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Oligosymptomatic tumors – Traps for doctors and patients

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Abstract

English:

Few patients are fortunate enough to get detected in the early stages of tumors whether benignant or malignant. This chance, with multiple hidden ethical issues, has pitfalls for both doctors and patients. We are presenting two cases, a male and a female with diagnosis problems successfully managed even if they are not convinced about the necessity of the surgery. The male, aged 63 years, non-smoker, with occupational exposure for 41 years, oligosymptomatic, during a preoperative routine X-ray and thorax CT for a left hydrocele operated in June 2020, was identified an acidophilic tumor formation, located in the anterior mediastinum. Additional investigations revealed a left vocal cord paresis and the transthoracic needle biopsy raised suspicion of thymoma with glandular areas and clear cells, also confirmed by surgery, an N0 stage. In the second case, a 42 years female with a recent history of SARS-COV-2 viral infection, mild clinical form, while performing a CT scan to assess COVID status, discovered a tumor mass located in the anterior mediastinum. ENT examination establishes the diagnoses of subacute laryngitis, dysphonic syndrome under etiological observation, and chronic rhinitis. The excision of the mediastinal formation is performed with favorable postoperative evolution. Histopathological examination highlighted changes that argue the diagnosis of mature intrathymic teratoma. Apparently, there were fortunate cases with curative resection, but being oligosymptomatic also involved substantial efforts to convince the patient and the caregivers about the need for urgent surgery.

Keywords

thymoma • mature intratimic teratoma • oligosymptomatic

Tumori oligosimptomatice – capcane pentru medici și pacienți

Rezumat

Romanian:

Puțini pacienți au șansa de a fi detectați în stadii incipiente ale tumorilor, fie ele benigne sau maligne. Această șansă are multe aspecte etice ascunse, capcane atât pentru medici, cât și pentru pacienți. Vă prezentăm două cazuri, un bărbat și o femeie, cu probleme de diagnostic, gestionate cu succes în ciuda caracterului refractar asupra necesității intervenției chirurgicale. Bărbatului, în vârstă de 63 de ani, nefumător, cu expunere profesională timp de 41 de ani, oligosimptomatic, în cadrul unei evaluari preoperatorii pentru hidrocel stâng, operat în iunie 2020, i s-a identificat o formațiune tumorală acidofilă, localizată în partea anterioară a mediastinului. Investigațiile suplimentare au evidențiat pareză a corzii vocale stângi, iar puncția-biopsie transtoracica cu ac, a ridicat suspiciunea de timom cu zone glandulare și celule clare, confirmat ulterior prin intervenție chirurgicală, stadiu N0. În cel de-al doilea caz, o femeie de 42 de ani cu antecedente recente de infecție virală SARS-COV-2, formă clinică ușoară, în timpul efectuării unui CT pentru evaluarea statusului post - COVID, a descoperit o masă tumorală localizată în mediastinul anterior. Examenul ORL stabilește diagnosticele de laringită subacută, sindrom disfonic de etiologie neprecizată și rinită cronică. Excizia formaţiunii mediastinale se realizează cu evoluţie postoperatorie favorabilă. Examenul histopatologic a evidențiat modificări care susțin diagnosticul de teratom intratimic matur. Aparent, au fost cazuri cu circumstanțe favorabile, beneficiind de rezecție curativă, însă întocmai caracterul oligosimptomatic a implicat eforturi substanțiale pentru a convinge pacientul și aparținătorii de necesitatea unei intervenții chirurgicale urgente.

Cuvinte-cheie

timom • teratom matur intratimic • oligosimptomatic

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Introduction

Early detection of malignant diseases in patients is a real problem for the doctors and patients. Thymic epithelial tumors are the most common neoplasms arising from the anterior mediastinum (1). It is difficult not only to preoperatively predict the WHO malignancy grade and the invasive potential of thymic epithelial tumors but also of other types of tumors located in the anterior mediastinum. The practitioner has also other additional problems. Irrespective of size, a tumor may be considered high-grade and could invade the surrounding organs (2). We are trying in this presentation to describe the diagnosis and therapeutic problems found in two cases of mediastinal tumors.

