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Atypical behavior of thymic carcinoma

AIM: *To describe the case of a thymic carcinoma with atypical clinical behavior that has arisen with a voluminous metastasis at the right hemidiaphragm while the primitive thymic neoplasm was initially occult.*
CASE REPORT: *A 42 years female patient came to clinical observation for a voluminous thoraco-abdominal mass located in right side, infiltrating the diaphragm. The patient was submitted to surgical excision of the mass; definitive histological examination: non-keratinizing spinocellular carcinoma suggestive for neoplasia on ectopic thymic tissue or metastasis from carcinoma of the thymus. Three 3 months after surgery MR and CT-scan restaging identified the presence of anterior mediastinal mass of about 3 cm of diameter, compatible with thymical origin; thymectomy was performed (histology: Lymphoepithelial thymoma). Eight months after the first surgical procedure a restaging by CT, MR and PET CT showed the presence of disease recurrence at the right diaphragmatic level. The patient underwent surgical exploration, with right thoracotomic approach: a metastasis in the hepatic segment VII was found and radically removed. Six months after liver metastasis resection, CT scan showed disease progression in mediastinum, with involvement of pericardium and aorta; the patient died for disease recurrence five months later, 22 months after the first surgical procedure.*
CONCLUSION: *Thymic neoplasms are the most common tumors of the mediastinum; a small percentage of these tumors are however extremely aggressive carcinomas. Rare but not exceptional findings are also cancers arising from ectopic thymic tissue.*

KEY WORDS: Cancer, Metastasis, Thymus

Introduction

Thymic neoplasms are the most common tumors of the mediastinum, usually presenting an indolent clinical course [1]. A small percentage of these tumors are however extremely aggressive carcinomas, with typical tendency to mediastinal invasion, pleural dissemination, metastatisation [2] and poor survival rates [3]. Rare but not exceptional are also cancers arising from ectopic thymic tissue [4].

Case report

A 42 years female patient came to clinical observation because of right hemithorax, right hypochondrium pain and worsening dyspnea.
The thorax–abdomen CT scan and MR discovered the presence of a 9 cm voluminous mass located in right side of the chest, infiltrating the diaphragm (Fig. 1). No other pathological findings were detected.

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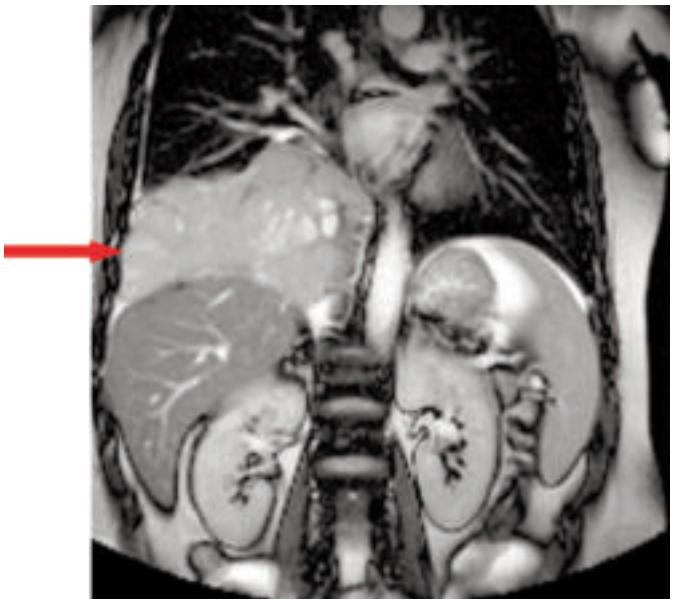

Fig. 1: CT scan with coronal reconstruction: thoracic mass located in right side, infiltrating the diaphragm.

