The Daily Dose: Study Tips for Exam and Board Preparation

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The Daily Dose: lymphoid, histiocytic and granulomatous diseases EXERCISE AND FEEDBACK

Regarding five cases that I provided as study preparation:

- EBV related mucocutaneous diease
- nodular sclerosing Hodgkin lymphoma
- Langerhans cell histiocytosis
- Rosai Dorfman Disease (sinus histiocytosis with massive lympadenopathy)
- Kikuchi-Fujimoto Disease (necrotizing histiocyticlymphadenitis)

I made the following comments on the respondent(s) diagnostic lines, which included:

- Malignant lymphoproliferative disorder favor CHL
- Malignant lymphoproliferative disorder favor ???
- Langerhans cell histiocytosis
- Sinus histiocytosis with massive lymphadenopathy
- Features of necrosis associated with histiocytes and lymphocytes favor Kikuji Fujimoto disease (histiocytic necrotizing lymphadenitis). clinical correlation and IHC needed to rule out infection, SLE and lymphoma

As the reader (pretending I am the surgeon or clinician reading the report) the communication was clearer and I could better understand the diagnostic impression.

In cases 4 and 5, considering the phrase "rule out diffuse large blue cell lymphoma" be careful... I expect what was meant was "rule out diffuse large B cell lymphoma" (that may draw the attention of the examiner and make them look for other inconsistencies); the abbreviation 'CHL' was used which I expect meant to 'classical Hodgkin lymphoma' so I would caution against using abbreviations and write the name out so the reader knows what is meant. I admit that I'm not very adept at categorizing these, so I myself might just revert back to 'LYMPHOMA, FAVOR HODGKIN LYMPHOMA' or if the case was consistent 'LYMPHOMA, FAVOR NON-HODGKIN LYMPHOMA or FAVOR LARGE B CELL LYMPHOMA' since it communicates well i.e. that it's a lymphoma, and then the lesion can be described and iHC/low cytometry/molecular tests (all of which are more or less mandatory for lymphoma diagnosis) can be discussed. It's also reasonable to consider the diagnosis of 'MALIGNANT LYMPHOPROLIFERATIVE DISORDER or PROCESS' or 'ATYPICAL LYMPHOID PROLIFERATION' or 'ATYPICAL LYMPHOHISTIOCYTIC PROLIFERATION' if there are cells that resemble histiocytes.

Cases 6 and 7 were relatively obvious since the Langerhans Cell histiocytosis (LCH) case had numerous eosinophils and the case of Rosai Dorfman Disease (RDD) had more easily identifiable emperipolesis; be aware that these diseases, especially for extranodal variant, may lack the numerous eosinophils or the emperipolesis and only histiocytes or cells resembling histiocytes may be present...therefore, using the diagnostic line such as 'ATYPICAL LYMPHOHISTIOCYTIC PROLFERATION' or 'ATYPICAL LYMPHOHYSTIOCYTIC PROLIFERATION WITH MARKED EOSINOPHILIA' and favoring either RDD or LCH may be reasonable.

For case 8, this was again a relatively straightforward case, since there were a lot of histiocytes and clearly necrosis, but bear in mind that infectious diseases can present this way as well (see the comments which follow).

Let's take a step back and review some diagnostic terms that may be worth consideration:

ATYPICAL LYMPHOID or LYMPHOHISTIOCYTIC PROLFERATION

It may be difficult to determine if some of the cases are benign and reactive, benign and infectious in origin, or malignant... picture if you will an infectious disease like a fungal infection such as histoplasmosis with acute and chronic inflammation and large histiocytes that may have engulfed Histoplasma spores... and then review text(s) for the following:

- Wegener granulomatosis
- Rosai Dofrman Disease
- NK/T cell lymphoma

I like to consider these as 'dirty inflammatory diseases' and I may not be able to decide if the lesion is benign or malignant. This is where a panel that may include CD3/CD5/CD20, CD163 or CD68 to identify histiocytes, and perhaps some stains for fungal organisms (PAS-F and GMS) or AFB for mycobacterium may be of use; if separate or sparse T and B cell populations that don't seem to coexpress CD3/CD5 and CD20 are present but fungal organisms ARE identified within histiocytes, then there may be confidence that the lesion is infectious rather than malignant [I think this is one of the most challenging of dilemmas, so having this type of strategy is, I think,helpful in these types of cases]

LYMPHOMA

Just 'lymphoma' with perhaps a lean toward either 'large cell' or 'small cell' or 'Hodgkin' or 'non-Hoddkin' is (I think) acceptable, and then use IHC/flow/molecular tests to better characterize, understanding that it will almost always be appropriate to seek Hematopathology consultation

NECROTIZING or NON-NECROTIZING GRANULOMATOUS INFLAMMATION

- analysis with PAS-F/GMS and AFB for infectious origin, and perhaps a few IHC stains like CD163 or CD68 to verify histiocytes and even a CD3/CD5/CD20 to see if there's an aberrant B or T cell population if uncertainty exists
- polarized light viewing (for foreign body); additionally, consider this resource for morphologic comparison to known foreign body materials: http://www.aaomp.org/atlas/

When there are eosinophils, consider at least the following:

- LCH
- angiolymphoid hyperplasia with eosinophilia (ALHE) and perhaps Kimura Disease which is a distinct lesion from ALHE
- variants of Hodgkin lymphoma (hint: HL may be thought of as type of large B cell lymphoma)
- eosinophilic abscesses that may be seen with or without granulomatous inflammation in disorders like inflammatory bowel disease/Crohn's Disease
- TUGSE or traumatic ulcerative granuoma with stromal eosiniphila versus EBV/CD30 related mucocutanous disease (TUGSE and EBV/CD30 related diseases can look very similar, so a case of TUGSE with abnormal Reed-Sternberg like cells, then an IHC panel of CD3/CD5/CD20/CD30/EBER might be reasonable to consider

- When there is necrosis: the aforementioned necrotizing granulomatous inflammation (which should lead to consideration of infectious disease such as mycobacterial infection)
- suspicion for other infectious diseases (including bartonella from cat scratch, psittacosis from birds and tularemia from rabbits) which should be supported by clinical and laboratory testing such as serology
- necrotic lymph node associated with primary or metastatic lymph node disease (consider both lymphoma and metastatic carcinoma or melanoma and investigate those IHC panels if the history and cytomorphology is consistent with these)
- rheumatologic and autoimmune disease, such as systemic lupus (which should be supported by clinical and laboratory testing)