The Daily Dose: Study Tips for Exam and Board Preparation

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The Daily Dose: An Exercise in Histopathology (Feedback)

Recently, I shared raw images from three 'blue cell tumor' cases as an exercise in histopathologic interpretation and report writing. The cases included (in no particular order):

- alveolar rhabdomyosarcoma (ARMS)
- esthesioneuroblastoma
- Merkel cell carcinoma

I'd like to share with you one set of responses (shared with permission) and my comments; the comments are cursory responses and may not represent the entire spectrum of examinations and tests that may be required in these cases; they're simply responses and suggestions to move the participant(s) in the right direction and facilitate development of a more elegant and more relevant sign-out methodology and to improve communication between the signing pathologist and the clinician (or examiner) who may read the report or response. I think taking time to review this type of feedback and asking questions has value and I appreciate the opportunity to share results and engage in dialogue.

First, a few overall recommendations to aide in consistency when reviewing any case:

Identify whether you think what you're looking at is benign or malignant; this may be the biggest challenge, for example…

> POORLY DIFFERENTIATED MALIGNANCY, FAVOR NEUROENDOCRINE VS MELANOMA VS POORLY DIFFERENTIATED CARCINOMA

…and then discuss tests and stains

If you can't decide, especially for some of the inflammatory or granulomatous or infectious diseases, don't hesitate to be undecided, but communicate this, for example…

> ATYPICAL LYMPHOID PROLIFERATION, FAVOR INFLAMMATORY ORIGIN

…and then discuss tests and stains

NOTE: I think the term 'small round cell tumor' is all right, but may not be the right descriptor for some lesions that may not be so round or may have spindle cell features.

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Consider whether you favor the lesion to be epithelial in origin, versus a spindle cell lesion, versus lymphoid (and so on); I think it's all right to start with this as a diagnostic line; for example(s):

MALIGNANT SPINDLE CELL NEOPLASM, FAVOR SMOOTH MUSCLE ORIGIN
vs
ADENOCARCINOMA, LOW/HIGH GRADE
vs
MUCIN PRODUCING ADENOCARCINOMA, LOW/HIGH GRADE
vs
LYMPHOMA, FAVOR B CELL ORIGIN

In most or all of these cases, IHC would be necessary and strong consideration should be given to molecular testing (especially for the sarcomas), flow cytometry (especially for the lymphoid lesions if lymphoma is suspected) and other tests, as well as clinical/laboratory/imaging correlation.

NOTE: I chose 'small round blue cell tumors' for this exercise because they incorporate many of these elements and tests that would be considered

My recommendation in describing additional histologic features like rosettes (suggestive of neuroendocrine origin), 'salt and pepper' features (also suggestive of neuroendocrine origin), plasmacytoid or rhabdoid features (which in these three tumors might suggest melanoma or things like atypical rhabdoid tumor) would be to include these as part of the explanation or report comments rather than part of the diagnostic line. My inclination is that the sooner the diagnosis or preliminary impression can be communicated, the better since it communicates a line of thinking and allows the comments and explanations to explain the response.

In these 'small round blue cell tumor' cases I recommended to the responden(s) to scan the entire slide and examine the lesion for any squamous features or keratinization which may lead one to consider entities such as sinonasal undifferentiated carcinoma, lymphoepithelial carcinoma or the more recently described translocation associated carcinomas such as those lesions associated with the *NUT* and *SMARCB1* locuses.

When considering and ordering additional tests, provide reasoning; examples from the individuals' responses follow:

Case # 1, the respondent(s) wrote:

SMALL ROUND CELL TUMOR RULE OUT EWING SARCOMA, RHABDOMYOSARCOMA, NEUROBLASTOMA
IHC: CD99, DESMIN, MYOGENIN, S100, CAM5.2, EMA, CHROMOGRANIN, SYNAPTOPHYSIN

MY SUGGESTION WAS TO CONSIDER INSTEAD
Case 1: CD99 (to favor vs exclude Ewing sarcoma)
desmin, myogenin (to favor vs exclude tumor of smooth or skeletal muscle origin, ex. rhabdomyosarcoma)
S100 (favor vs exclude melanoma)
Cam 5.2, EMA or cytokeratin (for epithelial origin)
chromogranin, synaptophysin (for neuroendocrine origin)

Case # 2, the respondent(s) wrote:

BLUE ROUND CELL TUMOR WITH RHABDOID FEATURES AND SOME AREAS SHOWS HOMER WRIGHT ROSETTE LIKE FEATURES RULE OUT MELANOMA, OLFACTORY NEUROBLASTOMA AND RHABDOMYOSARCOMA
IHC: S100, HMB-45, CHROMOGRANIN, SYNAPTOPHYSIN, DESMIN, MYOD1

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MY SUGGESTION WAS TO CONSIDER INSTEAD
Case 2: S100, HBM-45 (to favor vs exclude melanoma)
chromogranin, synaptophysin (to favor vs exclude neuroendocrine origin)
desmin, myoD1 (to favor vs exclude smooth vs skeletal muscle origin

Case # 3, the respondent(s) wrote:

> SMALL ROUND BLUE CELL TUMOR WITH SALT AND PAPER FEATURES AND CHOMEDONECROSIS ROLL OUT EWS/PNET, MELANOMA, SMALL CELL CARCINOMA (PRIMARY, METASTATIC)

MY SUGGESTION WAS TO CONSIDER INSTEAD
Case 3: CD99, Fli-1 (to favor vs exclude Ewing sarcoma)
CD56 (presuming this was considered for neuroendocrine features, but may stain for many other things)
TTF-1 (excluding metastatic small cell carcinoma)
CDX2 (I was curious about this choice, as I thinking about CDX2 first for an intestinal type adenocarcinoma)
S100, HMB-45 (favor vs exclude melanoma)
chromogranin, synaptomysin (favor vs exclude neuroendocrine)

WHAT I LIKED (PERSONALLY)

Consistent with IHC panels and a choice of stains that should provide a fairly confident picture of tissue of origin in these undifferentiated tumors; my preference is to think of 'small round blue cell tumors' in this way (as undifferentiated tumors), since the first things I think of are poorly differentiated tumors of any origin (which can include carcinomas, so there should not be tremendous hesitancy to consider a cytokeratin set in any of these lesions, especially if suggestions of epithelial morphology or keratin production can be identified), melanoma (just about all the time, and the choice of S100 and either HMB45 or MelanA is reasonable, though there are some challenges in using HMB45 and MelanA in desmoplastic and amelanotic variants; SOX10 has been used in melanoma diagnosis and tumors of nerve origin as well) and neuroendocrine tumors (there is wisdom in using at least two stains, with chromogranin and synaptophysin considered to be complementary in their sensitivity).

THINGS TO BE CAREFUL ABOUT

Spelling and neatness

Writing things out versus making lists; I prefer lists for three reasons:

1. they are easier to read and provide a clearer picture of the train of thought
2. the reader(s) should and will look for neatness; listing to me is neater
3. the risk of forgetting something is reduced and items can more easily be added to a list

I didn't see any comments in the three cases relating to molecular testing, which could be additionally helpful for some of the diagnoses that might be considered, such as:

- chromosome 22 trranslocations in Ewing sarcoma
- t(1;13) and t(2;13) when considering alveolar rhabdomyosarcoma as a diagnosis

FINAL COMMENT(S):

I think there is benefit in performing IHC drills, so I am working on putting together another set of practice cases to practice IHC considerations; I am also preparing some ‘unknown’ diagnoses to facilitate skills development in employing IHC panels that may be considered.

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