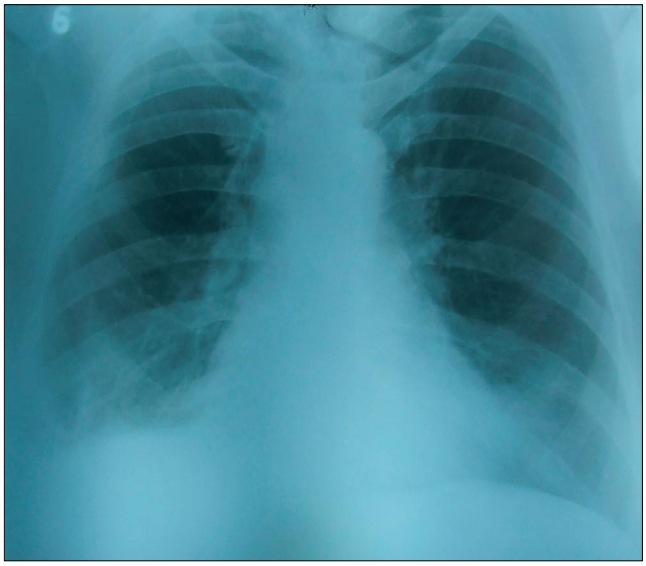
lesions throughout its mass. The thoracic aorta had a normal caliber (Figure 2, Figure 3).

The patient was thus referred to the Thoracic Surgery Clinic of the Emergency Central Clinical Military Hospital with the diagnosis of mediastinal tumor. Given the large size of the tumor and its proximity to the superior vena cava, a Carlens diagnostic mediastinoscopy was performed. Multiple biopsies were taken, causing the tumor to bleed profusely. Hemostasis was obtained with gauze packing. The histopathological report described small fragments of fibroconjunctive tissue with a diffuse small cellular infiltrate, suggestive of non-Hodgkin lymphoma or microcellular carcinoma. In order to arrive at diagnosis, immunohistochemical staining (IHC) was recommended. IHC was negative for epithelial cells and positive for B and T lymphocytes, but could not specify whether the tumor was lymphomatous. Therefore, a left anterolateral thoracotomy with access to the pleural cavity via the third intercostal space was performed. A tumor approximately 7 cm in diameter, renitent and highly vascular, located posteriorly and to the left of the superior vena cava and pushing the trachea

**Figure 4.**
**Postoperative chest x-ray**



posteriorly was encountered. There were great difficulties dissecting around the tumor due to its proximity to the superior vena cava, ascending aorta and trachea, which were not invaded. The highly vascular lesion proved to be very difficult to excise due to frequent bleeding, but in the end it was completely removed using careful, step-by-step dissection.

The patient's progress was favorable (Figure 4), she was discharged six days postoperatively. Histopathology of the resected specimen showed modified lymph nodes with features compatible with the diagnosis of Castleman's disease – plasma cell type.

## Discussions

Castleman's disease was first described by Benjamin Castleman in 1956[2]. It is an uncommon (and therefore poorly-known) disease characterized by the appearance of tumoral adenopathies.

According to its localization, it can be unicentric or multicentric. Histologically, three types can be described: hyaline-vascular, plasma cell and mixed[3]. Both sexes are affected equally and it can appear at any age, though it has been noted that patients with the multicentric form of the disease tend to be older adults aged 50-70[1].

The localized (unicentric) form presents as a slow-growing mass that frequently originates from the mediastinal, cervical or abdominal lymph nodes. Similar lesions have been known to appear in various non-lymphatic structures such as skeletal muscle, larynx, lungs, orbits[4] and even endotracheally[5]. The patients are usually asymptomatic and when manifestations do appear, they are primarily related to the compression of nearby structures. General symptoms occour quite infrequently and is generally not associated with the appearance of lymphomas or other tumors. Surgical resection is curative in 90-95% of all cases.

The hyaline-vascular type is generally unicentric. The plasma cell type is associated with the multicentric variant of the disease, although isolated forms can appear in 10% of all patients.