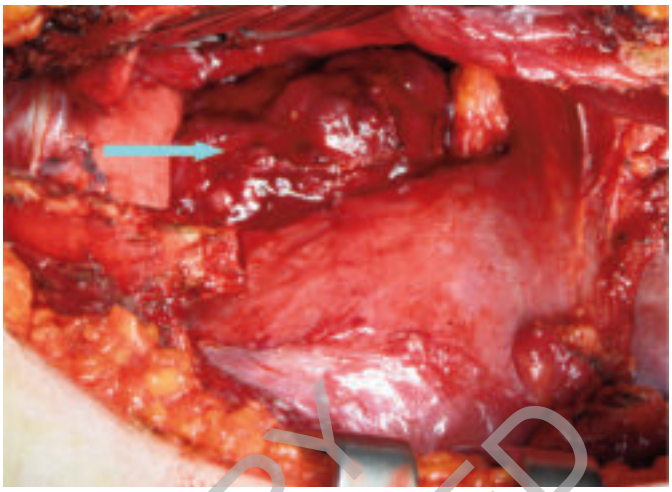

Fig. 2: Surgical exeresis of thoracic mass (thoraco – phreno- laparotomic approach).

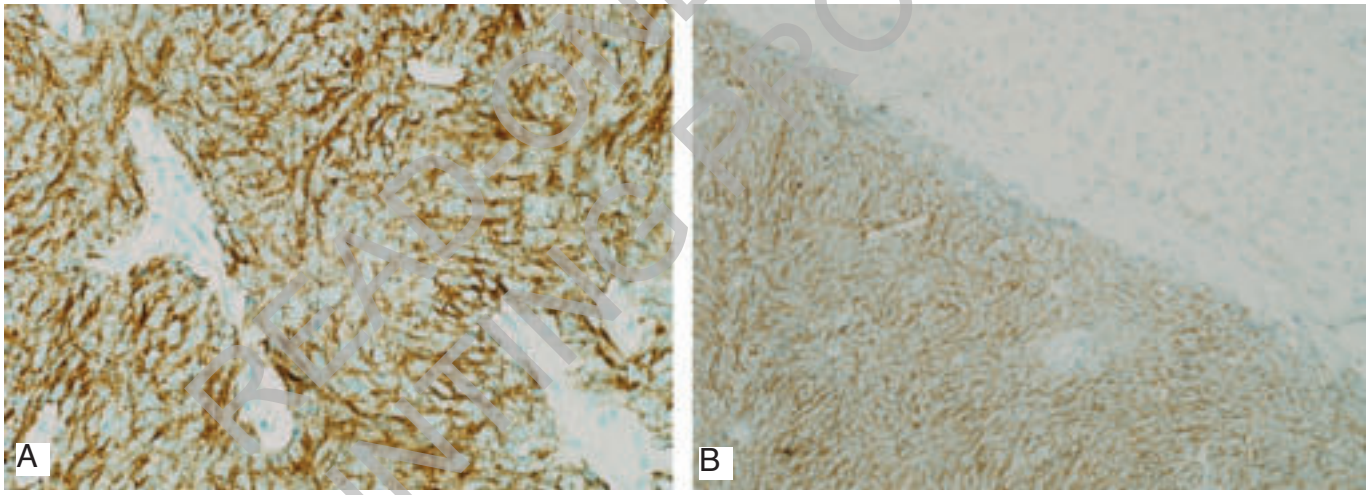

Fig. 3: Histology of the thoracic mass; A) (cytokeratin 5/6 coloration); pankeratin coloration; B) localization poor differentiated carcinoma of the thymus.

CT-guided biopsy confirmed the presence of spinocellular carcinoma K + p 63+.
The patient was submitted to surgical excision of the mass (Fig. 2). A thoraco – phreno laparotomy was performed and the mass resected en bloc with the right hemidiaphragm which was reconstructed with dual mesh. Definitive histological examination showed a non-keratinizing spinocellular carcinoma suggestive for neoplasia on ectopic thymic tissue or metastasis from carcinoma of the thymus (Figg. 3A and 3B).

