

## CASE REPORT

# A nodular hyperplasia of the thymic epithelium (so-called microscopic thymoma)

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### Abstract

We investigate a case of nodular hyperplasia of the thymic epithelium which was incidentally, microscopically discovered. Macroscopically there was no sign of tumor and the thymus was surgically removed for the therapy of the clinical symptoms of the myasthenia gravis worsened in two years of evolution. Histological in a general appearance of an involuted thymic tissue, a small nodular epithelial proliferation was identified. The epithelial proliferation was classified as A-type in the *WHO* histological classification of the thymic epithelial tumors. Generally, these microscopic thymomas range from 0.2 mm to 0.4 mm in size that corresponds to our finding that measured 0.25/0.35 mm. This lesion was singular; on additional sections examined, we did not find other areas. Even so, there is a tight connection between the myasthenia gravis, thymomas and these microscopic thymomas, the development of a thymoma from this lesion has not been proven.

**Keywords:** nodular epithelial hyperplasia, microscopic thymoma, myasthenia gravis.

### Introduction

Nodular hyperplasia of the thymic epithelium is a term suggested by some authors [1–4] to replace the old designation of "microscopic thymoma". This lesion is defined as an epithelial proliferation, smaller than 1 mm in diameter, which is usually found in patients suffering from myasthenia gravis and without a macroscopically evident tumor. Since the first report of the entity by Rosai J, 1976 [5], only eight cases are published in literature until now [4, 6–8].

We present such a case that was an incidentally finding in a young female, after thymectomy performed due to worsening of the clinical symptoms of myasthenia gravis in two years of evolution. Although the evolution of this entity to a conventional thymoma is not known, an improvement in the clinical evolution of the patients after surgical removal of the thymus was reported [4, 7, 8].

Therefore, there is a need to a complete microscopically examination of all the thymic tissue resected from the patients with myasthenia gravis, to detect areas of microscopic thymomas or microthymomas.

### Patient and Methods

We report the case of I.G., a 30-year-old female, diagnosed in 2006 with myasthenia gravis, up to now treated with prednisone. In December 2008, she was admitted in the Emergency County Hospital from Timisoara with worsening of the clinical symptoms of myasthenia. A mediastinal CT was performed, but any tumor or lymphadenopathy was not identified. The patient was transferred to surgery with proposal of

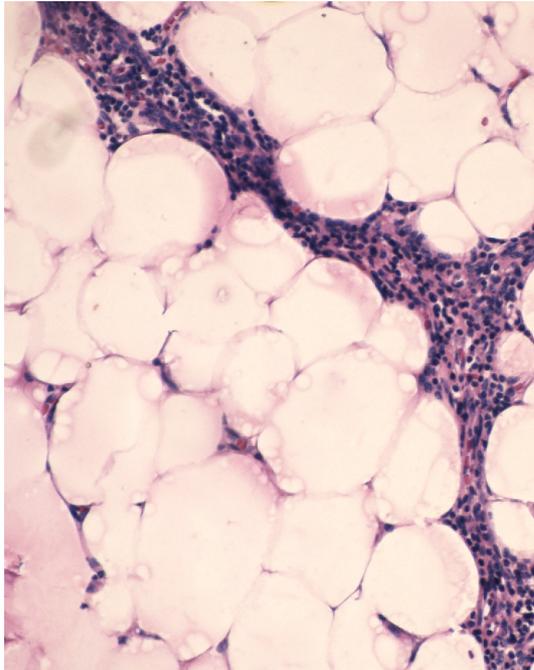
thymectomy. Finally, the surgery was performed through left thoroscopic approach. A thymic tissue was identified in the peripericardial adipose tissue. The thymic tissue had up to 3 cm in length and grey in color. The resected thymic tissue together with peripericardial fat was sent to the Pathological Department for diagnosis.

### Pathological findings

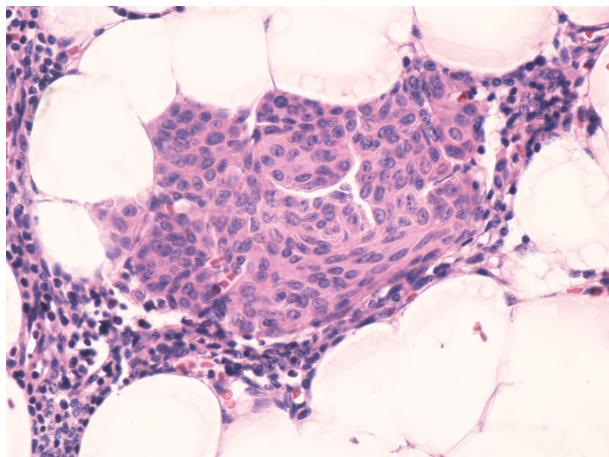
*Macroscopically* was identified a 6/6/2 cm fragment, adipose tissue-like. On cut-surface the aspect was mixed, on the yellow background of adipose tissue were visible gray and brown-hemorrhagic areas. On serial sections there was no evident tumoral mass macroscopically. Specimens were formalin-fixed paraffin-embedded using the standard histological technique.

