Immunohistochemistry in Tumor Diagnostics

1

Contents

1.1 **Expression Pattern and Diagnostic Pitfalls** 1

1.2 **Immunohistochemical Pathways for the Diagnosis Primary Tumors and of Metastasis of Unknown Primary Tumors** 2

References 9

1.1 Expression Pattern and Diagnostic Pitfalls

The following chapters provide an overview of the most common immunohistochemical markers used for tumor diagnosis in addition to the immunoprofile of the most common tumors. The expression pattern of targeted antigens is also listed as an important factor to consider in the interpretation of the immunohistochemical stains and includes the following expression (stain) patterns:

1. Nuclear staining pattern: characteristic for antigens expressed in cellular nuclei or on the nuclear membrane. Good examples for this expression pattern are transcription factors and steroid hormone receptors.
2. Cytoplasmic staining pattern: characteristic for antigens located in the cytoplasm. Common examples are the cellular skeletal proteins such as vimentin, actin, desmin, and cytokeratins. Some antigens display a further restricted cytoplasmic staining pattern and stain-specific organelles, as, e.g., mitochondria (leading to a granular cytoplasmic staining) or the Golgi apparatus (unilateral perinuclear pattern).
3. Membrane staining pattern: characteristic for antigens located within the cell membrane, typical examples are the majority of CD antigens.

M.S.A. Tuffaha et al., *Immunohistochemistry in Tumor Diagnostics*,
DOI 10.1007/978-3-319-53577-7_1

4. Extracellular staining pattern: this pattern is characteristic for extracellular and tissue matrix antigens in addition to the cell secretion products such as collagens and CEA.

It is noteworthy to mention that some antigens have different expression patterns depending on cell cycle phase or on differentiation stage such as the immunoglobulin expression in lymphoid tissue. Other antigens have a unique expression pattern characteristic for some tumors.

Finally, it is important to remember that the interpretation of immunohistochemical results is not the description of positive or negative stains. The conventional H&E morphology of the tumor in addition to the characteristics of each antibody and the expression pattern of targeted antigens must be considered as well as the results of internal positive and negative controls, which may be present in examined tissue sections.

1.2 Immunohistochemical Pathways for the Diagnosis Primary Tumors and of Metastasis of Unknown Primary Tumors

Because of the large number of available antibodies for immunohistochemical antigen profiling of tumors, it is important to choose an initial informative screening antibody panel. For the choice of such initial diagnostic panel, the histomorphology of the examined tumor, the tumor location and clinical data, as well as the specificity and the sensitivity of the available antibodies must be considered.

For tumors with an ambiguous morphology or tumors with undetermined histogenic differentiation, we found that the most informative, time-, and money-saving primary panel consists of antibodies reacting with epithelial, mesenchymal, neural, and hematopoietic cell lines (Algorithm 1.1) [1–4].

The following panel is an example for an initial screening panel:

1. Pan-cytokeratin (cytokeratin cocktail)
2. LCA (leukocyte common antigen)
3. S100 and HMB45 (or melanoma cocktail)
4. Oct4/SALL-4
5. Vimentin

Other tissue-specific markers can be added if the morphology of the tumors favors any differentiation line.

If tumors reveal the small round blue cell morphology, another screening antibody panel is necessary and can include the following antibodies (Algorithm 1.2):