Case 1

The first patient, M.G, a male, non-smoker, resident in Arges County, aged 63 years with occupational exposure for 41 years, came to our clinic being oligosymptomatic (only with dysfonia). On a preoperative routine X-ray and thorax CT for a left hydrocele operated in June 2020, it was detected an iodphilous tumor formation, anterior mediastinum, with diameters of 39/69/77 mm, with calcifications inside, with extension to the left lung and a fibrous nodule in the left upper place, subpleural, with small fluid collection at the anterior pericardial recess (Figure 1). The patient had a pathological history consisting of a cervical lipoma and a left vocal cord paresis identified by adjacent biological and mini-invasive investigations (bronchoscopy). The suspicion of thymoma with glandular areas and clear cells was raised by the transthoracic needle biopsy (Figure 2). Surgery highlighted an encapsulated thymoma, an encapsulated formation with polycyclic contour and focal calcifications, and staged N0 (Figure 3). The anatomopathological test confirmed that it was a type A thymom (Figure 4) and the patient needs to undergo chemo and radiotherapy.

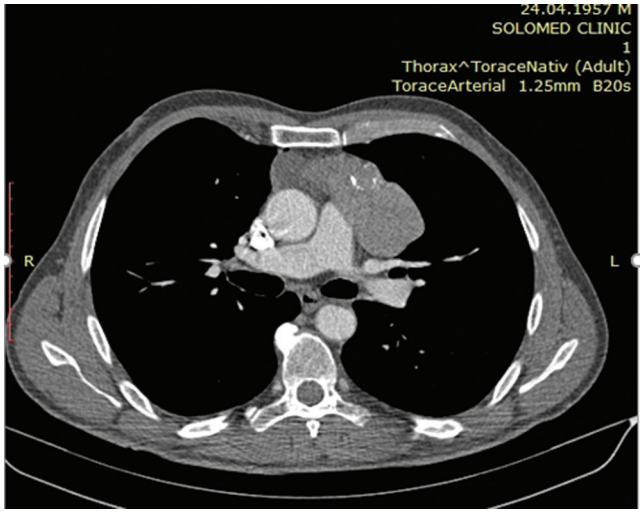


Figure 1. Iodophiltumor tumor formation of 36.6/69.6/76.8 mm at the level of the anterior left-hand mediastinum, with non-homogeneous structure, with calcifications on the inside. The tumour is in contact with the ascending aorta and the trunk of the pulmonary artery. No mediastinal adenopathy.

Case 2

The second one, a case was of a 42-year-old female patient, D.N.G, a non-smoker, a nurse by profession, known with a recent history of SARS-VOC-2 viral infection, a mild clinical form, circumstances to perform a chest CT scan to assess COVID status. Thus, reticular interstitial lesions are described, subpleural located, in association with discrete ground-glass areas, with bilateral basal subpleural predominance

