Extended Abstract

Update on the TNM 8th Edition—staging of thymic epithelial tumors, a pathologist's perspective

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Histopathological evaluation of mediastinal pleura, pericardium and lung invasion by thymic epithelial tumors (TET) defines the pT1b, pT2 and pT3 stages, as per the 8th tumor-node-metastasis (TNM) edition (1). Schematic diagrams produced by the International Thymic Malignancy Interest Group (ITMIG) (2) and recommendations produced by the International Collaboration on Cancer Reporting (ICCR) (3) clearly defined the macroscopic and histopathological criteria of invasion. It appears, however, that reproducibility of pT diagnosis on slides, even by experienced thoracic pathologists, was an issue in the RYTHMIC (French network dedicated to TET management) group (4). Checklists have been defined by the ITMIG (5) in order to avoid discrepancies between surgical and histopathological reports following pericardiac, mediastinal or pleural resection. It is crucial that the surgeon routinely orientates the resection specimen and marks areas of concern in, for example mediastinal pleura, pericardium, the innominate vein… Differentiating dissection areas from resection areas is also important to improve the R reproducibility of the pTNM. The pathologist should validate his report only after complete evaluation of the surgical report in order to avoid discrepancies (i.e., no mention of the pericardium in the pathological report despite pericardium resection in the surgical report). In addition, well-oriented and well-defined blocks describing the relationship of tumor to adjacent structures such as mediastinal pleura or pericardium would help the reproducibility of staging.

The pT1a stage combines Masaoka-Koga (MK) stage IIA and IIB and does not take into account the 0.3 cm threshold used by some pathologists to differentiate MK IIA from MK IIB (2). This differentiation in the RYTHMIC experience is tricky when considering measurement of invasion from the capsule or when the tumor is not encapsulated. Therefore, pT1a staging increases the concordance between pathologists for low stage TET. However, at least some countries (6) are still using MK staging for clinical decisions of tumor board and post operative radiotherapy trials (7).

One of the major difficulties for the pathologist when evaluating pT is the fact that in a significant number of cases, the tumor reaches the mediastinal pleura, pericardium or lung, but with a capsule. It is therefore difficult to differentiate the fibrous part of a capsule from the fibrous part of pleura or pericardium. An encapsulated tumor is for most pathologists considered as pT1a, even if it adheres to the fibrous part of the pericardium, although the surgeon cannot separate the pericardium from the TET. It is also very difficult to differentiate a thick TET capsule sticking to the lung from mediastinal pleura, which could even be fused with visceral pleura in very thick fibrous bands. Indeed, in such cases, pathologists could consider stage pT1a. It is easier to define pT1a when there is normal connective tissue beneath mediastinal pleura mesothelium and the TET capsule.

RYTHMIC experience showed that the ITMIG defined criteria for mediastinal pleural invasion (infiltration by tumor cells of the mediastinal pleural connective tissue above the elastic layer) is not easy to follow, as the elastic layer is not always present in the connective tissue of the mediastinal pleura. The easiest way therefore to define pT1b might be identification of invasion by the tumor cells beneath or adjacent to the mediastinal pleural mesothelium. Reproducible histological recognition between pathologists of the mediastinal pleura is also an issue.

Concerning pericardium evaluation, it is sometimes difficult to differentiate fibrous pericardium from the thymoma capsule, underlining the importance of well-defined and oriented blocks. Minimal invasion of the pericardium is also difficult to diagnose and should take into account the differentiation of the fibrous pericardium from the outer pericardial layer (OPL). Defining pT2 requires identification of infiltration of the fibrous pericardium by TET, whereas the invasion of OPL containing blood vessels and adipocytes is not considered as pT2.

Lung invasion (pT3) is defined by tumor infiltration of the lung parenchyma (alveoli) but also by the destruction and/or infiltration by the TET of the outer elastic layer (OEL) of the visceral pleura. The problem is that in some cases, particularly when there is a symphysis of the two pleuras sticking to the TET, the tumor cells invade visceral pleura but do not destroy the OEL. This minimal visceral pleural invasion is not defined today by the pTNM and should be taken into account in the next classification.

In conclusion, it appears important, in addition to histological definition of the different pT stages, to improve inter-pathologist reproducibility of pT evaluation. This is particularly important for mediastinal pleura, as well as minimal pericardium or lung invasion. Although immunostains such as p63 or p40 could help to identify tumor cells or calretinin and elastic stains to better evaluate the mesothelial and the elastic pleural layers, pT stage evaluation by the pathologist is difficult. It underlines the importance of the ongoing RYTHMIC/ITMIG pathology project on pT stage histological reproducibility.

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