Primary mediastinal seminoma

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Abstract

The primary mediastinal seminoma is a rare clinical entity included in the group of germ cell tumors of the mediastinum. In spite of its high malignancy and being symptomatic in about 80% of cases, often it is only suspected when it becomes so large that it is impossible to be completely resected. We report a clinical case of inoperable mediastinal seminoma occurring in a 41 years-old man making the review of the literature with emphasizes on the therapeutic strategy.

Keywords: germ cell tumors of the mediastinum, primary mediastinal seminoma, residual mass.

Introduction

The primary mediastinal seminoma is part of the group of mediastinal germ cell tumors.

Such location emerges with a frequency estimated in around 40% of all extragonadal germ cells. The retroperitoneal location comes in second place and on the pineal gland, extragonadal germ-cell tumors are extremely rare.[1,2,3]

Extragonadal germ cell tumors, particularly those located on the pineal and mediastinum, represent a malignant transformation of embryo cells located there, without a primary gonadal focus. Some researchers suggest that such distribution emerges as a consequence of an abnormal migration of germ cells during embryogenesis.[3,4] Most primary seminomas in the mediastinum are located on the anterior mediastinum, mainly in its antero-superior portion,[3] with symptoms resulting from the compression and sometimes the invasion of adjacent structures. Chest pain is the most common, but cough can also emerge, dyspnoea and obstruction of the superior vena cava. Weight loss and fever are the most frequent systemic symptoms. Around 20% of patients are asymptomatic, and in these, tumors are found on occasional thorax X-Rays.[3,5]

Many patients present a comprehensive involvement of the great vessels when they are diagnosed or, then, metastatic disease symptoms with the lung, liver and the bone as the most affected organs. [3,5,6]

The posterior anterior X-Ray and the thorax profile reveal changes in over 95% of cases, with the thorax CT scan helping to provide supplementary information, as the extension of the tumor and the involvement of adjacent structures. A β subunit of human chorionic gonadotrophin (βHCG) and the alpha-fetoprotein (AFP) are considered tumor markers useful to the diagnosis, staging and monitoring of the response to treatment of germ-cell tumors. [3,5] However, in the cases of mediastinum seminoma, AFP is usually negative and the βHCG shows itself increased in only to 10% of such tumors.[1,3]

Also, lactate dehydrogenase (LDH) deserves to be referred, as its increase is associated to a wider disease extension and together with βHCG, is part of the so-called prognosis factors.[1,5,6]

Particularly well studied by Hurt,[6] are the following factors: age above 25 years old, presence of upper vena cava syndrome, supraclavicular adenopathy and/or para-aortic, general signs as weight-loss and fever, incomplete exeresis, presence of metastases, particularly bone ones and at the end, a higher rate of βHCG, witnessing the presence of a wide number of syncio-trophoblast cells. [3,7]

Regarding the therapy strategy, the initial tradi-

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tional attitude was until a short while ago, a surgical exeresis as complete as possible, followed by radiotherapy.[7,8,9]

At present, the first course of action is often the surgical one, but only to confirm the histology diagnosis.[1,2] A total exeresis surgery is only possible in the case of an encapsulated tumor and this is seen only in 25% of cases. On the other hand, tumoral reduction surgery is arguable and should not be mutilating, as it causes a non-negligible morbidity and mortality. [8,9,10]

Post-surgical radiotherapy is recommended only in cases of invasive tumor or when its exeresis is incomplete or still when the residual tumor shows an active seminoma. Because such tumor is very radio sensitive, although less than the testicular seminoma, it can be controlled with radiotherapy, using doses a bit higher than those used in the testicular seminoma:[1,11] , i.e. , 45 Gy 5 to 6 weeks proving that a similar histology does not grant identical radio sensitivity, confirming a more reserved prognosis of mediastinal seminomas versus testicular seminoma. [9] In spite of that, the survival of such patients at 5 years is around 60%. [9,10] But such tumors are also very sensitive to chemotherapy, with a total response lower than 80% of advanced seminoma cases and 90% in seminomas only located in the mediastinum. Without a precise staging, the therapeutic strategy becomes difficult. Some authors propose a similar staging to the one used for the thyme tumors (*Table 1*), conditioning some strategies, namely in the case of exeresis to become impracticable, to make exclusively radiotherapy, except in bulky tumors (diameter above 50% of the thoracic diameter), or in the metastases.