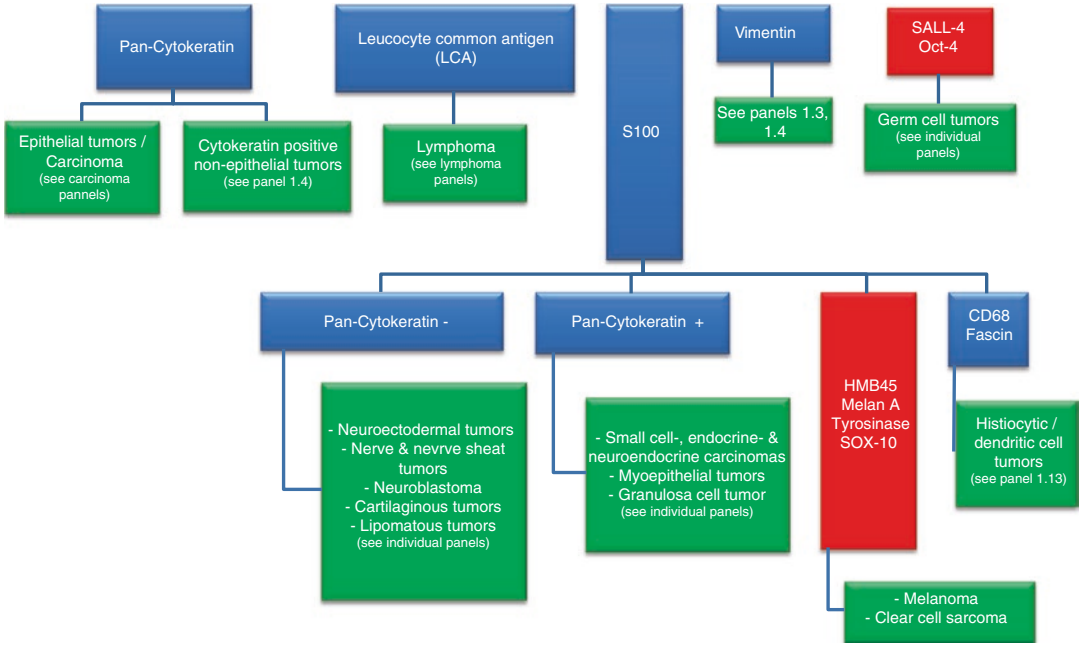
1. S100
2. Pan-cytokeratin (cytokeratin cocktail)
3. Desmin and/or myogenic transcription factors
4. LCA
5. CD99
6. CD56

This panel can be modified according to the age of the patient, tumor location, and clinical history. Adding one or more of tissue- or organ-specific markers to the initial diagnostic panel can give additional valuable diagnostic information.

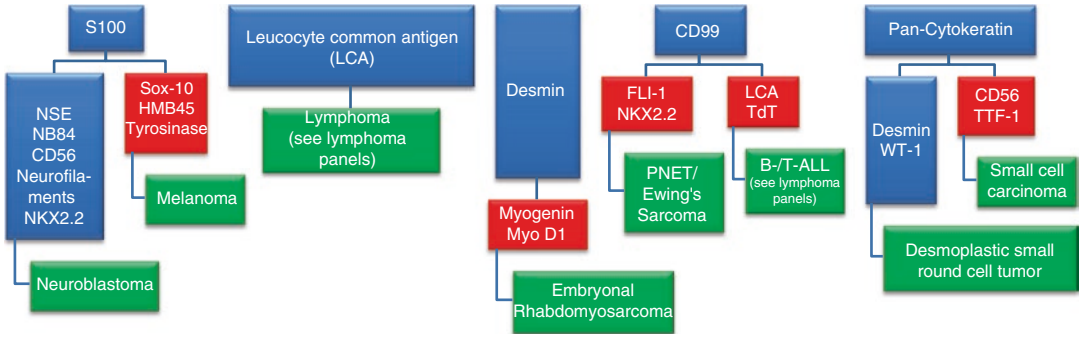
For orientation, we suggest a group of diagnostic algorithms to ease solving the most common diagnostic problems (Algorithms 1.1–1.13). According to the results obtained from the initial algorithm, a second panel with more selective antibodies can be assembled using tissue and/or tumor-specific markers for the final histopathologic diagnosis. The immunohistochemical conclusion must be made considering the histomorphology of the tumor and the expression profile of all antibodies in the used panel and always to remember that there is no antibody exclusively specific for a certain tissue type or particular tumor entity.

In the following 13 algorithms, general screening antibodies are placed in blue boxes,

