Editorial

Tumor epithelial tumors: do we expect a brighter or a grey future?

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Provenance: This is an invited Editorial commissioned by Section Editor Dr. Gang Shen, MMSC (The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China).

Comment on: Meurgey A, Girard N, Merveilleux du Vignaux C, *et al*. Assessment of the ITMIG statement on the WHO histological classification and of the eighth TNM staging of thymic epithelial tumors, of a series of 188 thymic epithelial tumors. J Thorac Oncol 2017;12:1571-81.

Submitted Sep 15, 2017. Accepted for publication Sep 22, 2017.
doi: 10.21037/jtd.2017.10.30
View this article at: http://dx.doi.org/10.21037/jtd.2017.10.30

Recent years have been very important for thymic epithelial tumors (TETs), due to several joined publications of the International Thymic Malignancies Interest Group (ITMIG) and International Association for the study of lung cancer (IASLC) (1-3). Together ITMIG and IASLC proposed a new TNM classification which was received by AJCC/UICC for the 8th edition of the TNM classification, while ITMIG alone (4) provided some consensus statements on the use of WHO histological classification.

A recent paper by Meurgey *et al*. (5), analyzing in a retrospective way prospectively recorded data, explores the feasibility and relevance of these two innovations among 188 TETs diagnosed and treated at Louis-Pradel Hospital, Hospices Civils de Lyon.

WHO histological classification has been questioned over time due to the ability of pathologists to well recognized different patterns (6-8): French paper underlines that the major criteria proposed by ITMIG are present in 100% of analyzed specimens in type A, AB, B1 and B2 thymomas as well as in 87% of thymic carcinomas (TCs). These results are certainly a step forward in recognizing different patterns of WHO classification, but not clearly demonstrate any reduction in inter-observer variability (cases were discussed together between a senior and a junior thoracic pathologist) which is up to 22% between non-expert diagnosis and expert review (9).

Anyway, WHO classification remains a major prognostic factor on time to recurrence (TTR) and is strictly related to stage (more aggressive features are present in more advanced disease).

TNM staging is generally shared as the most reliable prognostic factor among all tumor types. Data from the French trial did not record any difference in TTR or overall survival (OS) using the 8th TNM classification, while Masaoka stage catches some differences in TTR. OS is a questionable end-point particularly in thymoma, thus our reflections will consider the TTR only.

The big change in the 8th TNM classification is the inclusion of both Masaoka stage I and II in stage I, thus unifying encapsulated TETs along with those infiltrating mediastinal fat or mediastinal pleura. The French trial observed a great migration of their cases from more advanced stage as per Masaoka staging system to stage I per TNM classification that finally represents the majority of patients (from 28% of Masaoka stage I to 84% of TNM stage I).

If we look to process of invasion of TETs we can consider four layers: (I) capsule or pseudo-capsule; (II) adipose tissue, mediastinal pleura; (III) visceral pleura, pericardium, and great vessels; (IV) lung, hearth, intraluminary growth.

Masaoka staging system includes these anatomical criteria that disappeared in the new TNM. If we think to thymus surrounding tissue, visceral pleura pericardium and great vessels represents the same layers which can be interested just according to different tumor location. The new TNM seems to be more influenced by the ability of surgeons to achieve a R0 resection than to natural history of TETs.

Moreover, in French trial very few patients were included in TNM stage II (2%), no one in stage IIIb and 3% in stage IV disease. These data are similar to those recorded by ITMIG (1), where 82.5% of patients were classified as stage

I, only 3% as stage II, 9.8% as stage III (but only 0.4% with stage IIIB disease) and 4.7% with stage IV disease (4% with pleural or pericardial involvement).

Both ITMIG and French data suffer from a selection bias because evaluated patients are just those who underwent surgery. Thus, we need to collect data prospectively on those patients who do not receive any surgery for unresectable disease in order to assess their long-term results and prognosis.

The challenge for the near future will be to discriminate different disease among stage I disease and how to transfer old data on adjuvant treatment in such patients. Probably, the way to go will include the adoption of a risk stratification strategy according to stage, histology and R0 resection (10) along with the implementation of national database (11) with data about resected and un-resected patients.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: D'Angelillo RM, Ramella S. Tumor epithelial tumors: do we expect a brighter or a grey future? J Thorac Dis 2017;9(11):4180-4181. doi: 10.21037/jtd.2017.10.30