In these last circumstances, chemotherapy should be done first and the most voted is based on cisplatin combined with vinblastine, bleomycin, with or without doxorubicin, using standard doses for four cycles. [1,8,9,10,11] The therapeutic strategy also involves the treatment of the residual mass and depends on the size of the latter. If above 3 cm, should be referred to surgical exeresis. If the histology exam shows a negative seminoma, supplementary radio therapy should be carried out.[1,3,9,10]

If the residual tumor is below 3 cm, there should be a clinical and laboratorial monitoring with a monthly determination of the βHCG and AFP for one year and with thorax CT scan every three months, also for one year. On the following years, all such procedures must be made every six months.[1,3,5,10,11]

TABLE I

Stages of mediastinal seminomas

Stage 1
Encapsulated tumor, totally resectable Capsula invaded, totally resectable
Stage 2
Invasive tumor, totally resectable Invasive tumor, incompletely resectable Invasive tumor (<50% thoracic diameter)
Stage 3
Invasive and bulky tumor (>50% thoracic diameter Subclavicular and cervical ganglia Subdiaphragmatic ganglia
Stage 3
Bone metastases Other metastases
Adapted from P. Ruffié and J. P. Droz.

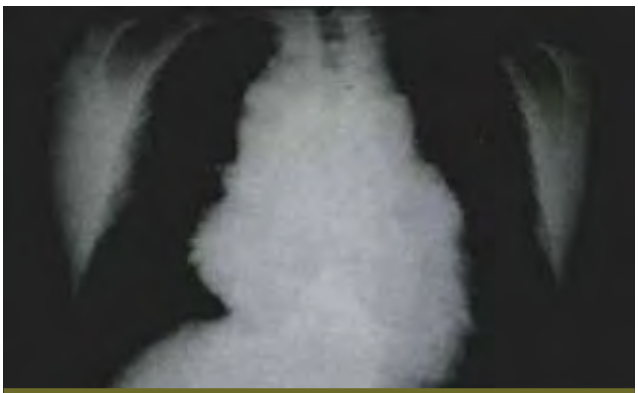
Due to its rarity, the authors report the clinical case of a primary mediastinal seminoma presenting simultaneously as a good demonstrative use of such therapeutic strategies and follow up.

Case report

41 years old man, Caucasian, sap tree collector, born and residing in Tondela county, was admitted on the 4th May 1993 for studying a mediastinum mass.

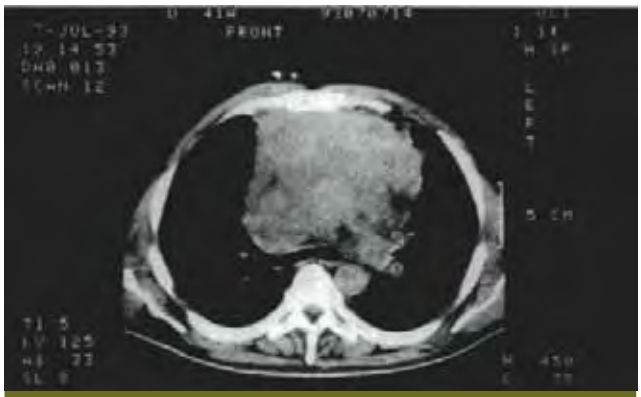
2 months previously, apparently a spontaneous grinding pain started on the left shoulder blade, without characteristic exacerbation or relief. Subsequently he had dry cough, light fever (37.5 – 38°C) and anorexia, being medicated by his family doctor with amoxicillin and paracetamol. As the symptoms persisted, added by dyspnoea mainly in dorsiflexion and dorsal decubitus, he underwent at the time a thorax X-Ray showing mediastinum enlargement (*Fig. 1*), leading to a thorax CT scan. Such test revealed in the anterior upper part of the mediastinum a bulky tumoural mass measuring 16.4 X 11.70 cm (*Fig. 2*). It was at once considered that this mass features had to be found through a histology study, as the diagnosis hypotheses were multiple (*Table 2*) and the patient was admitted into hospital.

From the personal background it should be highlighted that the victim had suffered a fall fracturing the right tibia, with a well-tolerated osteo-synthetic



PA Thorax X-Ray. Wider upper mediastinum.

FIG. 1



Thorax CT Scan. Reduced tumoral mass.

