Immunohistochemical markers (Non-core)

Reason/Evidentiary Support

Immunohistochemical analysis of thymic resection specimens may be performed for several reasons:

1. To exclude or confirm the presence of a tumour of thymic epithelial origin[1]
2. To aid in subtyping of thymomas[2]
3. To establish the origin of a thymic carcinoma as either a primary thymic carcinoma or a metastasis

The differential diagnostic spectrum of thymoma is related to either its epithelial component or to the lymphoid component. The lymphoid component of "B-type" thymoma and of thymic follicular hyperplasia may raise the suspicion of non-Hodgkin lymphoma, especially T-lymphoblastic leukaemia/lymphoma. Immunohistochemistry may be applied to type the lymphoid population [normally composed of immature, CD3/terminal deoxynucleotidyl transferase (TdT/CD1a/CD99+) lymphocytes], or to confirm the presence of an epithelial component, which may be highlighted by pan-cytokeratin and/or p63 stains. The epithelial component in thymic epithelial tumours with a sparse lymphoid component may raise the possibility of either a germ cell tumour or metastatic carcinoma.[1,3] Germ cell tumours may be diagnosed by appropriate immunohistochemical stains including SALL4, OCT4, CD117, CD30, D2-40, human chorionic gonadotropin (hCG), placental alkaline phosphatase (PLAP), and α-fetoprotein (AFP).[1]

Subtyping of thymomas is primarily based on histology; immunohistochemical stains (cytokeratin and/or p63) may be helpful in the evaluation of the density of the epithelial cells in B-type thymoma thus aiding the diagnosis of B1/2/3 thymoma. Similarly, cytokeratin stains may be used to confirm the epithelial nature of the spindle cells in type A, type AB and in metaplastic thymoma. Epithelial expression of CD20 is reported to be more frequent among type A and AB thymomas.[4] Neuroendocrine markers may be useful to rule out neuroendocrine tumours.[2]

Distinguishing thymoma (in particular type B3 thymoma) and thymic carcinoma may occasionally be problematic; there are no immunohistochemical markers that can reliably segregate these entities. However, CD5, CD117 and the recently described markers GLUT1 and MUC1 show a higher incidence of staining in thymic carcinoma (in particular, thymic squamous cell carcinoma) compared to thymoma.[5,6] Ki-67 labelling index in epithelial tumour cells of ≥13.5% has been suggestive of thymic carcinoma.[7]

The diagnosis of thymic carcinoma essentially involves the exclusion of metastasis; immunohistochemical analysis may support a diagnosis of thymic carcinoma but cannot establish the diagnosis with certainty. Expression of CD5, particularly in combination with CD117 positivity, lends some support to a diagnosis of thymic carcinoma. Several new markers (FoxN1 and CD205) may further support a diagnosis of thymic carcinoma. Other markers may be applied to rule out thymic carcinoma by confirming a non-thymic origin, such as TTF-1. However, given the great diversity in histological subtypes of thymic carcinoma, the specificity of markers routinely used to diagnose carcinoma of a particular origin may be considerably lower in this situation.[8]

References

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