Disorders of White Blood Cells and Lymphoid Tissues

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Case Study 9:

Max is a 60-year-old living in Iowa. For the 27 years, he has been working in the agricultural industry, particularly in the management of corn production. Recently he began to feel weak during work and tired easily. During the night he woke up sweating, and he often felt unusually warm during the day. Max was also surprised that, in spite of eating regularly, his weight was declining and his work pants were now too large for him. Upon physical examination, his physician noted his inguinal lymph nodes were swollen although Max said they were not sore. Subsequent laboratory tests confirmed follicular, non-Hodgkin lymphoma. Chemotherapy in conjunction with rituximab was immediately initiated.

1. What are the key cellular differences between non-Hodgkin lymphoma and Hodgkin lymphoma?
2. The early manifestations of non-Hodgkin lymphoma and Hodgkin lymphoma in lymphatic tissue appear differently. In terms of lymphatic presentation, how would these two diseases appear clinically?
3. What are the pharmacologic properties of rituximab, and what is its mechanism of action on malignant cells?
4. Outline the structure of lymph node parenchyma including the areas where B and T lymphocytes reside. Where did Max’s lymphoma arise?

Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL) are both a type of cancer that begins in a subset of lymphocytes that aid the body fight off infections and other conditions. Although the diseases may sound similar, the primary difference between them is in the specific lymphocyte each involves. Hodgkin lymphoma occurs with the presence of Reed-Sternberg cells, which are mature B cells that have become malignant. They are unusually massive by cellular standards and are up to five times larger than normal lymphocytes. They carry more than one nucleus. The initial sign of the Hodgkin lymphoma is the appearance of enlarged lymph nodes. In contrast, Non-Hodgkin lymphoma is marked by the absence of Reed-Sternberg cells. It is derived from either B cells or T cells and can arise in the lymph nodes or other body organs. Both the B and T cells play different roles in the response of the body immune to disease and infections.

Despite the two forms of lymphomas being marked by painless lymph nodes swelling, the lymphatic presentation of Hodgkin lymphomas and non-Hodgkin's lymphoma appear differently clinically. Hodgkin lymphomas begin with either a single enlarged node or within a local group. It likely arises in the upper portion of the body that is the neck, underarms, or chest primarily Asymptomatic lymphadenopathy that is above the diaphragm 80% of the time but also found under the arm or in the groin. Although presentation commonly occurs above the diaphragm, it may in some instances first present below the diaphragm resulting in frequently progressing to the spleen. Most of the Hodgkin’s lymphoma malignancies are found in the chest regions with very few cases demonstrating cancer outside the lymph nodes. The Hodgkin’s swellings are often not painful but can feel rubbery. Additionally, in Hodgkin's lymphoma, the progression of the condition is often quite orderly spreading in a downward pattern. The pattern is usually from the initial site of the attack to each lymph node, and its diagnosis rarely happens in stage IV. On the other hand, Non-Hodgkin lymphoma arises in lymph nodes throughout the body, but can also occur in normal organs. It is usually a multicentric condition in nature generalized by lymphadenopathy with several nodes involved. The lymph nodes become enlarged when it occurs close to the surface of the body like on the neck sides, in the groin or above the collar bone. They may be seen or felt as lumps under the skin are often tender to the touch (Shankland, Armitage, & Hancock, 2012). More often Non-Hodgkin lymphoma tumors commonly occur in the abdomen with most cases of lymphomas outside the lymph nodes. Most of the Non-Hodgkin lymphoma cases are likely to spread since it is a multicentric condition, but is not predictable in terms of progression. Because of the case presentations of Non-Hodgkin lymphoma is often diagnosed at stage IV.

Rituxan (Rituximab) is indicated for the treatment of patients with relapsed or refractory, low-grade or follicular, CD20-positive, B-cell, non-Hodgkin’s lymphoma; Rituxan is indicated for the first-line treatment of follicular, CD20-positive, B-cell non-Hodgkin’s lymphoma in combination with cyclophosphamide, vincristine, and prednisolone (a steroid) known asCVP chemotherapy(Genetech, 2017). Rituxan is a preservative-free liquid concentrate for intravenous administration. Rituxan is supplied at a concentration of 10 mg/mL in either 100 mg or 500 mg single-use vials.‘Rituxan is a genetically engineered human monoclonal IgG1 kappa antibody directed against the CD20 antigen found on normal and malignant surfaces of B lymphocytes; Rituxan is a medium of nutrient containing the antibiotic gentamicin, though it is not detectable in the final product’ (Genetech, 2017).Rituximab exerts its effect by binding a Tran’s membrane protein expressed on the surface of B cells, called the CD20 antigen, leading to depletion of this B-lymphocyte lineage. The binding involves a quick depletion of both the normal and damaged B cells, resulting in a reduction of their immunogenic properties. In addition to the CD20+ B-cells depletion per se, it also has other immunologic mechanisms like cellular and complement dependent cytotoxicity, induction of oncogenic-Myc and MHC class II expression, and direct apoptosis induction (Taylor & Lindorfer, 2014). These multiple mechanisms use the anti-CD20 chimeric monoclonal antibody in Rituximab to kills B cells. It also sensitizes cells to the effects of chemotherapy by mobilizing antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity effectors mechanisms (Niermann, Schulze, & Hallermann, 2013). The mechanisms of action of Rituximab in the elimination of tumor lymph nodes occur along the course of the lymphatic vessel and are organized lymphoid organs containing lymphocytes within a fine reticular stroma. They are small elongated bean shaped glands that occurs in clusters much like grapes. Along the lymph channels reside approximately 600 lymph nodes that act as filters that sieve off the harmful substances brought by the lymphatic channel and are sites of origin and production of lymphocytes for normal physiological functions. They react to both the substances of endogenous and exogenous with a variety of distinct morphological and functional responses.

The parenchyma of the lymph nodes contains reticular fibers, which support the lymphocytes. Its structures include the capsule, sub capsular sinus, cortex, paracortex, medullary sinuses, medullary cords and hilum. The primary structural division of lymph node parenchyma is medulla and cortex with germinal centers where the B cells multiply and later differentiate into plasma cells and follicles. The cortex contains collections of lymphocytes that consist of predominantly B and some T-lymphocytes. The maturation of B lymphocytes completely happens within the bone marrow while the T lymphocytes attain maturity within the thymus after exiting the bone marrow immaturely. The medulla contains the medullary cords and sinuses together with the lymphatic vessels. The sites for the B cells are the primary and secondary follicles of the lymph node cortex while that of the T-cells is the paracortex which is the deeper region of the cortex (Förster, Braun, & Worbs, 2012). Max’s lymphoma arose from the centroblasts and centrocytes in the germinal centers of the lymph nodes. This is because he was diagnosed with follicular lymphoma that is a condition of neoplasm composed of follicle center, i.e., the germinal center and the B-cells, typically involving both centrocytes and centroblasts which usually have at least a partially follicular pattern. Also, the follicular lymphoma accounts for about 30% of all non-Hodgkin lymphomas in adults (Lymphoma Research Foundation, 2012) which were the case of Max.

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