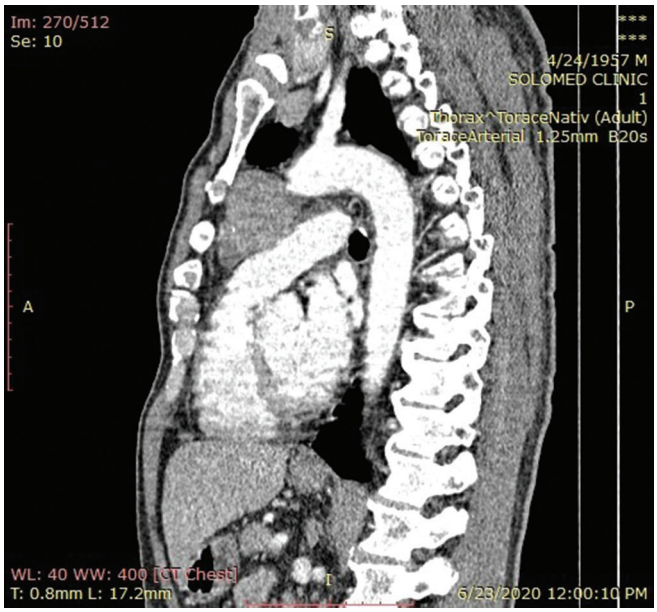


Figure 2. Thorax CT scan used for transthoracic puncture – Tumor fragments with a polymorphic appearance. Part of the fragments consist of an epithelial proliferation, either disseminated or aggregated in groups or beaches. Fusiform and oval epithelial cells have fine granular chromatin, small single wallnut and are intrigued with small lymphocytes with condensed chromatin. In other areas, tumor fragments are made up of cuboidal cells with hyperchromic cells, fine granular chromatin, pale cytoplasm, being arranged in glandular structures. Zonal is found a proliferation made up of cell nests with round nuclei, slightly pleomorphic, clear cytoplasm. Tumor nests are separated by conjunctive septums that are hyalinized. Timom with glandular difference aries and clare cell component.

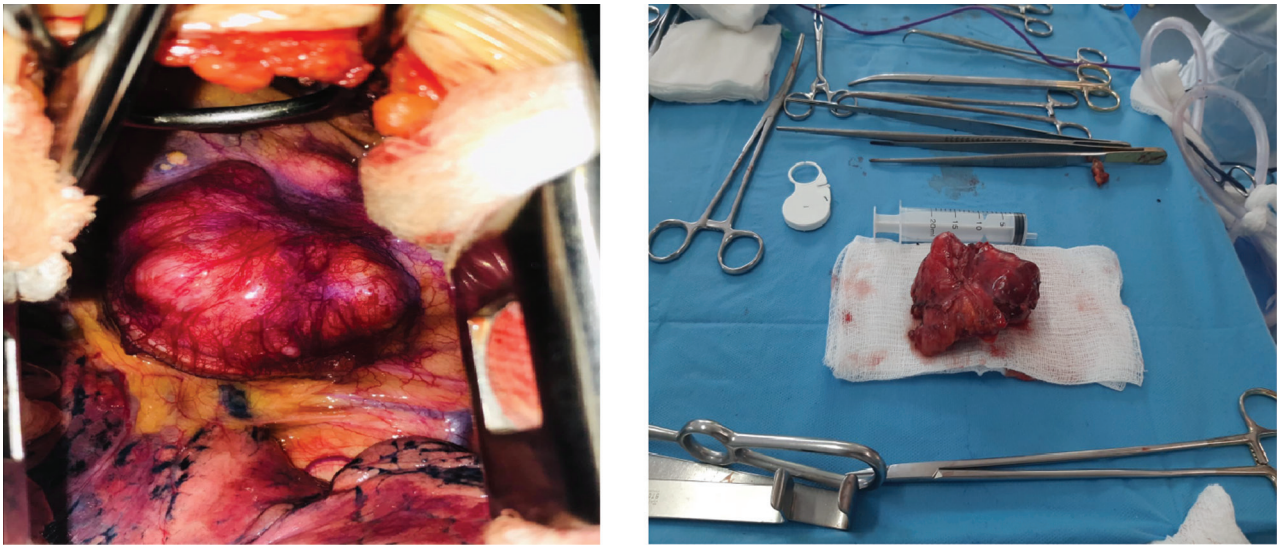
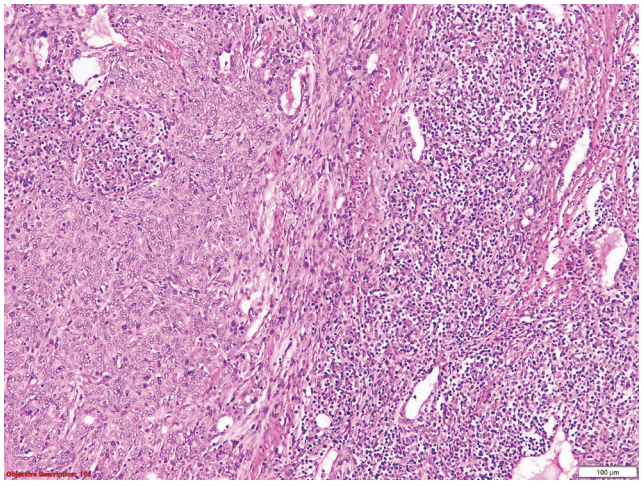


