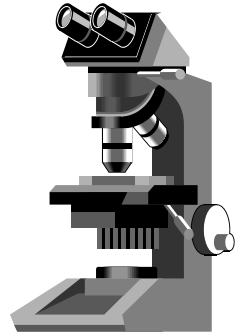


CALIFORNIA
TUMOR TISSUE REGISTRY

LYMPH NODE/SPLEEN PATHOLOGY

Minutes – Subscription A

September 2015



California Tumor Tissue Registry
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Currently Participants in 40 US States and 9 Countries Participated this Month

File Diagnosis:

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- Case 2: MULTIPLE MYELOMA, Ribs**
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- Case 10: SPLENIC MARGINAL ZONE B-CELL LYMPHOMA, Spleen**

CASE #1:

Accession No. 21957

DIAGNOSIS: MYCOSIS FUNGOIDES, Skin biopsy

Diagnoses submitted in decreasing order of frequency:

- Cutaneous T-Cell lymphoma
- Mycosis Fungoides
- Folliculotropic mycosis fungoides
- Mycosis fungoides with large cell transformation
- Follicular lymphoma vs follicular trophic mycosis fungoides
- Marginal for B-Cell lymphoma
- Follicular Lymphoma
- Cutaneous pseudolymphoma
- B-Cell cutaneous lymphoid hyperplasia
- Cutaneous NHL
- Dermatopathic lymphadenopathy
- Primary cutaneous follicle-center lymphoma
- B-cell lymphoma: follicular
- Leukemia cutis
- Primary cutaneous follicle center lymphoma
- MALT lymphoma
- Plasmacytoma
- Small cell lymphoma
- Dermatopathic lymphadenitis

Discussion

Mycosis Fungoides (MF) is the most common type of cutaneous T- cell lymphoma (CTCL). Patients are usually older adults, with a median age of about 55 years. Males are affected twice as commonly as females. The disease is more common in persons of Sub- Saharan African lineage. MF is a clonal disorder composed of T lymphocytes that have a convoluted, cerebriform nuclear appearance. There is usually a prolonged clinical course with infiltration of the skin with rash, patch and plaque-like lesions. It is often clinically misdiagnosed as psoriasis. With advanced disease there is involvement of the lymph nodes, blood and visceral organs. The epidermotrophic neoplastic lymphoid infiltrate is composed of small to intermediate-sized atypical lymphocytes with enlarged hyperchromatic cerebriform nuclei and clear cytoplasm (haloed cells, best evaluated in upper epidermis). There is a paucity of spongiosis. The neoplastic lymphocytes may infiltrate the basal epidermis in a linear manner ("string of pearls", "toy soldiers"), and in small or large aggregates (Pautrier microabscesses). The neoplastic T cells in MF are usually CD4+ mature T cells; 20% of early MF may display CD8+ phenotype and is more common in hypopigmented and hyperpigmented lesions and in pediatric cases. Diagnostic testing: Immunophenotypic abnormalities (an expanded CD4⁺ T-cell population with a CD4/CD8 ratio of more than 10; loss of any or all of the T-cell antigens CD7, CD2, CD3, CD4, and CD5; or loss of both CD4 and CD5). There is clonal rearrangement of T cell receptor genes. It is a slow indolent disease but may progress to Sezary syndrome (erythroderma and leukemia).

CASE #2:

Accession No. 12650

DIAGNOSIS: MULTIPLE MYELOMA, Ribs

Diagnoses submitted in decreasing order of frequency:

- Plasmacytoma
- Plasma cell myeloma, multiple myeloma
- Plasma cell neoplasm (High Grade)
- Plasmablastic lymphoma
- Granulocytic sarcoma

Myeloid Sarcoma
Immunoblastic lymphoma (plasmacytoid)
Diffuse large B-cell lymphoma with plasmablastic features
Diffuse large B-cell lymphoma, extranodal
Melanoma

Discussion

Multiple myeloma (MM)