In its multicentric variant, Castleman's disease consists of multiple adenopathies and hepatosplenomegaly in some cases. It is associated with plasma cell proliferation in 90% of all cases and hyaline-vascular disease in the remaining 10%[3]. It can also be associated with a variety of non-specific symptoms (the „B class" symptoms of lymphomas): fever, night sweats, weight loss and fatigue, anorexia, peripheral edema. Laboratory tests can demonstrate anemia, hypoalbuminemia, hypergammaglobulinemia. 20% of patients present with peripheral neuropathy. The systemic manifestations of this disease are caused by an excess production of $IL_6$. The multicentric form of Castleman's disease can be associated with a variety of illnesses such as: autoimmune hemolytic anemia, multiple myeloma, amyloidosis, pemphigus or multiple associations such as in POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammapathy, and skin changes). It has an aggressive evolution and can progress to non-Hodgkin lymphoma, often requiring systemic therapy.

The etiology of Castleman's disease has not been elucidated yet, although there are two current theories. One theory postulates that the lymphoid hyperplasia is due to chronic antigenic stimulation by a viral trigger. Human herpesvirus 8 (the Epstein-Barr virus) may be involved, as it readily populates B lymphocytes and has been connected to the pathogenesis of Kaposi's sarcoma, lymphoma and Castleman's disease. It also seems to play a role in the promotion of angiogenesis in the early stages of the latter[6]. The second theory states that the malady is caused by developmental growth disturbance of the lymphoid tissues, leading to the appearance of a vascular lymphoid hamartoma[7].

Diagnostic imaging plays a key role in the exploration of patients with Castleman disease, as the illness is frequently discovered incidentally in asymptomatic patients, especially in its localized variant.

Computed tomography shows a well-defined hypervascularized mass, that retains more contrast substance that lymphomas or thymomas and that is as iodophilic as a large vessel[1]. The fact that the mass is enhanced simultaneously with many large vessels is significant in establishing a positive diagno-

sis[8]. In our case the tumor was initially considered an aortic aneurysm on the first CT scan.

PET-CT is also very useful in evaluating patients suffering from Castleman's disease. Standard uptake values (SUV) are generally lower than those seen in lymphomas. PET can also be used to evaluate the patient's response to therapeutic measures, as it can show a decrease of metabolic activity in the affected lymph nodes in the case of patients who are responding to therapy.

The diagnosis of Castleman's disease is primarily a histopathological one, requiring the excision or biopsy of the lesion. In order to arrive at conclusive findings, a greater amount of tissue is needed. A fine-needle biopsy is usually non-diagnostic and the disease is frequently confounded with a thymoma or lymphoma[9]. In our case, the diagnosis after mediastinoscopic biopsy was diffuse non-Hodgkin lymphoma or microcellular carcinoma but was infirmed by immunohistochemical staining.

The treatment of localized Castleman's disease consists of surgical excision. The tumoral mass is highly vascular and can cause important blood loss during its dissection. Preoperative angiographic embolization has been proposed in order to lower the risk of hemorrhage[1,7]. The administration of corticosteroids or rituximab and even radiotherapy have been used to reconvert voluminous, inoperable tumors or after partial resection.

The treatment of multicentric Castleman's disease includes chemotherapy, antiviral drugs (aciclovir, ganciclovir), corticosteroids, antiangiogenetic factors (thalidomide), anti-$IL_6$ and $IL_6$-R antibodies, anti-$CD_{20}$ antibodies (rituximab) and suramin – an antiparasitic drug that inhibits the proliferation of lymphoid cells[10,11]. So far, none of these methods has prevailed and a specific treatment protocol for the multicentric variant has yet to be defined.

The localized form has a good outcome, as complete surgical resection is generally curative. The multicentric variant with systemic symptoms has a less optimistic prognosis, and it is usually the patients with generalized Castleman's disease and peripheral neuropathy that have the worst prognosis of all.

In all cases of Castleman's disease, long-term follow-up is necessary in order to timely detect possible malignant changes[10].

## Instead of a conclusion

This case is a rare form of Castleman's disease, as the plasma cell type is rarely associated with the localized variant and devoid of general symptoms. Mediastinoscopy, a valuable minimally-invasive diagnostic method, can lead to severe bleeding not only by damaging any large blood vessels, but also by biopsing a highly vascular tumor, such as the one presented here.

Although it is a rare malady, the diagnosis of Castleman's disease must be taken into consideration when encountering mediastinal tumor with significant contrast enhancement upon a CT scan.

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