Figure 3. Macroscopic tumour image – The 10/7 cm tumor, of hard consistency and polylobulate appearance, was highlighted.

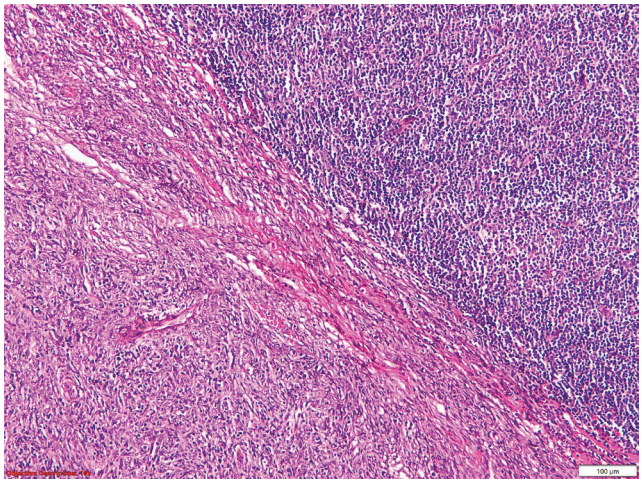
(Figures 5A and B), and, respectively, a tumor mass located in the anterior mediastinum (Figures 6A and B). In the context of the described facts, the patient was directed to our unit to establish the etiology and to adopt the appropriate therapeutic management. Medical history reports repeated episodes of chest tightness, intermittently present, associated with a recurrent dysphonic syndrome, which occurred paroxysmal during the last 2 years. Clinical examination at presentation was normal, subject to over optimal BMI values (25.35 kg/m^2). Lacking firm respiratory symptomatology, specific investigations are carried out to document the etiology of the tumor. The reassessment chest CT scan confirm on the anterior mediastinum a nodule of about 32/22 mm, with lipid inclusions and fine peripheral calcifications, complete remission of interstitial changes developed in the viral context, without other notable changes (Figures 7A and B). Biologic samples within normal limits, except for a discrete hepatic cytolysis syndrome (TGP 1.5 × upper limit of normal). In terms of respiratory function, we mention plethysmography, alveolo-capillary diffusion with normal values of lung volumes and ventilatory flows, slightly low alveolo-capillary diffusion, normal transfer constant (DLCO C 76.8%, KCO c 86.8%). Complementary to the previously mentioned investigations, a bronchoscopic examination is performed, which does not identify patent proliferative lesions in the explorable areas, noting the larynx with the present dynamics and a bilateral diffuse bronchial appearance, negative tumor cytology. The performed ENT exam establishes the diagnoses of subacute laryngitis, dysphonic syndrome under etiological observation, and chronic rhinitis, with the recommendation of a phoniatrics examination and phoniatric exercises, subsequently NFL fibroscopic reassessment. In the clinical and paraclinical background described above, practically an asymptomatic patient, incidentally diagnosed with mediastinal tumor mass on the prevascular area, it is considered opportune to evaluate the case from a surgical point of view, considering tumor resection, an indication firmly established after the examination. Undergoing general orotracheal anesthesia, a right side thoracic approach is performed with pleural access through the fourth intercostal space, upon entering the pleural cavity, finding normal lungs and pleura, secondary, being described on the anterior mediastinum a well-defined tumor formation, round-oval, with dimensions of about 4/5 cm. The excision of the mediastinal formation is performed with its reference to a histopathological examination, hemostasis control. Favorable postoperative evolution is noted, with no complications. Histopathological examination (Figures 8A and B) macroscopically describes, spherical tumor mass, encapsulated, of firm consistency, 25 g, with free resection margins (non-tumor), microscopic with cystic formation aspect, developed intrathymically, with a fibrous wall, associating intraparietal smooth muscle fibers, bone tissue, choroid plexus, mucous glands, seromucous, sebaceous glands, microcalcifications, changes that argue the diagnosis of mature intrathymic teratoma.