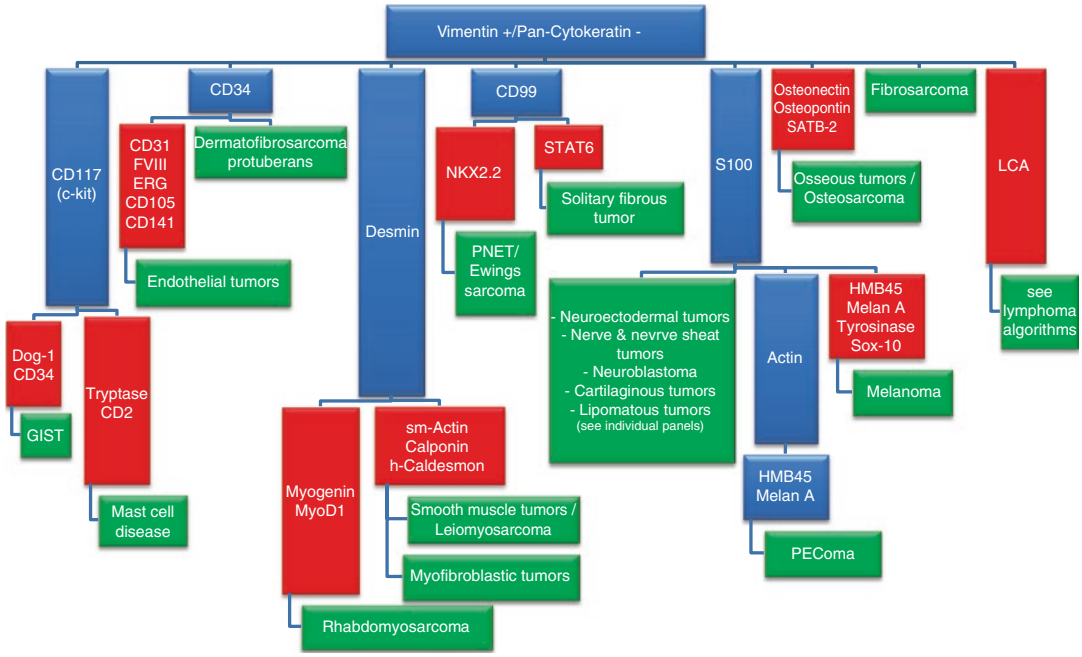
more specific antibodies in red boxes, and the most probable diagnosis in green ones. It is important to remember that the immunoprofile of tumors may be a subject of exceptions or aberrant expression of different antigens, which may cause misdiagnosis. Finally, all immunohistochemical markers have to be interpreted in the appropriate morphological context.



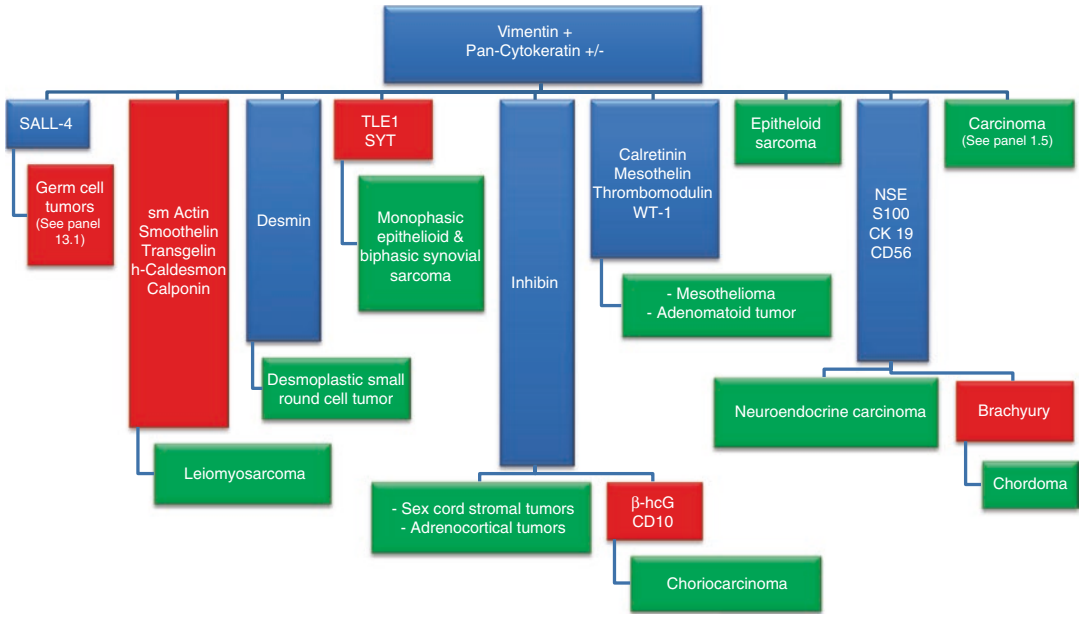
Algorithm 1.1 Primary Screening Antibody Panel



