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THYMIC CARCINOMAS DIAGNOSED AT THE PATHOLOGY DEPARTMENT AT JRA HOSPITAL

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ABSTRACT

Thymic carcinomas are rare epithelial tumours belonging to the group of epithelial tumours of the thymus. It is an aggressive lesion with a high frequency of metastases. Its local recurrence rate is over 50%, the survival rate between 5 and 10 years is less than 20%.

This study describes the epidemiological and histopathological features of thymic carcinomas with a review of the literature.

We report three cases including two men and one woman, respectively aged 20, 58 and 20 years old, who consulted for an anterior mediastinal mass. Surgical excision was performed in two cases and biopsies in one case. On gross findings, the specimens were firm non- encapsulated tumours. In all cases, histological examination suggested thymic carcinoma.

Thymic carcinomas present non-specific histological features. The diagnostic criteria for the primary tumour site are in most cases based on a combination of clinical and morphological data.

KEY WORDS: *Carcinoma, Madagascar, Thymus, Thymic Epithelial Tumour*

INTRODUCTION

Thymic epithelial tumours are rare pathologies but represent 20% of mediastinum tumours [1] and are the first cause of anterior mediastinal mass (35 to 50% of cases). According to World Health Organization (WHO) classification in 2004, thymic epithelial tumors are divided on three types: thymomas (80% of cases), thymic carcinomas and neuroendocrine tumours (5%) [2, 3]. Thymic carcinomas have an incidence of 0.2 to 0.5 per million people [4]. Itrepresent 5% of all malignant thymic tumours and 15% of thymic epithelial tumours. These are aggressive tumours [1, 5]. The overall survival rate at 5 years is about 30 to 50%, and it is less than 20% between 5 and 10 years [6, 7]. The aim of our study is to describe the epidemiological and histopathologicalfeatures of thymic carcinomas, diagnosed at the Department of Pathalogy, with a review of the literature.

Materials and method

This is a retrospective and descriptive study of thymic carcinomas diagnosed at the Department of Pathalogy at JRA Hospital, during 10 years from January 2010 to December 2019.

RESULTS

We collected three cases.

The first patient was a 20-year-old man. He presented chest pain revealing on imaging the presence of a left antero-lateral mediastinal mass with a nodule in the pleura opposite the mass, and without particularities for the other organs. He underwent excision of the mediastinal tumour and the pleural nodule for histological examination. On macroscopic examination, the nodule was greyish, firm, 1.5x1x0.5 cm. The mediastinal mass was brownish, firm, non-encapsulated measuring 10x8x5 cm. The sectioned surfaces were heterogeneous brownish-white. On histological examination, the two samples presented the same morphological structures. It was a malignant tumour proliferation made up of large polyhedral cohesive cells with hyperchromatic, nucleolated nuclei. There was no focus of necrosis The stroma was fibrous. The histological features suggested thymic carcinoma withpleural extension.

The second patient was a 58-year-old man who had a tumour in the anterior mediastinum associated with chest pain and whose imaging revealed no other tumour lesions in other organs. A surgical excision of the tumour was performed which, at the gross examination, was greyish, firm, non-encapsulated specimen, measuring 6x5x3cm. The sectioned surface was heterogeneous with multiple whitish nodules measuring 0.3 to 1.2 cm in diameter and foci of necrosis. On histological examination, it was lymphoid tissue infiltrated by carcinomatous cells, with moderate cytonuclear atypia, organized in clusters or strips or in a solid mass focally centered by necrosis. Three mitosis per 10 high-power fields (HPF) were observed. The diagnosis was a non-keratinizing squamous cell carcinoma whose thymic origin cannot be excluded.

The third patient was a 20-year-old woman with a mediastinal tumour, without any other particularities for the other organs. Biopsies were performed, and the specimens measured 1.5cm. The histological feature was a proliferation tumor of atypical cohesive cells (Fig 1), with a large hyperchromatic nucleus and scanty cytoplasm. No foci of necrosis were observed. The diagnosis was a thymic carcinoma.

DISCUSSION

Thymic epithelial tumours represent 35 to 50% of anterior mediastinal masses [1]. Several systems have been used in their classification. In 1999, the WHO published a histopathological classification of thymus tumours and classified thymoma into six types: A, AB, B1, B2, B3 and C. Thymic carcinomas are classified as thymoma type C in this first classification. It was updated in 2004 and then in 2015 and thymic carcinomas are considered to be a separate group from thymomas [1, 3, 7]. They represent less than 5% ofall malignant thymus tumours and 15% of epithelial tumours. They correspond to malignant epithelial proliferation arising from thymic epithelial cells [1, 5, 8]. We collected only three cases on 10 years, which can also testify to the rarity of thymic carcinomas reported in the literature.

Thymic carcinomas can occur at any age but are most common in adults between the ages of 30 and 60, with an average age of 46. In the literature, a male predominance is noted with a sex ratio of 1.5 as in the series by Suster and Rosai [8, 9], Chun-Hsiang Hsu et al [7]. In our study, two patients were 20 years old and one was 58 years old. Due to the small size of our cases, the peak frequency or the assertion of male predominance could not be determined.

From a clinical point of view, thymic carcinomas are often symptomatic due to their aggressive character from the outset. Most of the time, these are non-specific symptoms linked to local tumour invasion or to a mass effect in the mediastinum, such as cough, chest pain, superior vena cava syndrome or phrenic paralysis. In our study, the patients mainly presented with chest pain and the paraclinical examination revealed the existence of an anterior mediastinal mass leading to the realization of tumour excision in two cases and biopsies in one case.