MM a malignant tumor of terminally differentiated plasma cells most commonly seen in the bone marrow, and often presents with multifocal osteolytic lesions. Solitary bone or soft tissue lesions are designated as plasmacytomas. Thoracic involvement may produce thoracic skeletal abnormalities, plasmacytoma, pulmonary infiltrates, and pleural effusion¹. There is clonal proliferation of plasma cells often with production of monoclonal immunoglobulins or their fragments. MM is a disease of older patients, 50 – 80years; males and African Americans are more commonly affected. Bone marrow biopsy shows focal, interstitial or diffuse infiltrate with a variable number of plasma cells. Bone marrow biopsies should have >10% plasma cells to diagnose myeloma. The cells show variable maturation from plasmablastic to plasma cells. Eccentric nuclei, and perinuclear hof (due to prominent Golgi apparatus) are characteristic features. 10% have amyloid production. Tumor cells stain positively for Kappa or lambda light chains (one markedly more than the other), CD38, CD79a, CD138. There is variable staining for EMA. Differential diagnosis includes metastatic carcinoma, lymphoma, chronic osteomyelitis with abundant plasma cells.

CASE #3:

Accession No. 31108

DIAGNOSIS: CLASSICAL HODGKIN LYMPHOMA, Lymph Node

Diagnoses submitted in decreasing order of frequency:

Hodgkin lymphoma
Classical Hodgkin disease, nodular sclerosing
Hodgkin lymphoma (syncytial variant)
Classical Hodgkin disease, mixed cellularity
Hodgkin lymphoma, lymphocyte predominant
Hodgkin lymphoma, mixed cellularity type
Favor Hodgkin lymphoma, cannot rule out anaplastic large cell lymphoma
Small lymphocytic lymphoma, mixed cellularity type
Anaplastic large cell lymphoma

Discussion

Classic Hodgkin lymphoma (CHL)

CHL is a monoclonal lymphoid neoplasm (mostly of B cell origin) composed of mononuclear Hodgkin and multinucleated Hodgkin Reed-Sternberg (HRS) cells in a background of non-neoplastic small lymphocytes, eosinophils, histiocytes, plasma cells, fibroblasts and collagen. There are four subtypes: lymphocyte-rich, nodular sclerosis, mixed cellularity and lymphocyte-depleted CHL. Developed countries show a bimodal age distribution with one peak at 15-35 years of age and the second one in late life (after 54). In developing countries the disease presents at an earlier age, often in children younger than 10 years, and often mixed cellularity subtype. EBV infection may be involved in this type. Patients present with variable lymphadenopathy and constitutional B symptoms (fever, night sweats, weight loss, pruritus). Cervical group of lymph nodes are most commonly affected. Mediastinal involvement is mostly by the Nodular Sclerosing subtype. Positive stains: CD30 (membrane & Golgi zone), CD15, CD20. PAX5/BSAP shows weak nuclear expression in ~95% of cases, demonstrating the B cell origin. EBV (40-60% of mixed cellularity). Majority of cases are curable by modern therapy. Differential diagnosis: ALK1+ Anaplastic Large Cell lymphoma, Infectious mononucleosis, Non – Hodgkin Lymphoma.

CASE #4:

Accession No. 31857

DIAGNOSIS: COMPOSITE LYMPHOMA SLL/HL, Left inguinal

Diagnoses submitted in decreasing order of frequency:

- Hodgkin lymphoma
- CLL and Hodgkin Lymphoma, composite
- Small lymphocytic lymphoma/classical Hodgkin lymphoma, mixed cellularity subtype
- SLL/CLL
- Follicular lymphoma
- CLL w/ Hodgkin Lymphoma transformation
- CLL/SLL consistent with Reed Sternberg cells (Richter's transformation)
- Small lymphocytic lymphoma (CLL) with large B-cell lymphoma transformation
- Nodular lymphocytes predominant Hodgkin lymphoma
- Classic Hodgkin lymphoma, mixed cellularity type
- CLL with Richter's transformation (Hodgkin lymphoma)
- B-cell, large cell lymphoma

