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NEUROENDOCRINE CARCINOMA OF THE THYMUS. CASE STUDY

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A b s t r a c t

Thymic and/or mediastinal carcinoids (recently renamed as neuroendocrine carcinomas of the thymus) occur very rarely, manifesting themselves by either their endocrine activity or an appearance of pulmonary mediastinal symptoms. Two cases of this tumour were diagnosed in our departments. One patient was a 76-year-old woman in whom a small tumour resembling an enlarged lymph node was removed from the thymic region during cardiosurgical intervention. The other, a 50-year-old man, had an aggressively growing tumour in the anterior mediastinum. Neither of the tumours showed any endocrine activity.

K e y w o r d s

Neuroendocrine carcinoma of the thymus, Aggressive and non-aggressive types

INTRODUCTION

The term „carcinoid" was introduced by Oberndorfer in 1907 to denote small intestine tumours that were less aggressive than true carcinomas. The endocrine activity of these tumours was discovered some years later by Gosset and Masson. Cases of carcinoids in different locations were reported in the following years. Thymic carcinoid was described for the first time by *Rosai* and *Riga* (*1*). The mediastinal localisation of carcinoids has recently been studied by *Moran* and *Suster* (*2*). These authors coined the term „neuroendocrine carcinoma of the thymus".

CASE STUDY

Two cases of thymic carcinoids were diagnosed in our departments and are described below.

CASE ONE

A 76-year-old woman underwent a minor cardiac surgery. In the course of operation, a small, encapsulated tumour-like body (about 20x20 mm in diameter) resembling an enlarged lymph node was found in the mediastinum. Histological examination revealed atrophic thymic parenchyma with typical Hassall' bodies

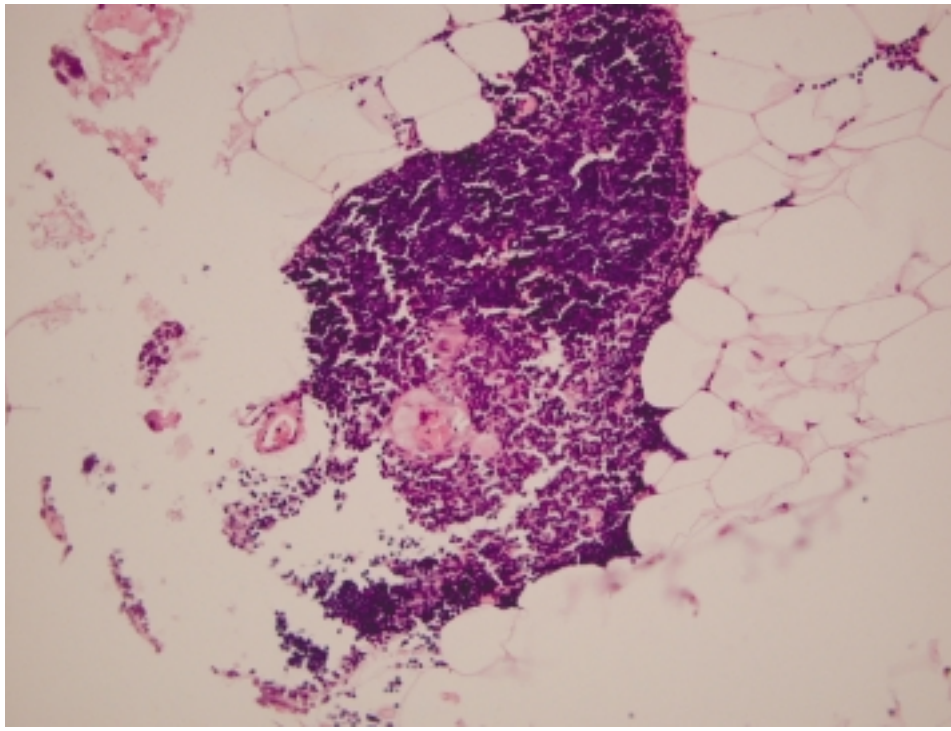

Fig. 1
Histological examination of thymic parenchyma

infiltrated with neoplastic cells and composed of proliferating thymic epithelia, and smaller cells that were arranged in an insular pattern. The nuclei of these cells contained fine chromatin structures and showed only rare mitoses. The cytoplasm showed granular argyrophilia. No sings of mucous secretion were observed (*Fig. 1*). Immunochemical staining showed positive reactions for membranous and cytoplasmic neuroendocrine markers (chromogranins and synaptophysin), and for cytokeratins (AEI/AE3) in the paranuclear region. The histological finding was indicative of thymic carcinoid (well differentiated neuroendocrine carcinoma of the thymic gland).

