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Please read this section first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will not issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.
The Thistle QA CEU No is: MT-13/00142.
Each attendee should claim THREE CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

DIFFERENTIAL SLIDES LEGEND

CYCLE 41 SLIDE 5

MANTLE CELL LYMPHOMA

Mantle cell lymphoma (MCL) is one of the rarest of the non-Hodgkin's lymphomas (NHLs), comprising about 6% of NHL cases. While it is difficult to treat and seldom considered cured, investigations into better treatments are actively pursued worldwide. Median survival times were about 3 years, but are now estimated as approaching 6 years for new patients. MCL is a subtype of B-cell lymphoma, due to CD5 positive antigen-naive pregerminal center B-cell within the mantle zone that surrounds normal germinal center follicles. MCL cells generally over-express cyclin D1 due to a t(11:14) chromosomal translocation in the DNA. More specifically, the translocation is at t(11;14)(q13;q32).

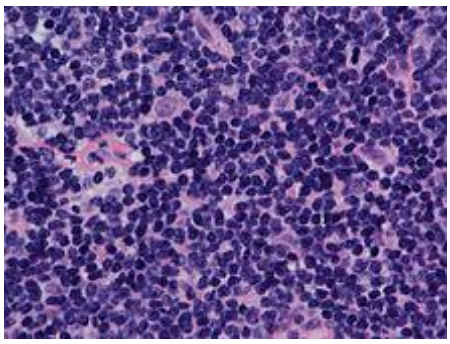
The cause is unknown and no inherited predisposition has been identified. MCL is not communicable. Essentially, it is an abnormal break and subsequent translocation in a gene that causes the cells to divide too early before becoming capable of helping to fight diseases. In addition, the cells do not die as they should and therefore accumulate in the lymphoid system, including lymph nodes and the spleen, with non-useful cells eventually rendering the system dysfunctional. MCL affected cells proliferate in a nodular or diffuse pattern with two main cytologic variants: typical or blastic. Typical cases are small to intermediate sized cells with irregular nuclei. Blastic (aka blastoid) variants have intermediate to large sized cells with finely dispersed chromatin and are more aggressive in nature.

Symptoms

The ratio of males to females affected is about 4:1. At diagnosis, typical patients are in their 60s and usually present to the oncologist with advanced disease. About half have fever, heavy night sweats, unexplained weight loss (over 10%) or some combination. Swelling of lymph nodes and spleen are usually present. Bone marrow, liver and GI tract involvement occurs in a very high percentage. It is common for a person to have initially noticed "a bump" on the neck or in the armpits or groin.

Diagnosis

Diagnosis generally requires stained slides of a surgically removed part of a lymph node. Other methods are also commonly used, including cytogenetics and fluorescence in situ hybridization (FISH). Polymerase chain reaction (PCR) and CER3 clonotypic primers are additional methods, but are less often used.



Mantle cell lymphoma.

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The immunophenotype profile consists of CD5+ (in about 80%),CD10-/+ (It is usually CD5+ and CD10) CD20+, CD23-/+ (though plus in rare cases). Generally, cyclin D1 is expressed but it may not be required. The workup for Mantle cell lymphoma is similar to the workup for many indolent lymphomas and certain aggressive lymphomas.

Mantle cell lymphoma is a systemic disease with frequent involvement of the bone marrow and gastrointestinal tract (generally showing polyposis in the lining). There is also a not-uncommon leukemic phase, marked by presence in the blood. For this reason, both the peripheral blood and bone marrow are evaluated for the presence of malignant cells. Chest, abdominal, and pelvic CT scans are routinely performed.

Since mantle cell lymphoma may present a lymphomatous polyposis coli and colon involvement is common, colonoscopy is now considered a routine part of the evaluation. Upper endoscopy and neck CT scan may be helpful in selected cases. In some patients with the blastic variant, lumbar puncture is done to evaluate the spinal fluid for involvement.

Causes
Attempts to determine causes of MCL have failed. It is not known what causes the translocation damage to the gene. Exposure to toxins is often mentioned as a possibility. The translocation damage to a gene is required in only one cell for the cancer to begin.

Prognosis
The overall 5-year survival rate for MCL is generally 50% (advanced stage MCL) to 70% (for limited-stage MCL). Prognosis for individuals with MCL is problematic and indexes do not work as well due to patients presenting with advanced stage disease. Staging is used but is not very informative, since the malignant B-cells can travel freely though the lymphatic system and therefore most patients are at stage III or IV at diagnosis. Prognosis is not strongly affected by staging in MCL and the concept of metastasis does not really apply.

MCL is one of the few NHLs that can cross the boundary into the brain, yet it can be treated in that event.
There are a number of prognostic indicators that have been studied. There is not universal agreement on their importance or usefulness in prognosis. Ki-67 is an indicator of how fast cells mature and is expressed in a range from about 10% to 90%. The lower the percentage, the lower the speed of maturity, and the more indolent the disease.

MCL cell types can aid in prognosis in a subjective way.

- Blastic is a larger cell type.
- Diffuse is spread through the node.
- Nodular are small groups of collected cells spread through the node.

Diffuse and nodular are similar in behavior. Blastic is faster growing and it is harder to get long remissions. Some thought is that given a long time, some non-blastic MCL transforms to blastic. Although survival of most blastic patients is shorter, some data shows that 25% of blastic MCL patients survive to 5 years. That is longer than diffuse type and almost as long as nodular (almost 7 yrs).

Beta-2 microglobulin is another risk factor in MCL used primarily for transplant patients. Values less than 3 have yielded 95% overall survival to 6 yrs for auto SCT where over 3 yields a median of 44 overall survival for auto SCT. This is not yet fully validated.

Testing for high levels of LDH in NHL patients is useful because LDH is released when body tissues break down for any reason. While it cannot be used as a sole means of diagnosing NHL, it is a surrogate for tracking tumor burden in those diagnosed by other means.

Treatments
There are no proven standards of treatment for MCL, and there is no consensus among specialists on how to treat it optimally. Many regimens are available and often get good response rates, but patients almost always get disease progression after chemotherapy. Each relapse is typically more difficult to treat, and relapse is generally faster.

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Fortunately, regimens are available that will treat relapse, and new approaches are under test. Because of the aforementioned factors, many MCL patients enroll in clinical trials to get the latest treatments.
There are four classes of treatments currently in general use: chemotherapy, immune based therapy, radio immunotherapy and new biologic agents. The phases of treatment are generally: frontline, following diagnosis, consolidation, after frontline response (to prolong remissions), and relapse. Relapse is usually experienced multiple times.

References

1. http://en.wikipedia.org/wiki/Mantle_cell_lymphoma

Questions

1. What is MCL?
2. Discuss the lab findings in a patient diagnosed with MCL.
3. Discuss the prognosis of a patient diagnosed with MCL.