FIG. 2

TABLE II

Antero-superior mediastinum diseases

Thyme pathologies (tumors, cysts, hyperplasia)
Intra-thoracic goiter
Lymphoma
Germ cell tumors
Endocrine tumors (thyroid, parathyroid, carcinoid)

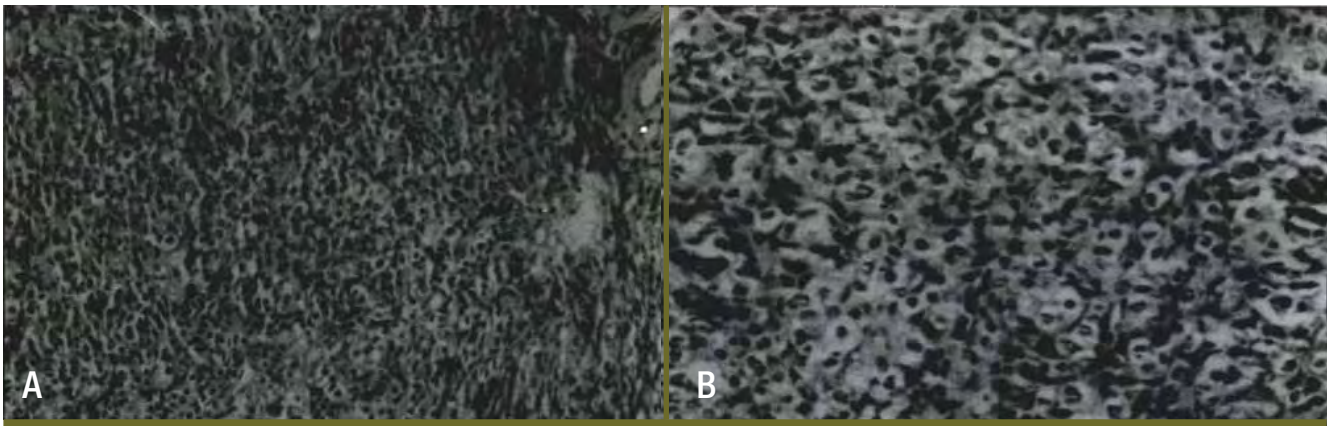
material, and a traumatism of the lumbar spine resulting in stress lumbar pain related with a probable disc hernia. Family background is irrelevant. The objective exam showed a good general condition (BMI = 26 kilograms/m^2) with blood pressure of 130/80 mm HG, rhythmic pulse, wide with 90 beats per minute and axillary temperature of 36.6°C. There was neither edema nor adenopathy. The thorax observation revealed multiple small melanic nevi, with the percussion revealing under dullness on the upper half of the left hemithorax, without modification of vocal vibration on palpation. The pulmonary auscultation was normal and the cardiac one has shown hypophonesis. A brief neurologic summary has shown to be normal. The laboratorial tests have highlighted a slight normochromic normocytic anemia (Hb= 10, 6 g/dL), a slight increase on hepatic enzymes (GGT=62 U/L and alkaline phosphatase = 119 U/L) and the erythrocyte sedimentation rate (120 mm on the first hour).

In the meantime, the patient underwent a biopsy guided by CT scan. As the histology study was inconclusive, due to the scarce sampling, a second biopsy was carried out with the same results. He was thereafter subject to a mediastinotomy in the Cardiothoracic Surgery Service, and some fragments were obtained enabling the histological diagnosis of seminoma (*Fig. 3A and B*). Before such diagnosis, a testicular ultrasound was made revealing only a slight bilateral varicocele. βHCG and AFP dosages were negative.

This way, testicular biopsy was not necessary and we established the diagnosis of primary mediastinal seminoma.

To complete the staging, respiratory functional tests were made (VC=84%, FEV1 = 80%; Tiffeneau Index = 84%) and for anatomical staging an abdominal CT scan was carried out showing no changes.

We concluded to be before a mediastinal seminoma in stage II C, according to the staging proposed by Ruffié & Droz this is, an unresectable bulky invasive tumor (less than 50% of the thorax diameter). The patient underwent radiotherapy in the Portuguese Institute of Oncology in Coimbra, with a total dosage of 40 Gy for four weeks. As the results were not satisfactory (tumor reduction in just a third of its initial size) it was proposed to the patient treatment with cytostatic drugs, after recovering the hemogram values. The patient refused and missed the monitoring appointments. Four months later he came to the Medicine 1 Service due to a localized pain on the left shoulder, being diagnosed a pathological fracture on the medium third joint with the external third of the left claviculae. He underwent thoraco- abdominal CT scan and bone scintigraphy, revealing "on the right pulmonary field, on the level of the upper lobe and

