Microscopic thymoma and myasthenia gravis

F Puglisi, N Finato, L Mariuzzi, C Marchini, G Fioretti, C A Beltrami

Abstract
A rare case of microscopically sized thymoma is described in a 56 year old man suffering from myasthenia gravis. Histological examination of the surgically removed thymus showed the presence of several epithelial thymoma-like islands. As controls, 100 thymuses obtained from consecutive necropsies were sampled: 4% of these cases showed epithelial islands. This case is further proof that "microscopic thymoma" is a true pathological entity and suggests that every thymus removed from myasthenic patients in which there is no macroscopic evidence of thymoma should be examined microscopically on serial sections.


Keywords: Microscopic thymoma, myasthenia gravis.

The first pathological report on microscopic thymoma, by Rosai and Levine, was published in 1976.1 The authors described a microscopic lesion (1 mm in diameter) having the histological features of a thymoma which was occasionally discovered in thymuses removed during cardiac surgery. Recently, Pescarmona et al2 reported three cases of microscopic thymoma in thymuses removed from patients suffering from myasthenia gravis, an autoimmune disease which often occurs in the presence of thymic abnormalities. Here we present a case of a patient suffering from myasthenia gravis whose thymus contained several foci of microscopic thymoma.

Case report
A 56 year old man with diabetes mellitus was admitted to a general hospital in September 1993 with a four year history of generalised weakness and mild fatigability of the skeletal muscles. No diagnosis was made. In December the patient was referred to the neurological department of the University of Udine because the symptoms were rapidly worsening. On examination, he had bilateral ptosis, diplopia, and easy fatigability, mostly of the muscles of the trunk and the lower limbs. A diagnosis of myasthenia gravis was made on the basis of the clinical findings, an anticholinesterase test, repetitive nerve stimulation (40% reduction in the amplitude of the evoked muscle action potential), and positive assay for acetylcholine receptor antibodies (0–10 pmol/ml). In view of the possibility of an associated thymic disorder, a computed tomographic scan was performed. No mediastinal enlargement was discovered. In February 1994 the patient had a surgical thymectomy by the sternum splitting approach. After thymectomy, there was progressive clinical improvement over a follow up period of seven months. Anticholinesterase agents were used as medical treatment before and after surgery.

Pathological findings
The thymus weighed 30 g. Macroscopically it was a lobulated soft yellow gland. As controls we examined 100 thymuses obtained from consecutive necropsies to verify the presence of "thymoma-like" epithelial solid nests. The donors were 41 females, age range <1 to 90 years (mean = 68), and 59 males, age range <1 to 95 years (mean = 65). Thirty five samples of the myasthenic patient's thymus and 3–10 samples from each of the control thymuses were processed for conventional histology. Tissue sections were stained with haematoxylin and eosin, PAS, and Gomori for reticulum; in order to identify epithelial islands, the sections were also stained for cytokeratin with monoclonal antibody (CAM 5.2, Becton Dickinson), using the avidin–biotin peroxidase technique. The thymus of the patient with myasthenia gravis showed a variable degree of involution. Several epithelial nests of round-oval cells, with nuclear dispersed chromatin and nucleoli, were histologically detected. Mitoses and nuclear atypia were not found (figure). The observed epithelial lesions were consistent with foci of microscopic thymoma. To determine their dimensions, we measured all the immunohistochemically identified epithelial areas by an image analyser (IBAS2000, Kontron). The morphometric data showed that the largest island has an equivalent area of 272 × 71 mm.

An epithelial nest histologically consistent with microscopic thymoma; it was mainly composed of oval to round cells with clear chromatin and definite nucleoli. Haematoxylin and eosin, × 295.
The 100 control thymuses showed several patterns of involution with a decrease in number of lymphocytes and relative preservation of the epithelial cells. In four of the 100 cases (age range 53–80 years), epithelial islands and rosette-like formations were seen. In other cases, the architectural arrangement was characterised by anastomosing strands of epithelial elements admixed with thymocytes.