Discussion

The majority of anterior mediastinal masses are thymic-derived and can be divided into neoplastic and non-neoplastic processes. Thymomas are uncommon and slow-growing tumors that arise from epithelial cells of the thymus gland. The overall incidence in the United States is estimated to

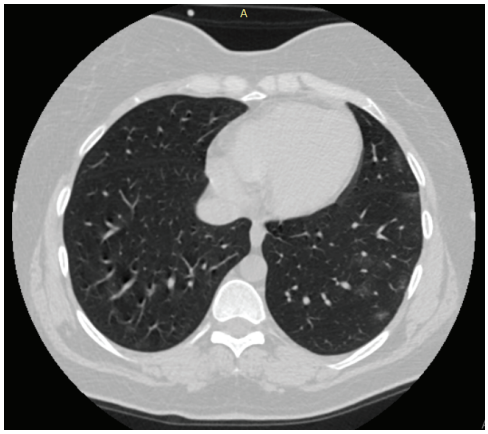


(A)

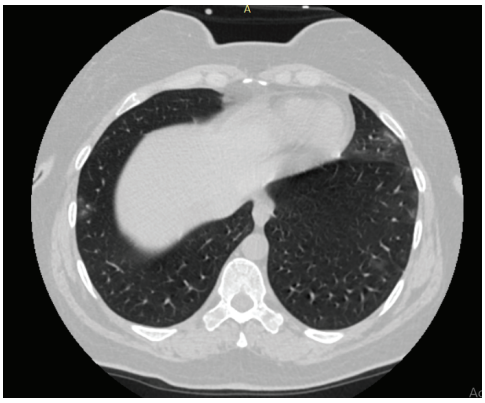


(B)

Figure 4. Histopatologic examination – From the resected tumoral block. Tumor formation of timic origin with integrated capsule, non-infiltrated, with septate nodular growth, of biphasic histological consistency, respectively with type A component, with proliferation of fusiform and cubic epithelial cells, on a poor lymphocytic background, intrigued with the predominant lymphocytic component. Mediastinal peritumoral – Fibroadipos connective tissue, which includes well-delimited stem tissue, identifies micronodular proliferation, consisting of an oval epithelial cellularity, without atipia. Thymom type AB, without capsular invasion, with satellite microthymomas.



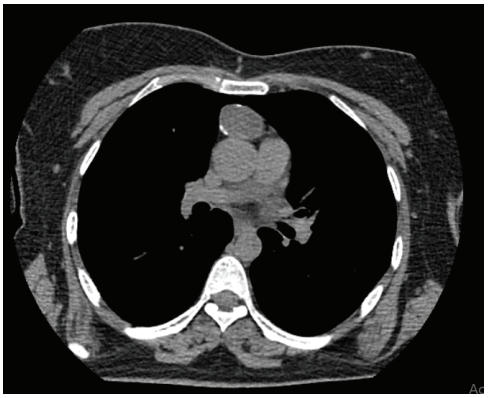
(A)



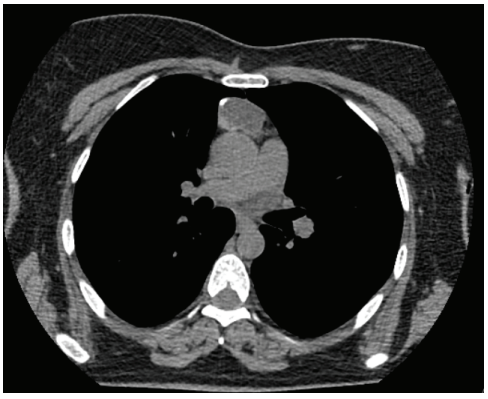
(B)