Three months after surgery MR and CT-scan restaging identified an anterior mediastinal mass of about 3 cm of diameter, compatible with thymus origin (Fig. 4); thymectomy was performed with median sternotomic approach; final histology showed the presence of lymphoepithelial thymoma .
The patient underwent adjuvant chemotherapy (Protocol ADOC, 3 cycles).
Eight months after the first surgical procedure, CT scan and MR detected a subphrenic pathological tissue sus-

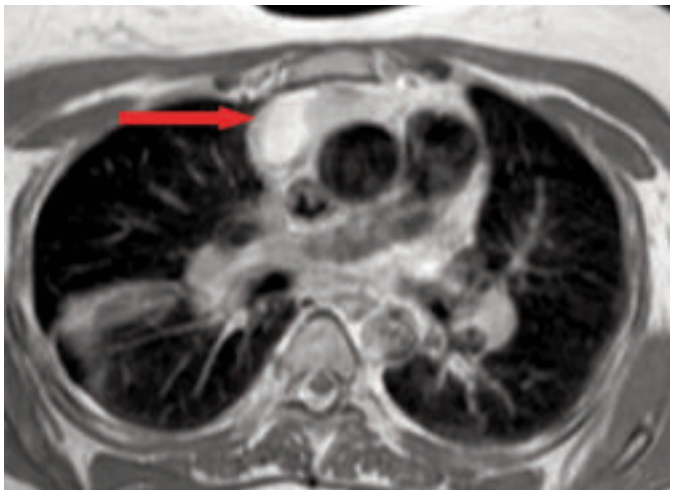

Fig. 4: Thorax MR showing an anterior mediastinal mass (suspect thymic cancer).

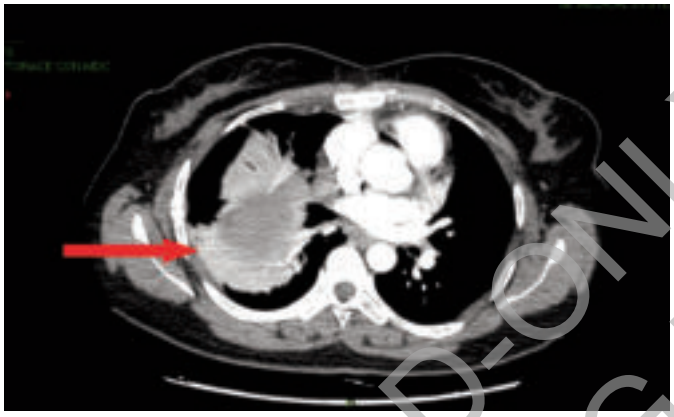

Fig. 5: Right subphrenic pathological tissue suspect of disease recurrence.

pected for disease recurrence; PET-CT also highlighted the presence of abnormal caption at right hemidiaphragm (Fig. 5).

The patient underwent surgical exploration, with right thoracotomic approach; no pathological findings have been found in the thorax; the dual mesh previously places in order to reconstruct the diaphragm was detached for right subprhenic space exploration; a metastasis in the hepatic segment VII was discovered and radically removed; the dual mesh was finally re-inserted.

Six months after the resection of liver metastases, CT scan showed disease progression in mediastinum, with involvement of pericardium and aorta (Fig. 6); a second line chemotherapy was started without any further surgical indications.

The patient died for disease progression five months later, 22 months after the first surgical procedure.

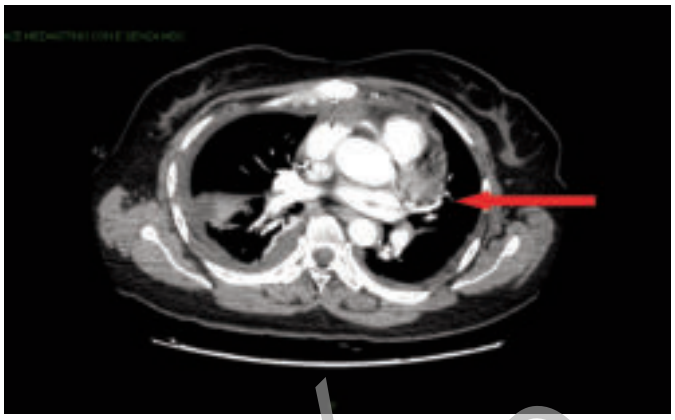

Fig. 6: Thorax CT scan showing disease progression, with neoplastic tissue infiltrating mediastinum, pericardium and aorta.