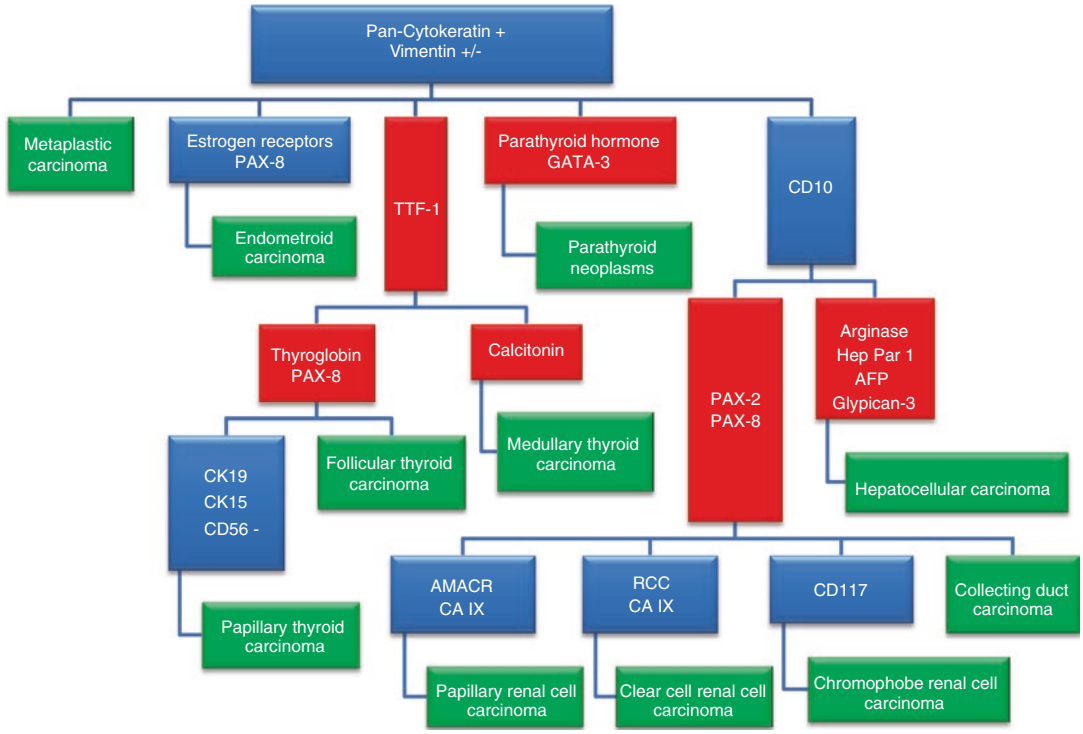
Algorithm 1.2 Antibody Panel for Tumors with Small Round Blue Cell Morphology



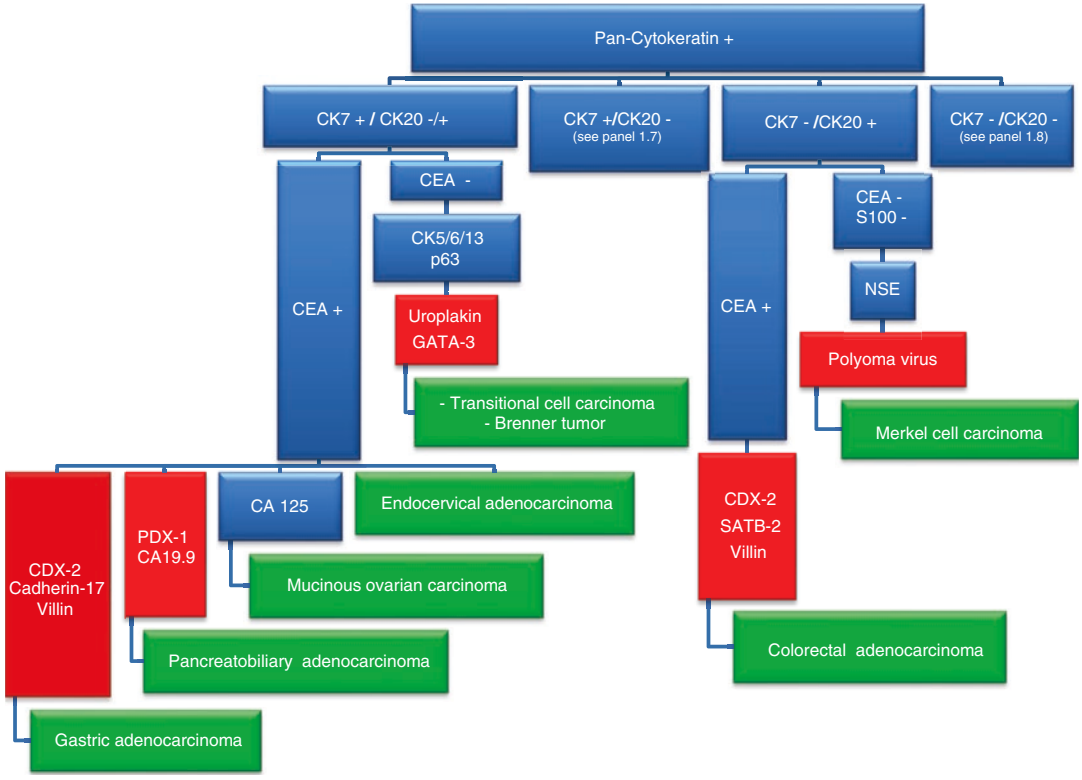
Algorithm 1.3 Cytokeratin-Negative Tumors



