantages is the limited availability of the equipment in hospitals in our country, mainly available in national centers or third-level hospitals. In our experience, thoracotomy continues to be an approach option since we do not always have the necessary equipment to offer the first option to patients; however, there is the necessary training to deal with this type of procedure with the techniques already described in the literature, their possible complications and the postoperative period.

The interaction of different specialties in decision-making for patients with thoracic tumors has proven to be the most forceful method to offer the best treatment to each patient individually. These sessions also called “tumor boards” confer the ability to discuss each case individually, with the purpose of offering unique and individualized treatments to each patient according to their pathology, international guidelines, identifying and referring patients in a timely manner, identification of compatible clinical trials, increase in cancer research, education for the professionals by sharing knowledge with the rest of the members [16]. The multidisciplinary team is made up of personnel from different medical areas and specialties, including: social work, psychology, pain medicine and palliative care, pulmonology, medical and surgical oncology, anesthesiology and pathology. In these sessions, the patient's lung health, radiographic and biochemical evaluation are discussed in order to formulate an appropriate treatment and follow-up plan based on current evidence, also having the interaction of the different specialties involved in the management of this type of patient.

It is for all the reasons previously mentioned that we present the experience of a second-level hospital, where it was decided to establish a multidisciplinary team to make diagnostic, therapeutic and follow-up decisions. Currently, the patients presented are undergoing treatment and strict follow-up in the clinic, hoping that in the future it will be possible to describe in a prospective study the time from the onset of symptoms to care, as well as to diagnosis and treatment, in addition to establishing whether the conformation of a multidisciplinary team locally impacts patient care. During the review of these cases, it is possible to notice that the patients present a clinical picture similar to that described in the literature with the presence of cough and low to medium-effort dyspnea as a common denominator, as well as a history of primary tumor, with breast cancer being present in all of the female patients. On the other hand, the majority of male patients had no previous relevant history, except for one presenting a previous history of colonic cancer. With the above, the diagnostic approach began with imaging studies such as chest tomography and computerized axial tomography of the lungs where the presence of a lesion suggestive of cancer was evident, for which they underwent a surgical procedure by thoracoscopy or thoracotomy.

4. Conclusions

Currently, tumor boards as joint sessions are essential for the comprehensive evaluation of a patient with oncological conditions. It has been demonstrated that multidisciplinary interaction in the management of lung and mediastinal tumors leads to better oncological outcomes since it improves decision making, coordination between different professionals improving communication channels with the consequent exchange of knowledge. Therefore, there is an improvement in the health system and the experience for both the patient and the specialist, as well as the association with the increase in quality of life, overall survival, adequate staging and pretreatment evaluation [16].

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