The mean diameter of the epithelial nests was 107 mm (range 41–237 mm).

Discussion

Approximately 75% of patients with myasthenia gravis have thymic abnormalities, namely lymphoid follicular hyperplasia or thymoma or both.14 Surgical thymectomy results in disease improvement in most myasthenic patients and in non-thymoma cases it is often curative,6 although the overall prognosis has not been significantly modified in large series of patients who have had thymectomy.6 The surgical approach is useful, however, in preventing spread of the thymoma. In this case we could not demonstrate the presence of a thymoma by computed tomography; nevertheless a thymectomy was performed for therapeutic purposes.

On histological examination, the islands of epithelial cells were interpreted as possible multiple foci of microscopic thymoma. This “microscopic thymoma” had a morphological pattern compatible with the descriptions of Rosai and Levine.1 Moreover, Pescarmona et al reported three other cases showing microscopic epithelial lesions (0.2–0.4 mm in diameter) consistent with foci of thymoma on the basis of their morphological appearance.

Since it is also possible to find epithelial clusters in involuted thymuses,5 we analysed as controls 100 consecutive thymuses with different degrees of involution obtained at necropsy. In four of these 100 cases, epithelial islands and very small rosette-like formations were observed. These microscopic changes were similar to those present in microscopic thymoma, especially the rosette-like formations. The findings of Rosai and Levine were similar, as were those of Pescarmona et al, and from a morphological point of view it is quite impossible to distinguish between the two conditions. Pescarmona suggested a possible multifocal origin of thymoma. Our case supports this suggestion and underlines the association between myasthenia gravis and multifocal thymoma not associated with lymphoid follicular hyperplasia of the thymus.

In conclusion, in order to establish the unequivocal presence of a thymoma in patients suffering from myasthenia gravis it is necessary to obtain histological samples of the entire gland, particularly in those cases without macroscopically evident lesions. Finally, it is important to realise that computed tomography of the chest is unable to detect microscopic sized thymomas.


Evaluation of the API-Campy System in the biochemical identification of hippurate negative campylobacter strains isolated from faeces

J Reina, M J Ros, A Serra

Abstract

The aim was to evaluate the efficacy of the API-Campy system in the biochemical identification of 62 hippurate negative campylobacter strains isolated from the faeces. The strains were identified manually as 34 nalidixic acid susceptible C. coli (NAS), 20 nalidixic acid resistant C. coli (NAR), and eight C. lari. The 34 strains of NAS C. coli were identified as such by the API-Campy system. Of the 20 strains of NAR C. coli, 15 (75%) were correctly identified by the commercial system. None of the five NAR C. coli strains which were also erythromycin resistant were identified as such by the system. The eight C. lari strains could not be identified by the API-Campy system because the bionumber obtained...
CD34 immunoperoxidase staining for the diagnosis of myelodysplastic syndromes and chronic myeloid leukaemia

Horny et al recently reported that immunoperoxidase staining of bone marrow biopsy specimens with the CD34/QBEND10 monoclonal antibody can be used to separate the myelodysplastic syndromes RA and RAEB-T from the RA and RARS subtypes. This report has now confirmed our previous findings that CD34/QBEND10 is a useful reagent for the study of conventionally processed, paraffin wax embedded bone marrow biopsy specimens. We have recently studied bone marrow biopsy specimens from 39 cases of primary myelodysplastic syndromes addressing the diagnostic value of CD34 staining in these conditions. We found that CD34 immunostaining can help in the detection of the increased number of blasts associated with the RAEB and RAEB-T subtypes. In addition, our study showed that QBEND10 represents a powerful prognostic tool for predicting survival and outcome in myelodysplastic syndromes. In primary RAEB cases median survival was 41 months in those with less than 1% CD34+ cells and 29 months in those with more than 1% CD34+ cells (p<0-05). Similar results were obtained in cases of therapy related myelodysplasia: CD34+ cases had a mean survival of 10 months compared with 43 months for the CD34− cases (p<0-005). The authors also suggest the potential usefulness of CD34 staining for identifying patients in the accelerated phase of chronic myeloid leukaemia. Our recently published study of 59 bone marrow biopsy specimens representing the three phases (stable, accelerated and blastic) of chronic myeloid leukaemia has indeed confirmed the finding of a statistically higher CD34 value in the two aggressive phases of this disease compared with the stable phase. Taken together, these data and those from Horny et al show that QBEND10 is a very useful reagent for the study of routinely processed bone marrow biopsy specimens and may provide useful diagnostic and prognostic information in myelodysplastic syndromes and myeloproliferative disorders. This type of approach may be especially valuable when a paraffin wax embedded specimen is the only material available for immunohistotyping.