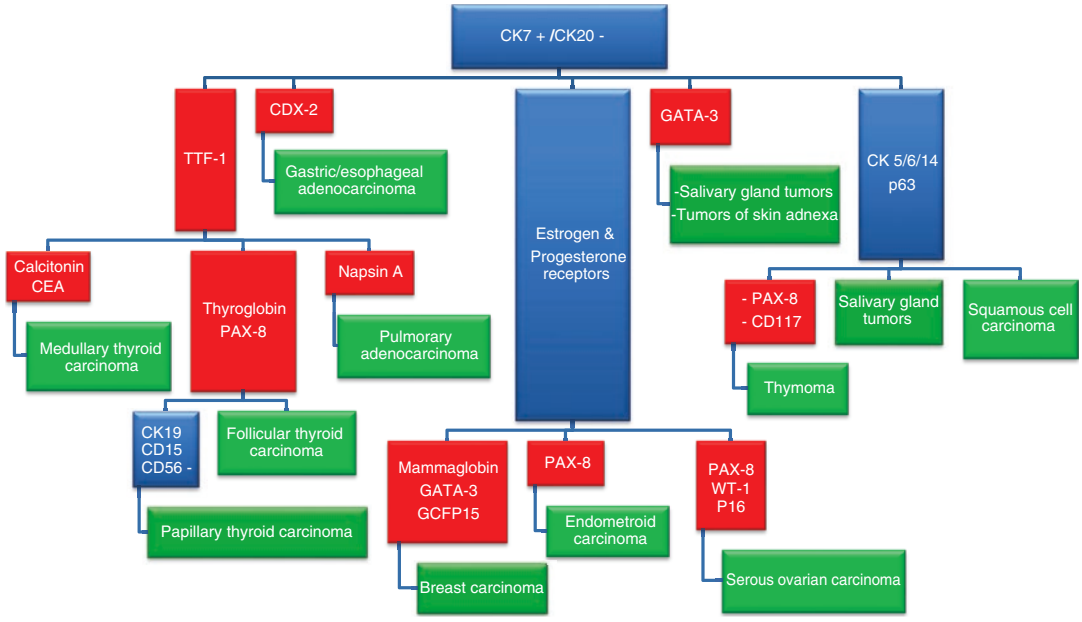
Algorithm 1.4 Tumors with Cytokeratin/Vimentin Co-expression