The diagnosis is histological. On gross examination, it is typically, in the series by Ayadi- Kaddour A. et al [10], a bulky mass of irregular contours measuring between 8 and 15 cm diameter, non-encapsulated, greyish-white in color, with cystic, hemorrhagic and/or necrotic changes. In our study, the specimen had 6 and 12 cm of diameter with macroscopic features resembling to those observed by Ayadi-Kaddour A. et al [10].

Histologically, primary thymic carcinoma is defined as a malignant epithelial tumour with cytological features of overt malignancy, having a primary location in the anterior mediastinum with no evidence of a similar tumour elsewhere [11]. The histological criteria to be specified, expect of the cellular type, are the extent of necrosis and the mitotic index

estimated at more than ten mitoses per 10HPF. The WHO histopathological classification specifies the different entities of thymic carcinomas. [10], with epidemiological particularities and different prognosis. Among the subtypes, squamous cell carcinoma (40%) and lymphoepithelial carcinoma (15%) are the most common [11, 12]. In our series, the diagnosis was suggested by the presence of malignant tumour proliferation composed by large, polyhedral and cohesive cells with hyperchromatic, nucleated nuclei. Foci of necrosis were seen in one case.
According to Ricardo V. Lloyd [13], thymic carcinoma of the keratinizing squamous type is composed of large polyhedral cells arranged in nests and cords. They are cohesive. The nuclei are vesicular or hyperchromatic, and the nucleoli are generally apparent. The cytoplasm is eosinophilic, with horny beads. Foci of necrosis are frequently observed, as the invasion of blood vessels within tumours. The non-keratinizing variant differs from the previous description only in the presence of less differentiation. Cytoplasmic eosinophilia and keratinization are absent, with a desmoplastic fibrous stroma [13].

Thymic carcinomas are distinguished by a significant locoregional extension and frequency of metastases. They are aggressive tumours and when establishing the diagnosis, 40% of patients already present lymph node metastases and 10% distant metastases [4, 12]. In our study, pleural extension was noted in one case.
The morphological aspects of thymic carcinoma can sometimes mimic a B3 thymoma type and a thymus location of a carcinoma from another site [1].

The distinction between an aggressive B thymoma type (B3) and a thymic carcinoma is not always clear, and the diagnosis is difficult especially on small biopsy fragments [12, 14]. Immunohistochemical (IHC) study is recommended in this case [7]. Antibodies to CD5 and CD117 are indicated and their co-expression by epithelial cells is an argument in favour of thymic carcinoma [15].

Thymic metastatic carcinomas also represent a differential diagnosis important to mention,as was the case in two of our cases and should be distinguished from mediastinal or thymic locations of primary extrathymic tumours, such as pulmonary location. Primary thymic carcinomas are morphologically like to carcinoma developed in other anatomical sites [16]. This makes the establishment of the diagnosis of a primary tumour difficult. In addition, primitive thymic carcinoma is in most cases immediately invasive. Eighty percent of patients have invasion of the organs adjacent to the thymus (vessels, pericardium, and pleura) at the time of diagnosis. As a result, it is sometimes difficult to determine if it is a primary tumour or metastasis [4]. Due to the highly non-specific histology of thymic carcinoma, diagnostic criteria should in most cases be based on a combination of clinical and morphological data, which was for our cases. The role of histological examination is mainly to confirm a diagnosis of malignancy and specify the histological type of the lesion (squamous, lymphoepithelioma-like, basaloid, sarcomatous, etc.). The diagonasis of exclusion requires clinical investigations and thorough X-rays to exclude the possibility of malignancy in another organ. Weissferdt A et al [17] state that there are no distinctive or pathognomonic features of thymic carcinomas that can help establish a definitive diagnosis based only on histological examination, especially on biopsy, but immunohistochemistry helps to straighten diagnosis. Primary thymic carcinoma is distinguished from metastatic carcinoma by positivity for CD70 and CD5 [16], which indicates the thymic origin of the tumour proliferation. In our study, the IHC examination could not be performed, but according to the clinical and paraclinical data (tumour of the anterior mediastinum associated with chest pain without other tumour lesions in the other organs), the possibility of primary thymic carcinoma has been raised.

CONCLUSION

Thymic carcinomas are rare and have non-specific histological features. Through this study, we reiterate that the diagnostic criteria for primary thymic carcinoma should, in most cases, be based on a combination of clinical, radiological Interdisciplinary consultation between surgeons, pathologists and oncologists is crucial for the assessment of diagnosis, tumour stage and patient management. The surgeon must specify sufficient clinical information and correct orientation of the surgical specimen.

Thymic carcinomas diagnosed at the Pathology Department at JRA Hospital

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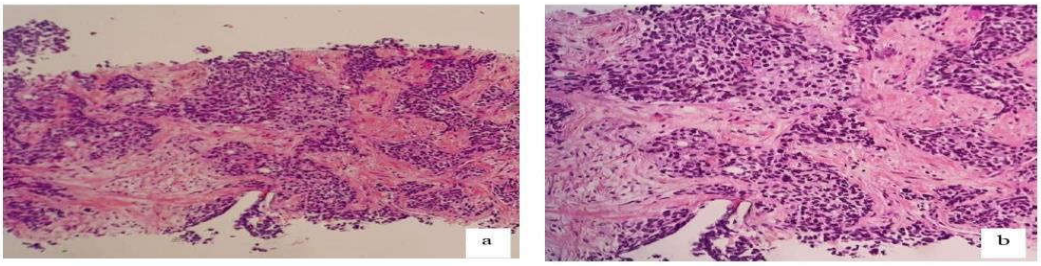

Figure 1 : Thymic carcinoma. HE x 100 (a) x200 (b).
Source : Department of Pathology at JRA University Hospital, Antananarivo Madagascar.

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