Discussion

Thymic carcinomas are rare and aggressive cancers often diagnosed at an advanced stage, with typically early mediastinal progression and a low survival rate at 5 years [5]. Scientific literature also reported rare but not exceptional cases of ectopic thymic tissue, derived from aberrations during the normal embryonic migration from third and fourth branchial pouch to the mediastinum; from these islands of thymic tissue, tumors can develop; ectopic thymic tissue locations have been described at the base of the skull, lung parenchyma, pleura and mediastinum. CT and NMR are useful diagnostic tools for the diagnosis of thymic masses; in addition, as suggested in a review of Literature [6], nuclear medicine imaging with Thallium-201, 99mTc-sestamibi, 99mTctetrofosmin, and also PET – CT scan, can provide additional information in cases of thymoma such as in differential diagnosis between thymic tumors, staging and restaging.

In our case, all the CT and MR scans have been revised after the definitive histological diagnosis had been made; no mediastinal nor thymic masses were definitively detectable. PET CT was not performed before the first surgical procedure because we thought that this procedure would not have been able to highlight any pathological capitation of an hypothetical primitive thymic mass, so small as to be invisible at thin slice CT and MR.

A proper histological type, early diagnosis, radical surgical excision with adequate adjuvant radio-chemotherapy are mandatory for proper clinical management of thymic carcinomas [7].

Surgery is the treatment of choice for thymic tumors and complete resection is the most important prognostic factor [8]; adjuvant radiation is recommended for invasive thymoma; a careful evaluation of signs of airway obstruction and cardiovascular complications is crucial for the management of anaesthesiological risks [9].

The treatment of recurrences, as observed in our case, remains still controversial; anyway, as suggested by experienced Authors, considering the particular spread of thymoma and the encouraging results of the aggressive surgical approach, re-resection should be recommended in resectable recurrent thymomas [10], even in cases of involvement of vital structures [11].

Conclusions

We have reported a thymic carcinoma with atypical clinical behavior, presented as a voluminous mass in the right chest infiltrating the hemidiaphragm while the primitive thymic neoplasm was initially occult.
The absence of normal thymic tissue on the mass seems to exclude the hypothesis of a cancer arising from ectopic thymus, with subsequent metastatization to anterior mediastinum and liver.
We also excluded that the appearance of the thymic nodule after 3 months could have been a recurrence due to incomplete resection of the mass on the mediastinal site during the first surgical procedure; the thoracic mass appeared as involving the right hemidiaphragm, without any infiltration of mediastinum.
An aggressive treatment lead to a relatively long survival after diagnosis in a young patient affected by a very aggressive disease; an hypothetical diagnosis of the primitive thymic cancer would not have changed our approach, as recommended in Literature about surgical management of invasive and recurrent thymomas.

Riassunto

INTRODUZIONE: I timomi, le più comuni neoformazioni del mediastino anteriore, hanno in genere un comportamento clinico indolente, ma in alcuni casi possono risultare carcinomi estremamente aggressivi.
Di riscontro raro ma non eccezionale sono le neoplasie derivanti da tessuto timico ectopico.
CASO CLINICO: Una paziente di 42 anni di età è stata ricoverata presso la nostra Divisione a seguito del riscontro di una massa a livello dell'emitorace destro; TC e risonanza magnetica non avevano evidenziato ulteriori reperti patologici di rilievo.
RISULTATI: La paziente è stata sottoposta ad intervento di asportazione della lesione con ricostruzione dell'emidiaframma destro (esame istologico: carcinoma squamoso non cheratinizzante compatibile con origine timica). A tre mesi dall'intervento chirurgico le indagini di follow up hanno evidenziato un nodulo di circa 3 cm di diametro a livello del timo, non presente alla TC pre operatoria; la paziente è stata sottoposta a timectomia con approccio sternotomico mediano. Ad otto mesi dalla procedura chirurgica è stata inoltre eseguita l'escissione di una metastasi a livello del VII segmento. A sei mesi dalla resezione epatica, è stata evidenziata progressione mediastinica di malattia. La paziente è deceduta cinque mesi dopo, 22 mesi dal primo intervento chirurgico.
CONCLUSIONI: Il caso da noi osservato mostra un comportamento clinico estremamente atipico di un carcinoma timico manifestatosi con una voluminosa massa metastatica all'emitorace di destra, con primitivo inizialmente occulto. L'assenza di tessuto timico normale nella massa rimossa chirurgicamente sembra escludere l'ipotesi di un carcinoma originatosi da tessuto timico ectopico successivamente metastatizzato al timo.