*Microscopically*, on routinely HE stain, islands of lymphoid tissue with predominant epithelial cells toward the periphery of these areas and scattered epithelial cells inside was observed (Figure 1). This aspect is correspondent to the involuted thymus. No Hassal's corpuscles have been identified nor perivascular spaces. On one of the sections analyzed, a small, distinct, nodular area of predominant epithelial cells was identified (Figure 2). The epithelial nest measured 0.25/0.35 mm on high power field ( $\times 40$ ) using Nikon E100 Eclipse microscope. This area was attached and continuous with an island of involuted thymic tissue. The epithelial cells were ovoid or polygonal in shape, well-defined borders, acidophilic cytoplasm, with ovoid, vesicular nuclei, some of them with one or more nucleoli. The appearance corresponds to the A-type thymoma in the *WHO 2004* histological classi-

fication of the thymic epithelial tumors. There was no lymphoid hyperplasia. The aspect was singular and on additional sections performed there were no other such areas identified.



**Figure 1** – *Involuted thymus with islands of thymic tissue composed predominantly of lymphocytes and a predominance of subcapsular epithelial cells (HE stain, ×200).*



**Figure 2** – *The lesion is represented by a small, distinct, nodular area, attached and continuous with the thymic tissue, composed of prominent epithelial cells (HE stain, ×400).*

## Discussion

Even after the puberty the thymus undergoes normal involution, the organ never disappear completely [1]. Some islands of thymic tissue are always encountered in adults, on microscopical examination of the serial section slide from the prepericardial fat. Usually these involuted thymic islands are composed predominantly of lymphocytes. Sometimes a trabecular or rosette-like formations of the subcapsular epithelial cells may be seen [9].

The term microscopic thymoma was first introduced by Rosai J in 1976 [5] and it is still recognized by

*WHO 2004* histological classification. It is defined as an epithelial proliferation, <1 mm in diameter, without a macroscopically evident tumor and that usually appear in patients suffering from myasthenia gravis [4, 6, 10]. Most of the reported cases range from 0.2 to 0.4 mm in size [3]. This entity must be differentiated from microthymoma, the term first proposed by Cheuk W *et al.* 2005 [2], which is a microscopic-sized thymoma >1 mm, but <1 cm in diameter, and exhibits the typical histological features of the conventional thymoma. Because microscopic thymoma is identified as a small thymic epithelial island, incidentally found, without the morphological features of the conventional thymoma (lobulation, perivascular spaces, immature T-cells and medullary differentiation) and because are no data regarding the role in the development of the conventional thymoma, the more appropriate term to define this lesion should be nodular hyperplasia of the thymic epithelium [1–4].

The connection between myasthenia gravis and thymic lesions is well documented. 70% of the patients with MG have morphological changes of lymphoid hyperplasia, and 10–20% of the patients have or will develop a thymoma [11]. The prevalence of microscopic thymoma in autopsy specimens among patients with clinical symptoms of myasthenia is 15% [6]. In these patients the typical clinically presentation is with neurological or eye-related symptoms.

Nodular hyperplasia of the thymic epithelium (microscopic thymoma) is an extremely rare lesion; only eight cases were reported in literature until now (Table 1).

The case that we describe in this paper was an incidentally finding in a patient with eye-related symptoms of myasthenia gravis that aggravated in two years of evolution. The pathogenesis of myasthenia gravis is related to an abnormal activation of thymic B-lymphocytes, in lymphoid hyperplasia or in contact with the epithelial cells in thymoma [4]. In our case there was no evidence of lymphoid hyperplasia so this finding shows a relationship between nodular epithelial hyperplasia and myasthenia, also suggested by Pescarmona E *et al.* [6].

The causes, pathogenesis and functional significance of the nodular hyperplasia of the thymic epithelium are unknown. Also, the role of myasthenia gravis in the pathogenesis of this lesion is not defined, the patients showing a long-lasting clinical improvement after thymectomy.

Histological the lesion was A-type thymoma in *WHO* classification. Even this histological type is not frequently associated with myasthenia gravis; all the cases published were A-type thymoma. The finding was singular; no other areas were identified on additional sections performed. This suggest a careful examination of all macroscopic non-neoplastic myasthenic thymus, and the need to make many paraffin-embedded blocks from resected thymic tissue, in order to a good detection of the microscopically areas of thymoma.

The prognosis and the evolution of the patient depend on the clinical manifestation of the myasthenia

gravis and not on the thymic nodular hyperplasia. We have no data concerning the clinical progression of the myasthenia gravis in our case, but in literature

is reported an improvement of the clinical symptoms of myasthenia gravis after the resection of this lesion [4, 7, 8].

**Table 1 – Clinical, radiological and histological features of our case and the published cases (modified after Chalabreysse L et al. [4])**

Author	Sex/Age [years]	Clinical symptoms	Tomography thymus	Histological type	Lymphoid hyperplasia
Our case	F/30	Diplopia, ptosis	Normal	A	-
	F/58	Diplopia, dysphagia, ptosis, fatigability	Normal	A	-
Chalabreysse L et al. [4]	M/29	Diplopia, ptosis	Calcifications	A	+
	F/38	Diplopia, dysphagia, legs fatigability	Enlarged	A	+
	F/32	Unknown	Unknown	A	-
Pescarmona E et al. [6]	M/38	Unknown	Unknown	A	-
	F/42	Unknown	Unknown	A	+
Poulard G et al. [7]	F/59	Deglutition troubles, muscle weakness	Normal	A	+
Puglisi F et al. [8]	M/56	Ptosis, diplopia, fatigability of trunk and limb muscles	Normal	A	-

## ☒ Conclusions

We report a case of nodular hyperplasia of the thymic epithelium (also called microscopic thymoma), a very rare finding lesion. The importance of this lesion is that it may be misinterpreted as a microthymoma; on the other side the evolution to a conventional thymoma it is unknown. Also, the relationship with the myasthenia gravis and the role of this lesion in the pathogenesis of the myasthenia is not elucidating, especially in the cases without lymphoid hyperplasia.

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