A ORAZI
Associate Professor of Pathology
Director, Section of Immunohistochemistry
Department of Pathology and Laboratory Medicine
University Hospital 4430
Indiana University Medical Center
550 North University Blvd
Indianapolis, Indiana 46202-5283, USA


Book review

If you wish to order or require further information regarding the titles reviewed here, please write to or telephone the BMJ Bookshop, PO Box 295, London, WC1 9JR. Tel 071 383 6244. Fax 071 383 6662. Books are supplied post free in the UK and for British ForcesPosted Overseas addresses. Overseas customers should add 15% for postage and packing. Payment can be made by cheque in sterling drawn on a UK bank or by credit card (Mastercard, Visa, or American Express) stating card number, expiry date, and full name. (The price and availability are occasionally subject to revision by the Publishers.)


This textbook deals in depth with what is a very highly specialised subject, bronchiorial pathology. The editor is an established expert in pulmonary disease and has asked many experts, particularly clinicians, to contribute to the book. The book provides us with the minute information on what is known about bronchiorial disease. It concentrates on occupational, occupational disease, obliterative bronchiolitis, and bronchiolitis organising pneumonia (BOOP), the last two conditions which in the past have been lumped together but which this book clearly separates and clarifies as being different entities with vastly different prognoses. There are excellent chapters on history, anatomy, imaging, pathology, and the various causes of bronchiorial disease. The clinicians' viewpoint is emphasised. However, the penalty of being a multi-author book is that there is discontinuity and a lot of repetition. The editor should have exercised more control over this aspect of the book which makes it very annoying and boring at times when the same references and observations are made by several authors. While not of general interest I would recommend it to pathologists interested in pulmonary pathology as it deals in great depth with what has been pathologically and clinically a very confusing and poorly illustrated area of lung disease in the past.

M N SHEPPARD

Postgraduate course

Current concepts in surgical pathology

November 6–10 1995

The Department of Pathology, Massachusetts General Hospital, Harvard Medical School, will present a postgraduate course in Surgical Pathology under the direction of Drs Nancy L Harris, Robert H Young and Eugene J Mark. This course is designed for pathologists at resident and practitioner levels. It will provide an in-depth review of diagnostic surgical pathology with emphasis on morphologic features, newly recognised entities, and specific pathologic processes, presented by the faculty of the Department of Pathology, Massachusetts General Hospital. Instruction will be primarily by lecture, but will also include discussion periods. Each participant will receive a comprehensive course syllabus.

The course has Category 1 accreditation for approximately 35 hours CME credit by the American Medical Association. The fee for the course is $825.00 (£522.00) (residents and fellows $610.00 (£386.00). For further information, please contact: Department of Continuing Education, Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA (tel: (617) 432-1525).

Notices

Texas Society of Pathologists
75 Years Young
presents
Pathology: Past, Present and Future
Diamond Jubilee Celebration
February 1–4 1996

For further information, please contact: Paula Riling, Texas Society of Pathologists, 401 West 15th Street, Austin, Texas 78701-1660, USA.

Correction

Microscopic thymoma and myasthenia gravis (J Clin Pathol 1995;48:682–683). The authors apologise for the errors which appeared in the Pathological findings section of their report. In the last line of the first paragraph, 272 x 71 mm should read 272 x 71 mm. In the final paragraph, 107 mm (range 41–237 mm) should read 107 mm (range 41–237 mm).