Discussion

Composite Lymphoma: Small Lymphocytic Lymphoma (SLL) /Chronic Lymphocytic Leukemia (CLL) and Hodgkin Lymphoma, Nodular Sclerosis Type. The nodal architecture is replaced by small lymphocytes with proliferation centers. This pattern occupies about 70% of the node and suggests CLL/SLL. In addition, there are nodules of apparent classic Hodgkin Lymphoma characterized by a mixture of Reed-Sternberg cells, Hodgkin cells, lacunar cells, eosinophils and lymphocytes. Focal fibrous bands were seen traversing the lymph node in some sections. The flow cytometry results were consistent with CD5+ B cell lymphoma. The lack of FMC7 supports CLL/SLL, as does the histology. Also the CBC showed 67% lymphocytes. This is a remarkable case of composite SLL and CHL lymphoma involving the same lymph node. The simultaneous occurrence of unrelated, morphologically and genetically distinct lymphomas in the same mass is a rare finding and is defined as composite lymphoma. In many cases the so-called composite lymphomas are genetically identical owing to different transformation events of a common precursor cell. This holds especially true for the occurrence of classic Hodgkin's lymphoma (CHL) and non-Hodgkin's lymphoma in the same patient, where fundamental morphological and immunophenotypical discrepancies superimpose onto the common cellular origin. Composite lymphomas occur as a combination of either two different B cell or two different T cell lymphoma components or one B cell lymphoma and one TCL. Composite lymphomas consisting of CHL and B cell NHL are believed to originate from a common precursor B cell with identical *IgH* gene rearrangements of both B cell lymphomas. In contrast, true composite lymphomas consisting of two clonally unrelated lymphomas, such as CHL and TCL are rare. There are various explanations for the development of CHL and NHL in the same patient, such as induction by chemotherapeutic agents or immunological defects. There is an almost threefold risk of CHL in patients successfully treated for NHL. Especially, lymphomas occurring with a delay of many years after chemotherapy of a first lymphoma are often considered to be treatment induced. Other known factors associated with high rates of lymphoma are autoimmune diseases such as Sjögren's syndrome, primary or acquired immunodeficiencies and autoimmune lymphoproliferative syndrome.

CASE NO #5:

Accession No. 31605

DIAGNOSIS: DIFFUSE LARGE B-CELL LYMPHOMA, Right testicle

Diagnoses submitted in decreasing order of frequency:

- B cell lymphoma
- Testicular non-Hodgkin lymphoma, favor DLBCL
- Diffuse large B-cell lymphoma
- High grade B-cell lymphoma
- Hodgkin Lymphoma
- Burkitt lymphoma
- Anaplastic lymphoma

Discussion

Diffuse Large B cell Lymphoma (DLBCL), Right testicle Primary testicular lymphoma constitutes 1-2% of Non-Hodgkin's lymphoma and 1-10% of testicular neoplasms affecting elderly men greater than 60 years of age. It is associated with a grave prognosis. The most frequent histology is DLBCL and has a predilection for extra nodal sites, especially the contra lateral testis and central nervous system. The incidence has increased over the last two decades with the emergence of human immune deficiency virus infection. The vast majority of the primary testicular lymphomas of the DLBCL type belong to the non-germinal center B-cell-like subgroup and all exhibit high proliferative activity, and Bcl-2. The uncommon primary testicular lymphoma of germinal center B-cell-like type may correlate with a positive HIV status. Factors that have been linked to more favorable outcomes include younger patient age, localized disease, and presence of sclerosis at pathologic analysis, smaller tumor size, lower histological tumor grade and lack of epididymal or spermatic cord involvement.

