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In this issue

Thymoma: a clinicopathological correlation of 1470 cases☆

Annikka Weissferdt MD, FRCPath[a], Neda Kalhor MD[a], Justin A. Bishop MD[b], Se Jin Jang MD, PhD[c], Jae Ro MD, PhD[d], Fredrik Petersson MD, PhD[e], Bingcheng Wu MD[e], Gerald Langman MBChB, FRCPath[f], Hollie Bancroft BSc[f], Yalan Bi MD[g], Yunxiao Meng MD, PhD[g], Filomena Medeiros MD[h], Hans Brunnstrom MD, PhD[i], Dominic Spagnolo MBBS, FRCPA[j,k], Siaw Ming Chai MBBS, FRCPA[j,k], Andrew Laycock MBBS, FRCPA[j,k], Paul E. Wakely Jr MD[l], Goran Elmberger MD[m], Fernando A. Soares MD[n], Antonio H. Campos MD[n], Derya Gumurdulu MD[o], Isabel Alvarado-Cabrero MD[p], Domenico Coppola MD[q], Arlene M. Correa PhD[r], David Rice MD[r], Reza J. Mehran MD[r], Boris Sepesi MD[r], Garrett Walsh MD[r], Larry Kaiser MD[s], Cesar A. Moran MD[a,*]

[a]*Department of Pathology at MD Anderson Cancer Center, Houston, TX, USA*
[b]*The Johns Hopkins Hospital, Baltimore, MD, USA*
[c]*Asan Medical Center, Ulsan University School of Medicine, Seoul, Republic of Korea*
[d]*Methodist Hospital, Houston, TX, USA*
[e]*National University Hospital, Singapore*
[f]*Heart of England NHS Foundation Trust, Birmingham, United Kingdom*
[g]*Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, and Peking Union Medical College Hospital, Peking, China*
[h]*Serv Anatomia Patologica, Hospital Pulido Valente, Centro Hospitalar Lisboa Norte, Lisboa, Portugal*
[i]*Lund University, Laboratory Medicine, Department of Clinical Sciences Lund, Pathology, Lund, Sweden*
[j]*PathWest Laboratory Medicine Western Australia; University of Western Australia, School of Pathology and Laboratory Medicine, Nedlands, Western Australia, Australia*
[k]*University of Notre Dame, Fremantle, Western Australia, Australia*
[l]*The Ohio State University, Columbus, OH, USA*
[m]*Department of Laboratory Medicine, Pathology Orebro University Hospital, Orebro, Sweden*
[n]*A.C. Camargo Cancer Center, Sao Paulo, Brazil*
[o]*Cukurova University Faculty of Medicine, Adana, Turkey*
[p]*Mexican Oncology Hospital, Mexico City, Mexico*
[q]*Moffitt Cancer Center, Tampa, Florida, USA*
[r]*Departments of Thoracic Surgery at M D Anderson Cancer Center, Houston, TX, USA*
[s]*Temple University School of Medicine, Philadelphia, PA, USA*

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* Corresponding author at: Department of Pathology, MD Anderson Cancer Center, Houston, TX.
E-mail address: cesarmoran@mdanderson.org (C. A. Moran).

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Summary We present 1470 surgical resections for thymoma identified in the pathology files of 14 institutions from 11 countries with the purpose of determining and correlating a simplified histological classification of thymoma and pathological staging with clinical outcome. The study population was composed of 720 men and 750 women between the ages of 12 and 86 years (average, 54.8 years). Clinically, 137 patients (17%) had a history of myasthenia gravis, 31 patients (3.8%) of other autoimmune disease, and 55 (6.8%) patients of another neoplastic process. Surgical resection was performed in all patients. Histologically, 1284 (87.13%) cases were thymomas (World Health Organization types A, B1, and B2, and mixed histologies), and 186 (12.7%) were atypical thymomas (World Health Organization type B3). Of the entire group, 630 (42.9%) were encapsulated thymomas, and 840 (57.9%) were invasive thymomas in different stages. Follow-up information was obtained in 1339 (91%) patients, who subsequently were analyzed by univariate and multivariate statistical analysis. Follow-up ranging from 1 to 384 months was obtained (mean, 69.2 months) showing tumor recurrence in 136 patients (10.1%), whereas 227 died: 64 (28.2%) due to tumor and 163 (71.8%) due to other causes. Statistical analysis shows that separation of these tumors into thymoma and atypical thymoma is statistically significant ($P = .001$), whereas tumor staging into categories of encapsulated, minimally invasive, and invasion into adjacent organs offers a meaningful clinical assessment with a $P = .038$. Our findings suggest that our simplified histological schema and pathological staging system are excellent predictors of clinical outcome.

1. Introduction

The classification and staging of thymomas have generated significant interest and controversy over the last 2 decades. Of note, some earlier publications have also shed important light on the pathology of the thymus. In 1955, in the first series of fascicles of the Armed Forces Institute of Pathology [1], under the designation of *Atlas of Tumor* Pathology, Section V—Fascicle 19, the author stated, "Many attempts have been made to classify thymomas on the basis of cell type." In addition, the author stated, "… it is both difficult and hazardous to classify tumors of such cell derivatives,… there are so many variations within a given tumor … no attempt is made to give a special name to any particular variant." Interestingly, only recently has such a statement been proven in a study of 630 thymomas evaluated for the impact on histologic heterogeneity [2]. In 1975, in the second series of fascicles from the Armed Forces Institute of Pathology [3], the authors stated, "… once the term thymoma is restricted to the tumor of epithelial thymic cells, with or without lymphocytic component, all further subdivisions are artificial."

In 1961, Bernatz et al [4] put forward a classification system based on the proportion of lymphocytes and separated thymomas into lymphocyte rich, epithelial rich, and mixed thymomas in which the tumor shows approximately equal proportion of lymphocytes and epithelial cells. In a subsequent publication of 181 thymomas, Bernatz et al [5] clearly stated that all histological variants might become invasive neoplasms. In 1985, Marino and Müller-Hermelink [6] proposed a new histological classification so-called histogenetic classification, separating thymomas by "cell of origin" into cortical and medullary types. However, contrary to the system of Bernatz et al [4], which predicts clinical outcome based on tumor stage at the time of diagnosis, this so-called histogenetic classification bases its prediction of clinical outcome on histology—cortical or medullary type.

With the lack of an official classification for thymomas, the World Health Organization (WHO) organized a panel of experts who in 1999 produced their first official publication on the *Histological Typing of Tumours of the Thymus* [7]. However, this initial WHO classification was a compromised approach comparing the Bernatz et al [4] and the Marino and Müller-Hermelink [6] classification schemas. In the WHO proposal, a system of letters and numbers was put forth as a "facilitator" of those schemas. Two important statements, quoted below, emerged as a highlight of this initial WHO schema [7]:

> "… the terminology chosen here is a non-committal one based on a combination of letters and numbers. It is not proposed as a new classification, but mainly to facilitate comparison among the many terms and classification schemes."

> "… the committee wishes to stress the importance of independently evaluating thymic epithelial tumours on the basis of their presence and degree of invasiveness and their cytoarchitectural features."

Furthermore, the committee offered an additional statement: "It will be appreciated, of course, that the classification reflects the present knowledge and that modifications are almost certain to be needed as experience accumulates." The last 2 publications from the WHO (2004 and 2015) [8,9] have ignored the advice from the members of the 1999 committee and the abundant evidence on the subjectivity of this schema. In addition, the authors have also perpetuated a schema that was clearly not intended as a new classification.