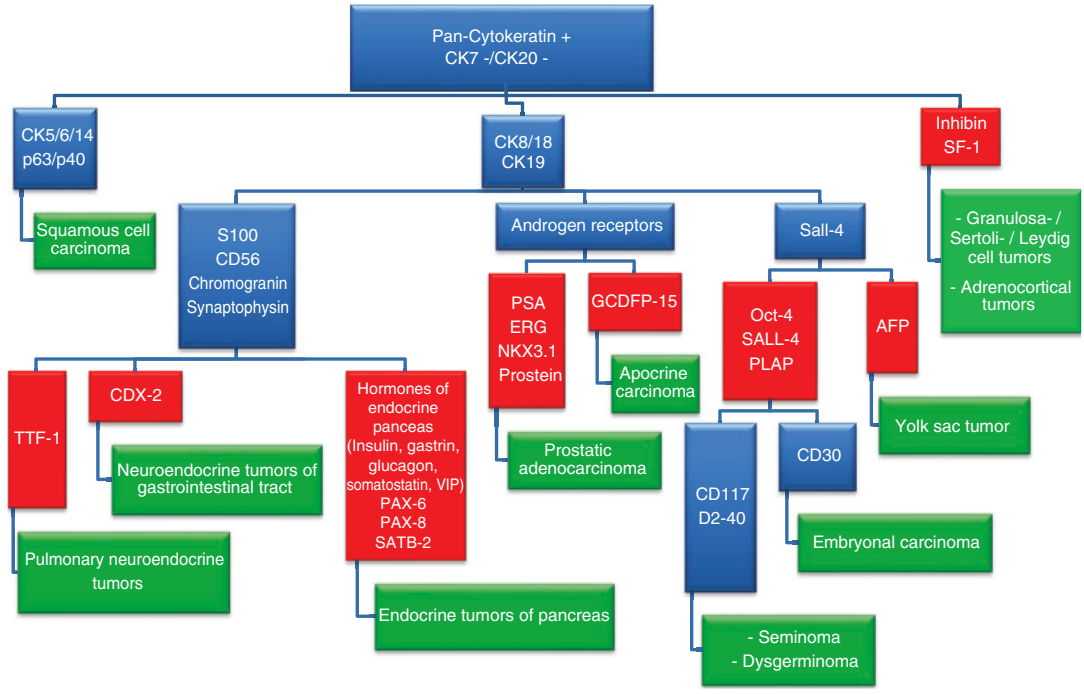
Algorithm 1.5 Carcinomas with Cytokeratin/Vimentin Co-expression



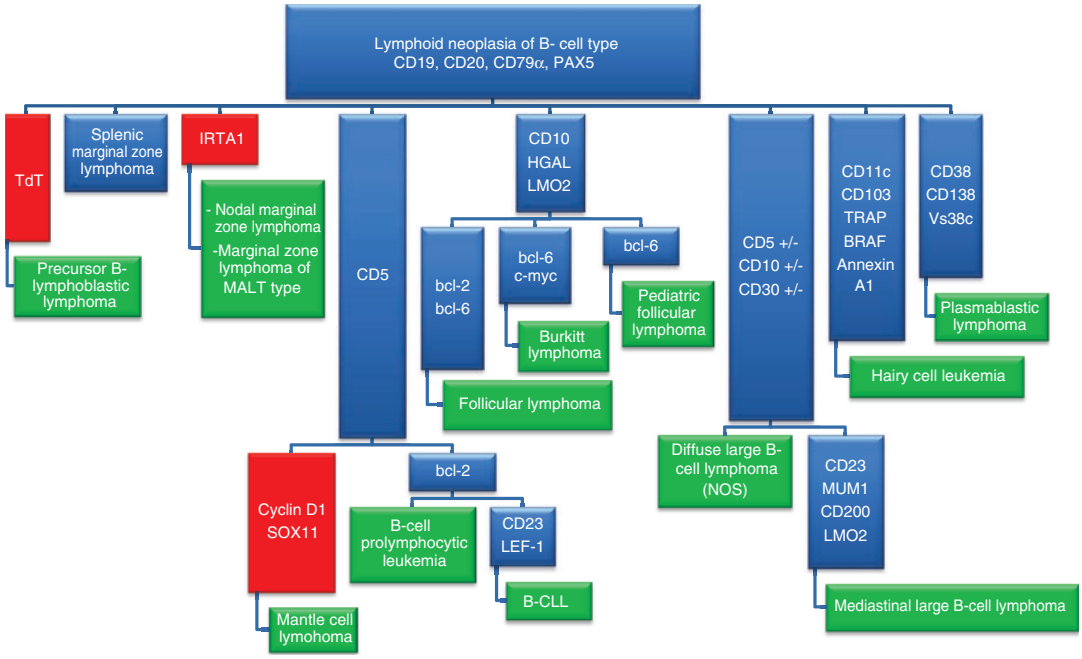
Algorithm 1.6 CK7/CK20 Expression Pattern in Carcinomas