CASE #6:

Accession No. 21382

DIAGNOSIS:HAIRY CELL LEUKEMIA, Spleen

Diagnoses submitted in decreasing order of frequency:

- Hairy cell leukemia / Lymphoma
- Hairy cell leukemia versus splenic marginal zone lymphoma
- Littoral Cell angioma
- Low grade B-cell lymphoma
- Splenic marginal B-cell lymphoma
- Splenic lymphoma, favor lymphoplasmacytic type
- CLL/SLL
- Splenic marginal zone lymphoma
- Hemangioendothelioma
- Splenic hamartoma
- Congestive splenomegaly
- Bacillary angiomatosis
- Splenic T-cell lymphoma
- Acute myeloid leukemia
- Splenomegaly possible IM
- Langerhans cell Histiocytosis

Discussion

Hairy cell leukemia (HCL) is a rare chronic B cell lymphoproliferative disorder characterized by the accumulation of small mature B cell lymphoid cells with abundant cytoplasm and "hairy" projections within the peripheral blood, bone marrow, and splenic red pulp. This typically results in splenomegaly and variable cytopenias, bleeding, and an increased risk of infection. The pathogenesis of HCL is largely unknown. Older white males are more commonly affected. Studies indicate that most cases are associated with a V600E activating mutation in the serine/threonine kinase BRAF implicating BRAF signaling in HCL. Exposures to ionizing radiation, Epstein-Barr virus, organic chemicals, woodworking, and farming have been mentioned as possible causes. Familial cases have been described, with family

members sharing the same HLA haplotype. HCL is postulated to arise from a late, activated memory B cell. Patients develop diffuse splenomegaly with involvement of the red pulp by the tumor cells, often with atrophy of the white pulp. No phagocytosis is seen. Tumor cells stain positively for CD11c, CD19, CD20, TRAP (tartrate resistant acid phosphatase), PCA1 (plasma cell antigen-1), FMC7, surface IgH. The findings of pancytopenia and splenomegaly in the presence of circulating cells that are TRAP positive and a dry bone marrow aspirate with biopsy material showing infiltration with a mononuclear cells that have a fried-egg appearance are diagnostic of hairy cell leukemia. The differential diagnosis includes Splenic Marginal Zone Lymphoma (different staining pattern), B cell Prolymphocytic Leukemia (morphology is different).

CASE #7:

Accession No. 32027

DIAGNOSIS:HISTIOCYTIC SARCOMA, right neck/tonsil

Diagnoses submitted in decreasing order of frequency:

- Histiocytic sarcoma
- Anaplastic large cell lymphoma
- Rosai-Dorfman
- Histiocytosis
- Myeloid sarcoma
- Atypical retriculohistiocytoma
- ALK positive anaplastic lymphoma
- Rhabdomyosarcoma

Discussion

Histiocytic Sarcoma, Tonsil / Right Neck

Microscopic sections of this large mass reveal an undifferentiated pleomorphic epithelioid proliferation composed of round to oval to focally grooved nuclei, small to focally prominent eosinophilic nucleoli, abundant eosinophilic cytoplasm, some with a vacuolated appearance, and increased mitotic activity, including atypical mitoses. In addition there are multinucleated tumor cells with associated mixed inflammatory cell infiltrate and lesional cells with phagocytic activity. Based on the microscopic features and IHC findings this case was diagnosed as a Histiocytic Sarcoma. This rare tumor is of macrophage lineage, and is very aggressive. The differential diagnosis includes reactive Histiocytosis, DLBCL, and carcinoma.

CASE #8:

Accession No. 29433

DIAGNOSIS:BURKITT LYMPHOMA, Mesentery

Diagnoses submitted in decreasing order of frequency:

- Burkitt lymphoma
- Burkitt lymphoma, endemic type
- Lymphoblastic lymphoma
- High grade B cell lymphoma
- Diffuse large cell lymphoma
- Enteropathy associated T-cell lymphoma
- Malignant lymphoma
- Malignant lymphoma, small non-cleaved
- Large cell lymphoma