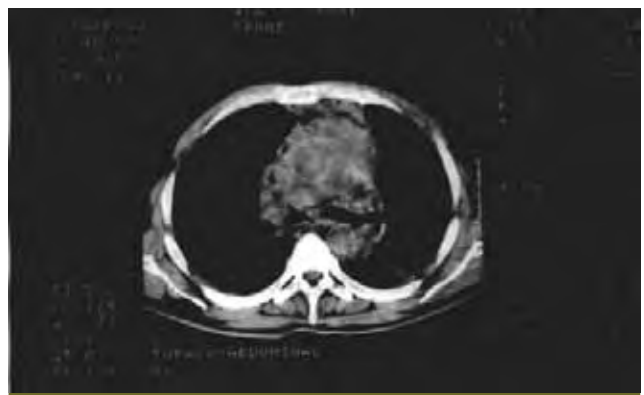


Mediastinal seminoma: round and ovoid cells pattern, with abundant cytoplasm and prominent nuclei; (A) – HE x 250 (B) – HE x 400.

FIG. 3

with peripheral location, several small nodes images compatible with metastases". The abdomen study showed some nodular formations located on the diaphragm and absence of changes on the hepatic parenchyma and adenomegalies in the lumbar-aortic chains. Such clinical condition placed the patient on stage IV of the above mentioned classification, being proposed again chemotherapy which he accepted. He underwent therapy scheme involving four cycles, each one made in the first week for cisplatin and on the third week for vinblastine, bleomycin and doxorubicin.

The treatment was reasonably well tolerated, with metastases disappearing and a reduction on the general mass to around 5 cm in the highest diameter (*Fig. 4*). Nuclear Magnetic Resonance restated a very intimate relationship between the residual tumor and crucial mediastinal structures as the aorta and the pericardium. In the absence of dissecting surface, its exeresis became impracticable. The patient was discharged with a reserved prognosis, referred to the outpatient clinic for follow-up.



Thorax CT Scan. Bulky tumoral mass in the antero-superior mediastinum.

FIG. 4

Comments

The primary mediastinal seminoma occurs mainly in the male gender, from the 20ties to the 40ties, representing the female gender only 5% of cases. [1,2,3]

The first problem in handling patients with mediastinal tumor is naturally the histological diagnosis. [3] However an increase on the serological tumor markers as AFP and βHCG in a young patient with a mass in the mediastinum is very suggestive of germ-cell tumor. In the case of seminoma, AFP is usually negative and βHCG is only increased in 5 to 10% of cases, justifying the resource to a needle biopsy, driven by CT scan, before any therapy attitude is taken.[3,6,7] As it was verified with this patient, the tumor was adherent to the subjacent structures, without cleavage surface, being an obstacle to its total exeresis. Sometimes a puncture by needle biopsy does not allow enough material for the histological diagnosis, and supplementary procedures are needed. Mediastinotomy is the best alternative searching for the diagnosis. [3]

Heroic efforts in tumoral exeresis must be avoided

as an initial approach of such cases because these tumors are extremely radiosensitive [8,9] what did not succeed with this patient, very likely due to big size of the tumor, a fact that on its own reveals its malignant potential.[2,3,5]

The development of bone metastases, one of the places more frequently reached immediately after the lymphatic system, [8] made the patient to accept carrying on treatment, now with cytostatic drugs. Patients in advanced stage of the disease, i.e., with metastases of bulky tumors, must be subject to treatment based on cisplatin (VBA + cisplatin). The virtues of such therapy scheme are rather clear in the excellent results obtained lately in the treatment of advanced testicular seminomas [3] starting already to emerge series relating to the primary mediastinal seminoma,[2,8,11] revealing rates of complete remission ranging from 80% to 100%.

But patients with a bulky seminoma may present a residual tumor after radiotherapy and/or chemotherapy, with a therapeutic solution remaining controversial, as it may or may not contain an active seminoma. Most authors make surgical exeresis to depend on the size of the tumor, i.e., if it is above 3 cm. [3,6,8,11]

In the described case, the patient even got the residual mass of higher size, but the absence of a cleavage plan between the tumor and adjacent structures has prevented surgery. Therefore, monitoring was kept through thorax CT scan with regular dosages of β HCG, AFP and LDH. [1,3,6] Regarding prognosis and considering the mentioned factors in the introduction, it is a reserved one, as we are before a patient over 25 years of age with a development of bone, pulmonary and ganglionary metastases where in spite of the regression with cytostatic drugs, still remained a residual tumor which is bulky and unresectable, gathering a high probability of keeping an active seminoma.[1,3,6,9,1] ■

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