CASE TWO

A 50-year-old man was a heavy smoker for about 30 years. He was a hypertensive, had hyperuricemia and suffered from recurrent erysipelas of the right lower extremity. He was allergic to penicillin. His family history was insignificant. Ten years ago he was ill with an influenza-like diseases

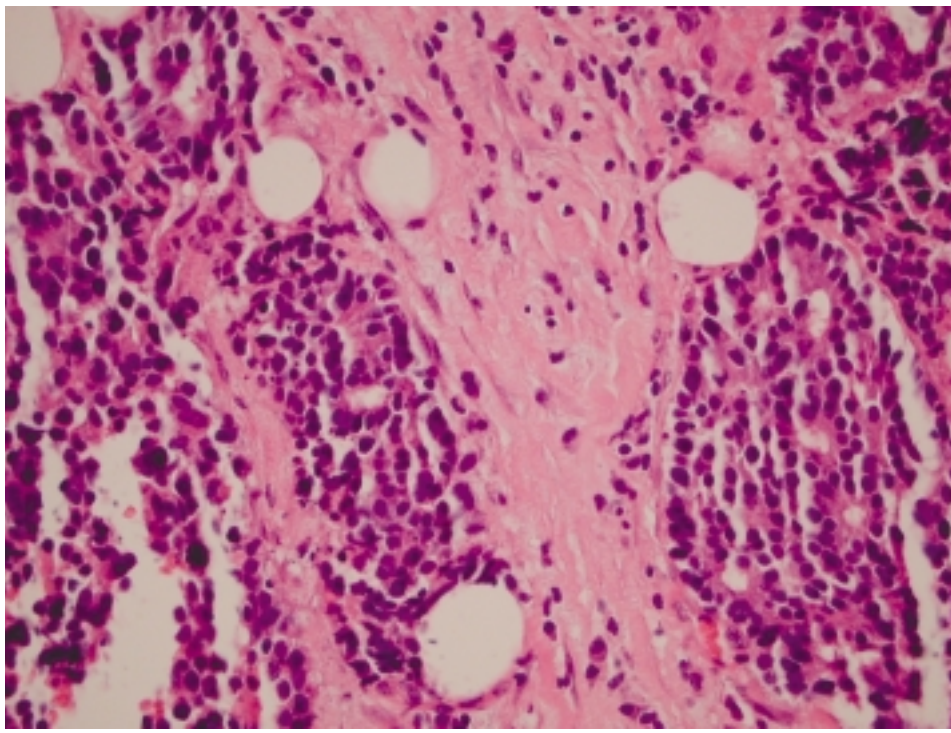

Fig. 2
Moderate positivity of synaptophysin and chromogranin (markers of neuroendocrine differentiation)

accompanied by paroxysmal dyspnoea occurring also at rest. Radiography revealed an infiltration of the hilar region of the left lung. Subsequent repeated pneumological examinations, including bronchoscopy, revealed no endobronchial infiltration but the hilar bronchus was evidently compressed owing to mediastinal tumorous enlargement. Repeated transbronchial bronchoscopic biopsy was negative. Thoracic CT showed neoplastic infiltration of the anterior mediastinum that extended into the pulmonary artery and the distal oesophagus. The mediastinal lymph nodes were enlarged. Thoracoscopic biopsy was indicated and was performed by harvesting a sample of tissue from the right hilar region; this was found to be densely infiltrated with tumorous tissue.

The patient soon recovered *per primam* and was discharged from hospital. Considering the histological and clinical findings, there was no indication for surgical treatment but radiotherapy was recommended and carried out.