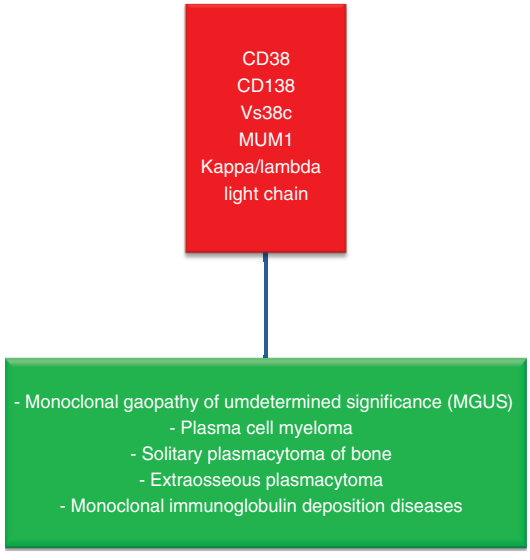
Algorithm 1.7 Cytokeratin CK7+/CK20− Carcinoma



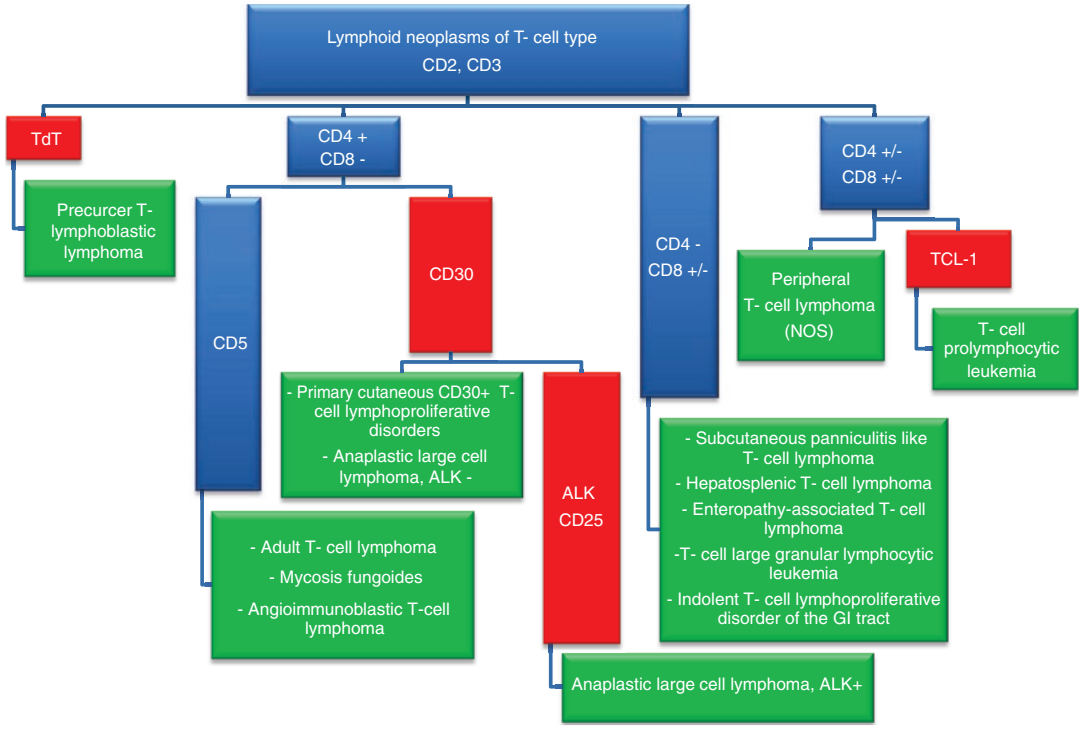
Algorithm 1.8 Cytokeratin CK 7−/CK 20− Carcinoma