Figure 5. Initial CT scan – Reticular interstitial lesions are described, subpleural located, in association with discrete ground-glass areas, with bilateral basal subpleural predominance.

be approximately 0.15 cases per 100,000 person-years, which translates to around 400 cases per year for the entire country (3). The current World Health Organization (WHO) classification of tumors of the thymus supports the approach introduced in 1999 by Rosai and Sobin (4), which divides thymomas based on the shape of the neoplastic thymic epithelial cells and the amount of background lymphocytes into five groups: type A corresponds to tumors in which the neoplastic cells are oval or spindle-shaped. Type A thymoma, the tumor diagnosed in the first case, is characterized by its great variability of morphologic growth patterns and, as such, the possibility of mimicking a wide variety of other neoplastic mediastinum disorders (5). In particular for the first case, if we compare the output of the transthoracic needle biopsy with the final result of the tumor extracted by surgery we can only reconfirm what the experts are sustaining, that the final diagnosis should be reserved until after the examination of the completely resected specimen has been carried out (6). In adults, the most common mediastinal tumors are epithelial (46%), followed by hematopoietic (23%), endocrine (16%), and germ cell tumors (15%) (7). Thymomas represent the most common type of thymic tumors and are classified based on the appearance and proportion of the neoplastic epithelial cells. Thymoma is the most common thymic epithelial tumor and it accounts for 15–21.7% of tumors in the mediastinum and 47% of tumors in the anterior

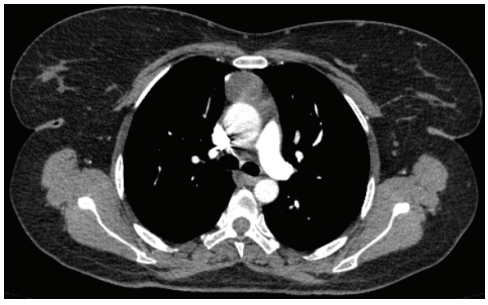


(A)

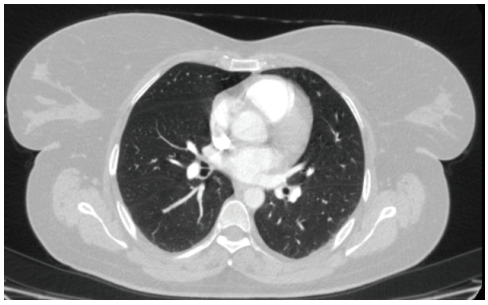


(B)

Figure 6. Initial CT scan – A tumor mass located in the anterior mediastinum.



(A)



(B)

Figure 7. Repetead CT scan. Anterior mediastinum a nodule of about 32/22 mm, with lipid inclusions and fine peripheral calcifications, complete remission of interstitial changes developed in the viral context, without other notable changes.