The histological findings were as follows: In an intraoperative sample, the tissue was partly necrotic and haemorrhagic. The sample consisted of solid

alveolar tissue. Cells were arranged partly in rosettes, partly in solid and alveolar structures. The cells were medium-sized, oval in shape, with eosinophilic cytoplasm and large, dark basophilic nuclei and only indistinct nucleoli. Neoplastic cells, separated by fibrous septa, penetrated into fibroadipose tissue. The mitotic activity was moderate. Immunoreactivity was significantly positive in AEI/AE3 and MNF (cytokeratin coctails). Synaptophysin and chromogranin (markers of neuroendocrine differentiation) showed a moderate positivity. The diagnosis made on the basis of the histological findings and immunological profile was that of a neuroendocrine carcinoma of the mediastinum, possibly of thymic origin (*Fig. 2*).

DISCUSSION

The histological diagnosis of carcinoids does not present any problem. This may appear when their biological nature and topical identity are evaluated. Biopsy samples sometimes show the absence of thymic tissue or its residual structures. Such tumours reveal malignant features in almost 80% of the cases (*3*) while lung carcinoids are less malignant (in about 25% of the cases studied). Mediastinal carcinoids show pecularities that do not correlate with malignity (fusiform cells, oncocytes, pigmented cells or stromal regressive changes such as mucinosis or amyloidosis). These changes are found in larger tumours and were not observed in our cases. The grading of malignity recommended in some textbooks of diagnostic pathology (*4,5*) is useful particularly in autopsy cases. The thymic origin of carcinoid tissue in case one was confirmed by the presence of Hassall's bodies in the neoplastic tissue. In case two, which was diagnosed as an aggressive mediastinal carcinoid, the origin was difficult to identify for certain because of the small size of tissue available. The malignity of carcinoids presented here was assessed as low in the first case and high in the second one.

The validity of immunohistochemical methods used in the diagnosis of carcinoid tumours is high (*2*); it is 90% for the keratin ratio and about 70% for chromogranins and synaptophysin.

The clinical diagnosis of thymic carcinoids remains marginal in importance, as also shown by our cases. Clinical signs of thymic carcinoids are not distinct and are present in only about 30% of the patients *(6)*.

Differential diagnosis of thymic carcinoids is complicated and depends on histological findings. We must distinguish among paraganglioma, thymoma, malignant lymphoma, adenoma of the parathyroid gland, medullary carcinoma of the thyroid gland, etc. The identification of neuroendocrine carcinoma is generally successful by means of histology and routine immunochemical methods for detection of synaptophysin, chromogranins and keratins. We did not have to use any other special methods in our cases.

As for the location of neuroendocrine thymic tumours, there exists no sharp borderline between true thymic and anteriomediastinal lesions, especially in cases where a vast mediastinal infiltration is evident. In both our cases, pulmonary origin was excluded. Some authors support the view on the marginal relevance of precise distinction between thymic and mediastinal carcinoids (*7*). In our study, we could rule out the coincidence of thymic carcinoid with MEN syndrome but we could not exclude a possibility that an acccidental carcinoid tumour is present elsewhere in the body of our patients. Metastatic carcinoids, which generally display hormonal activity, were not considered in our patients

At the end we pay attention to the evolution of carcinoid nomenclature. The original term „carcinoid" seems no longer suitable because of the results obtained by current immunohistochemical methods that can detect the neuroendocrine character of this carcinoma. The term „neuroendocrine carcinoma" is now widely accepted (*7,8*). *Gould* prefers the name „neuroendocrinoma" (*6*).

Some authors suggest that the diagnosis of thymic carcinoids is accurate only in autopsy cases, but this seems exaggerated. However, studies on this rare tumour are generally published only as case reports (*9,10,11*).

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NEUROENDOKRINNÍ KARCINOM THYMU

S o u h r n

Karcinoidy thymu (mediastina) nově zvané „neuroendokrinní karcinomy" se vyskytují vzácně a upozorní na sebe spíše inkreční aktivitou (paraneoplasticky) než místními příznaky. Měli jsme možnost diagnostikovat histologicky a imunohistochemicky tento tumor u dvou osob. U 76leté ženy, kde byl náhodným nálezem při kardiochirurgickém zákroku, a u 50letého muže už jako inoperabilní tumor v předním mediastinu. Oba tumory postrádaly inkreční aktivitu, což nás však neodrazuje preferovat výstižnější, v současnosti převažující termín „neuroendokrinní karcinom" thymu či mediastina.

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