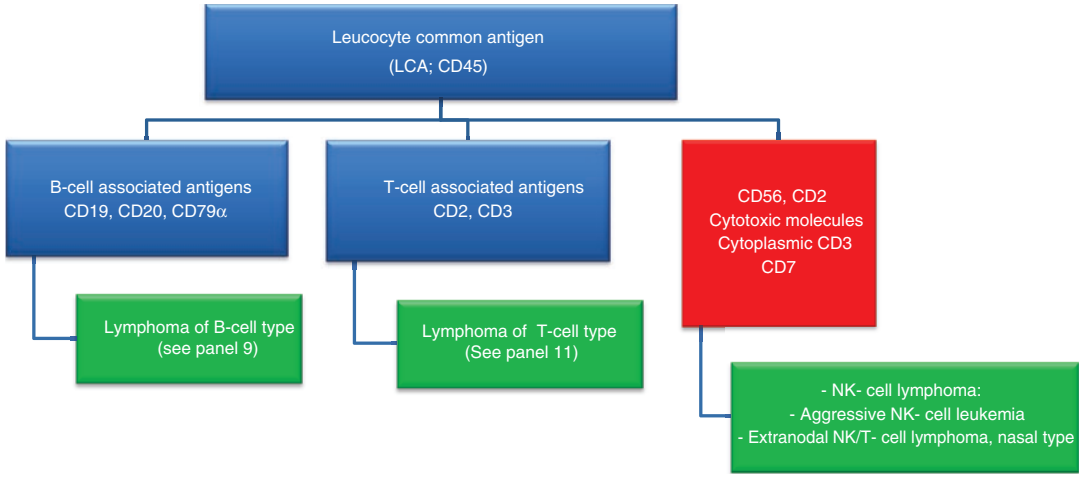
Algorithm 1.9 B-cell Neoplasms



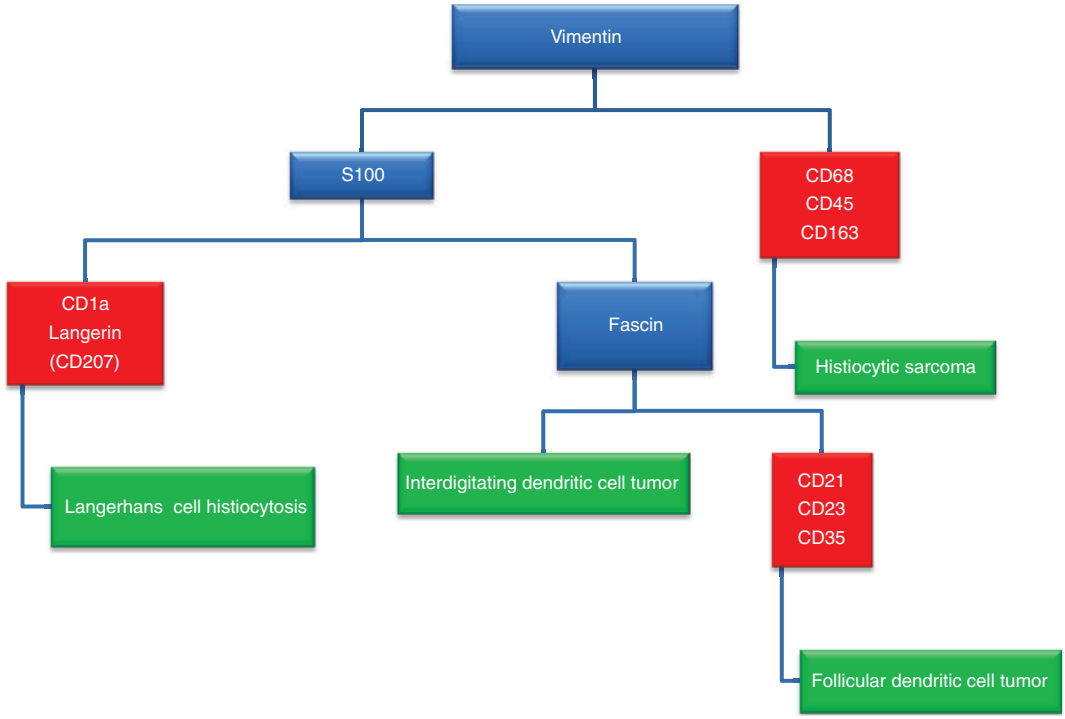
Algorithm 1.10 Plasma Cell Neoplasms



Algorithm 1.11 T-cell Neoplasms



Algorithm 1.12 T/NK-cell Neoplasms



Algorithm 1.13 Histiocytic and Dendritic Cell Tumors

References

1. Bahrami A, Truong LD, Ro JY. Undifferentiated tumor true identity by immunohistochemistry. Arch Pathol Lab Med. 2008;132:326–48.
2. Moll R. Initiale CUP-situation und CUP-syndrom. Pathologe. 2009;30:1–7.
3. Iwata F. Immunohistochemical detection of Cytokeratin and epithelial membrane antigen in leiomyosarcoma: a systemic study of 100 cases. Pathol Int. 2000;50:7–14.
4. Sweedlow SH, Campo E, Pileri SA, et al. The 2016 revision of the world health organization classification of lymphoid neoplasms. Blood. 2016;127:2375–90.