mediastinum (8). These tumors can have aggressive behaviors such as invasion of adjacent thoracic, with involvement of the pleura and pericardium; however, long-distance metastatic disease is rare (9). Our first patient had a pericardial involvement and satellite micro-thymomas. The most important prognostic indicator is the tumor stage, which is determined by the extent of invasion into the surrounding soft tissue, involvement of adjacent organs, and distant spread. In the mediastinum, the most common modalities for procuring biopsy samples from mass lesions include fine-needle aspiration, percutaneous core needle biopsy, and video-assisted thoracoscopic biopsy. The various morphological variations and overlap between subtypes cannot be assessed in aspirates or even in core biopsies. This happened with our first case where the transthoracic puncture only raised the possibility of a thymoma. Both tumors where discovered by chance, in a CT scan performed for an evaluation after preoperative investigations for another intervention, and, the second one., after a regularly check in CT scan for a COVID 19 infection. Probably this was chance for both because they were oligosymptomatic and were not aware of the existence of a lung disease. Among patients with thymic carcinoma, a number of 230 (42.0%) underwent initial surgery, and 124 (53.9%) received subsequent radiotherapy and chemotherapy (10). Thymic carcinoma tended to be diagnosed more frequently in advanced stages, and 106 (19.4%) affected patients underwent primary surgery, whereas 83 (15.2%) received initial chemotherapy and subsequent radiotherapy and surgery (10). Our first patient was successfully managed with the combinations of these three therapeutically options. The danger of postponing or delaying the intervention in such a case is because of the lack of symptoms for long period during tumor evolution. Approximately half of the discovered thymomas are asymptomatic, whereas the other half present paraneoplastic syndrome (PNS) (11). An extremely rare diagnostic is that of the teratoma mature intra thymic tumor. They form the commonest germ cell tumors (GCTs) and represent only 8–13% of all mediastinal tumors; they are more commonly found in the gonads, retroperitoneum or sacrococcygeal region (12, 13). Common differentials include thymoma, teratoma, thyroid disease, lymphoma,

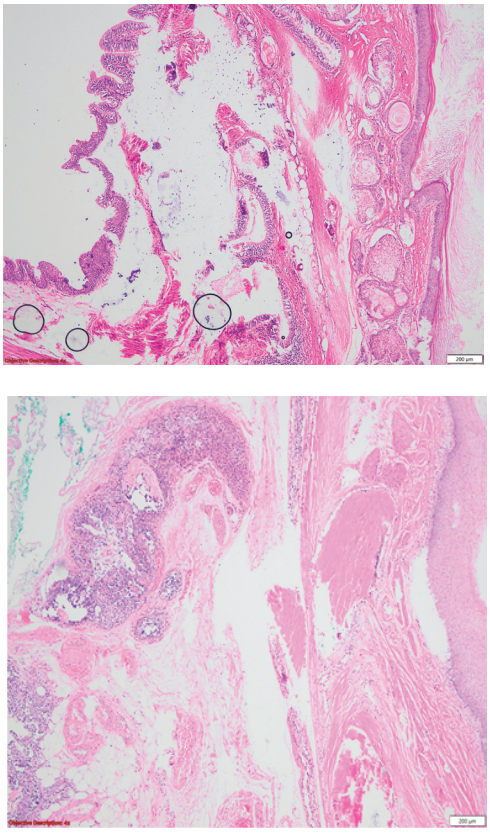


Figure 8. Histopathological evidences. Spherical tumor mass, encapsulated, of firm consistency, 25 g, with free resection edges (non-tumor), microscopic with cystic formation aspect, developed intrathymically, with a fibrous wall, associating intraparietal smooth muscle fibers, bones tissue, choroid plexus, mucous glands, sero--mucosa, and sebaceous glands, microcalcifications, changes that argue the diagnosis of mature intratimic teratoma.

cystic lesions, as well as neurogenic tumors. A small proportion of mature teratomas (<1%) have the potential to undergo malignant transformation. It was not the case for our patients. They are asymptomatic in up to 53% of cases and are often an incidental finding on a routine chest radiograph. This happens also in our patient after COVID-19 infection. Complete surgical resection is the recommended treatment for all mature teratomas not only for confirming the diagnosis but also for preventing future complications from this type of tumor. Survival rates have been reported to approach 100% at 5 years (14).

Conclusions

The common features of both cases are:

1. Both were discovered incidentally after investigations (X-ray and CT scan) for other diseases;
2. They were oligosymptomatic and it was difficult to convince them to be adherent to the radical solution of surgery;
3. Finally, even if we are speaking about a malign or benign thymic tumor, the cases where solved in a multidisciplinary working team, with hopes of long-term survival for these patients.

Ethical approval

Inform consent was obtained from the patient in order to participate to the study and write the article.

Conflicts of interest

The authors have no conflicts of interest to declare. All co-authors have seen and agree with the contents of the article and there is no financial interest to report. We mention that the patients' consent was obtained for the publication of the cases.

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