Discussion

Burkitt Lymphoma, Mesentery, Lymph Node

The mesenteric mass and lymph node show a mitotically active, monotonous non-cleaved lymphoid infiltrate with a starry sky background. The tumor cells show prominent nucleoli and coarse chromatin. Burkitt lymphoma (BL) is a highly aggressive B-cell lymphoma. The 3 different clinical variants of Burkitt lymphoma (BL) described (endemic, sporadic, and immunodeficiency related) with varied clinical presentations. The endemic form of Burkitt lymphoma (eBL) is most commonly seen in patients in equatorial Africa, with jaw and facial bone (orbit) involvement occurring in more than 50% of cases. Other clinical presentations include abdominal masses (ileal, cecal, etc), as in this case. Flow cytometry of biopsied tissue may reveal surface immunoglobulin M (IgM) (most common), as well as other mature B-cell markers such as CD20, CD22, CD79a, and CD10. Tdt, CD5, CD23, and CD34 are negative. Cytogenetic studies to identify c-myc mutation will aid in the diagnosis. Expression of CD21 (Epstein-Barr virus [EBV]-C3d receptor) is present only in EBV-positive patients (endemic BL). Differential diagnosis includes DLBCL, Lymphoblastic Lymphoma, Mantle Cell Lymphoma.

CASE # 9:

Accession No. 29546

DIAGNOSIS:MANTLE ZONE LYMPHOMA, Spleen

Diagnoses submitted in decreasing order of frequency:

- Small lymphocytic lymphoma/ chronic lymphocytic leukemia
- Splenic B-cell lymphoma, unclassified
- Splenic marginal zone lymphoma, Splenic lymphoma (B-Cell) with villous lymphocytes
- Lymphoplasmacytic lymphoma
- B-cell prolymphocytic lymphoma
- Mantle cell lymphoma
- Prolymphocytic leukemia
- Diffuse large B-Cell lymphoma
- Follicular lymphoma
- B-cell prolymphocytic lymphoma
- Mantle cell lymphoma (cyclin D1 negative)

Discussion

Mantle Cell Lymphoma, Spleen

This aggressive disease usually presents with splenomegaly. Postulated normal counterpart is naïve pre-germinal center B cell of inner mantle zone. Microscopically splenic parenchyma shows confluent tumor nodules in white pulp or enlarged lymphocytic coronas surrounding germinal centers. Tumor cells are small cells with irregular, often indented, hyperchromatic nuclei. Tumor cells show positive staining for surface IgM/IgD, CD5, CD20, CD43, bcl1/cyclin D1. Confirmed by characteristic (11,14)(q13;q32) translocation. Differential diagnosis: Splenic marginal zone lymphoma, SLL/CLL, reactive follicular hyperplasia.

CASE #10:

Accession No. 31289

DIAGNOSIS:SPLENIC MARGINAL ZONE B-CELL LYMPHOMA, Spleen

Diagnoses submitted in decreasing order of frequency:

- Small lymphocytic lymphoma
- Marginal zone B cell lymphoma
- Low grade B-cell lymphoma (favor marginal zone lymphoma)
- Lymphoplasmacytic lymphoma
- Splenic B-cell lymphoma, unclassified
- Hairy cell leukemia
- Splenic diffuse red pulp small B-cell lymphoma

Mantle cell lymphoma
MALT
Splenic lymphoma with villous lymphocytes

Discussion

Splenic Marginal Zone B cell Lymphoma

Splenic marginal zone lymphoma (SMZL) is a specific low-grade small B-cell lymphoma. Characteristic features are moderate to massive splenomegaly, moderate lymphocytosis with villous morphology, intrasinusoidal pattern of involvement of various organs. SMZL constitutes 8% to 14% of lymphoma in surgically removed spleens involved by lymphoproliferative disorders. The median age of patients is 68 years. Histologically, the hyperplastic white pulp shows expansion of marginal zones with frequent merging and coalescence. Neoplastic cells extend from the marginal zone to the red pulp with variable involvement. Involvement of splenic sinuses is typical. The sinuses are filled up with neoplastic cells morphologically identical to the cells seen in the marginal zones. There is neoplastic proliferation of small to medium sized lymphocytes with a diffuse growth pattern. There are occasional transformed lymphocytes. Mitotic figures are rare. Clonal rearrangements of IgH and IgL are common. Differential diagnosis: Hairy Cell Leukemia, B- CLL, Mantle Cell Lymphoma, Lymphoplasmacytic Lymphoma

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