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Commento e Commentary

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Sopravvivenza a lungo termine e qualità di vita sono le finalità principali che si propone le chirurgia nei pazienti affetti da cancro.
Questa osservazione si riferisce ad un paziente giovane affetto da un cancro del timo, che sopravvisse "soltanto" 22 mesi dopol'intervento. I chirurghi erano rimasti sorpresi di trovare un cancro del timo in una massa intratoracica a destra che recidivò dopo tre mesi, ed il paziente venne sottoposto ad un altro intervento prima del decesso.
Una revisionerecente condotta su 68 casi di carcinoma timico trattati in vario modo ha dimostrato una sopravvivenza media di tutti i pazienti di 36,4 mesi (con intervallo di confidenza del 95% di 23,7-56,4 mesi), laddove per pazienti allo stadio II, III, IV a la sopravvivenza era rispettivamente di 65,8, 24,6 e 27,3 mesi [1]. Da ciò sorge l'ovvio interrogativo: come per la metastasectomia polmonare [2]: qual è il limite che giustifica un intervento chirurgico per un cancro timico in stadio avanzato?
Quando la chirurgia non è efficace, come nell'esempio del mesotelioma pleurico [3], bisogna cercare nuovi trattamenti multimodali per dare speranza ma non illusione senza speranza ai nostri pazienti. Ad esempio un recente contributo dimostra che S-1 ha un rilevante effetto contro il cancro timico recidivo in un paziente che sopravvisse per più di 48 mesi [4]. Sulla base di questo singolo caso è stato iniziato uno studio prospettico di fase II per valutare l'efficacia del S-1 nei confronti del cancro timico recidivo. Chirurgi ed oncologi hanno ben presente che è molto difficile condurre trial randomizzati e controllati per una malattia così rara come il carcinoma del timo, che rappresenta meno di 1-4% dei tumori epiteliali del timo.
Nel Regno Unito nel 2006 la NICE (National Institute for Health and Clinical Excellence) ha lanciato una iniziativa per identificare interventi segnalati dal (National Health System) che non producono beneficio ai pazienti.
È dunque necessario sapere qual è lo standard per accettare di insistere con una particolare procedura su pazienti oncologici [5]. Nel futuro bisogna fare sforzi per dimostrare con evidenza che la procedura per ciascuna malattia oncologica di interesse chirurgico abbia efficacia a prolungare la sopravvivenza e migliorare la qualità di vita.

* * *

Long term survival and quality of life are the most important goals when surgery is performed in patients with cancer. This case reports a young patient with thymic cancer who survived "only" 22 months after the first operation. The surgeons have been surprised to find a thymic cancer in the intrathoracic right mass which recurred after 3 months, and the patient underwent another operation before death.
A recent review performed on 68 patients treated with various modalities for thymic carcinoma showed that the median survival time for all patients was 36.4 months (95% confidence interval, 23.7-56.4 months), whereas for patients with stage II, III, IVa were 65.8, 24.6, and 27.3 months, respectively [1]. The question that arises is obvious: as for pulmonary metastasectomy [2] what are the limit to justify an operation for advanced stage thymic cancer? When surgery "does not work" as for example is pleural mesothelioma [3], new multimodality treatments must be searched to give hope but not hopeless illusion to our patients. For example a recent report shows that S-1 has a remarkable effect against the relapsed thymic carcinoma in one patient who survived more than 48 months [4]. On the basis of single case reports, a prospective phase II study has been initiated to evaluates the efficacy of S-1 against relapsed thymic carcinoma. Surgeons and oncologist keep well in mind that it is very difficult to perform randomized controlled trial in rare diseases as thymic carcinoma which is a rare tumour accounting for less than 1–4% of thymic epithelial tumors,
In united kingdom in 2006 NICE (National Institute for Health and Clinical Excellence) launched an initiative to identify interventions delivered by the NHS (National Health System) that do not benefit patients. It is therefore necessary to know what is the standard to accept to persist with a particular practice in oncologic patients [5]. In the future efforts must be done to demonstrate evidence that the practice for every surgical oncologic disease is effective to prolong survival and improve quality of life.

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