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Advancements in Treatment for Non-Hodgkin's Lymphoma

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Abstract. In our past and in modern society, fragmentation has been prevalent because of diseases throughout history, whether it is the flu, or life threatening illnesses, they have always found a way to impact our lives. Many phenomenons have arised, and one seems to always foment a spark and multitude of debates and controversy, which is the enervating malignancy of cancer. And upon researchers, the non-Hodgkin's lymphomas are among the most diverse and challenging diseases to treat. Non-Hodgkin lymphoma comprises a diverse group of cancers originating from immune system cells, often presenting as swollen lymph nodes or solid masses. With the latest World Health Organization classification identifying over 50 distinct subtypes, the classification of these lymphomas remains intricate and constantly evolving. However, for general physicians, a more practical approach is to categorize them as either low-grade, or sometimes even high-grade, as this difference plays a crucial role in predicting disease progression and guiding treatment strategies. This update focuses on essential principles of diagnosis and management relevant to doctors who are not specialists, who may have patients that are diagnosed with non-Hodgkin lymphoma at various stages, from initial symptoms to treatment and ongoing care. Upon being the seventh most commonly diagnosed malignancies, Hepatosplenomegaly, abdominal masses, or compression of internal organs like the gastrointestinal tract, blood vessels, airways, spinal cord, ureters, or bile ducts; or localized tumors of parenchymal or visceral organs are common presenting findings. Other common symptoms include hematologic cytopenias, drenching night sweats, unexplained fevers, or weight loss exceeding 10% of baseline (B symptoms). Advancements in molecular oncology have started to uncover the underlying causes of their formation.

Keywords: Non-Hodgkin's Lymphoma, B-cell Lymphoma, Targeted therapy, Chemotherapy regimes, Environmental risk factors.

1. Introduction

In epidemiology, because of the heterogeneity Non-Hodgkin's lymphoma accounts for among malignant neoplasms of the lymphoid system, the United States NHL incidence rate has been rising around 3-4% each year since the early 1980s. The mortality rate from non-Hodgkin lymphoma (NHL) is increasing by an estimated 2% each year. This increase can only be explained in part by variations in the diagnostic standard and well known risk factors, such as family history, HIV, immunosuppressive disease or drug use [1].

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2. Pathogenesis of non-Hodgkin's lymphoma

Numerous risk factors for non-Hodgkin lymphoma (NHL) have been previously identified and reviewed. Genetic factors include a potential relative history of NHL or other types of possible cancers, as well as inherited immunodeficiencies. Environmental risk factors encompass exposure to high doses of radiation, viral infections, and conditions such as AIDS, along with the use of phenytoin. Certain occupations have been linked to an increased risk of NHL, including those in farming, pesticide application, grain milling, forestry, chemistry, cosmetology, machining, printing, and industries like oil, latex, polymers, and artificial materials. Although cigarette smoking has been shown to increase the risk of NHL in most studies, it is not consistent across all research on the subject [1]. Agricultural exposures have also been linked to non-Hodgkin's lymphoma, as farmers have an increased risk of non-Hodgkin's, with multiple studies finding sources of risks for NHL among producers or sprayers of pesticides. Though some findings may be inconsistent across countries and studies, overall it is evident that there is an increase in correlation to the disease among production workers, and professional pesticide sprayers with heavy exposure. Some research has identified links between general pesticide exposure and non-Hodgkin lymphoma, although there are exceptions. These studies encompass not only adults but also children, particularly in cases where parents have used pesticides [2]. Herbicides are also prevalent to the risk of NHL, as focus has been more particularly fixed on the phenoxy herbicides. This includes chemicals such as 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and 2,4-dichlorophenoxyacetic acid (2,4-D). 2,4,5-T has garnered particular attention due to its contamination with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). While 2,4-D and other frequently used phenoxy herbicides are not infected with TCDD, they do contain other dioxins and dibenzofurans [2].

Mature B-cell non-Hodgkin lymphoma (B-NHL), which makes up about 83% of all NHL cases, is a diverse group of cancers where B cells in the body start multiplying uncontrollably. While the exact cause of B-NHL is not fully understood, it is clear that changes in the immune system are a key factor. Conditions that weaken the immune system, such as congenital immunodeficiencies, HIV/AIDS, and transplant patients on immunosuppressive drugs, are well-established risk factors. Chronic infections with viruses like Epstein-Barr (EBV), H. pylori, or hepatitis C, especially when the immune system is not functioning properly, also increase the risk of B-NHL. Autoimmune diseases like rheumatoid arthritis, lupus, and Sjögren's syndrome have also been linked to a higher chance of developing B-NHL. On the other hand, conditions like asthma, hay fever, and eczema might actually lower the risk. A common theme in these conditions is the disruption of cytokines, which are key players in immune system function. These cytokines can boost B-cell growth, prevent them from dying off, and help them undergo processes that make it easier for genetic changes, such as chromosomal translocations, to occur. These genetic changes can activate cancer-causing genes or turn off tumor-suppressing genes, leading to the development of B-NHL. So, it is likely that cytokines play an important role in the development of B-cell lymphoma [3]. In T-cell lymphomas, normal T-cells become cancerous, leading to their unchecked growth and survival. This transformation typically involves genetic mutations and chromosomal changes that interfere with the normal regulation of the cell cycle and cell death. Specific alterations, such as mutations in the T-cell receptor (TCR) signaling pathway or in crucial transcription factors, play a key role in the development of these malignant T-cells [4].

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3. Classification of non-Hodgkin's lymphoma

Non-Hodgkin lymphoma can show up in different ways. Most people will first notice swollen lymph nodes or an enlarged spleen. This could involve one node or several. In cases of low-grade lymphoma, the swelling tends to develop slowly over months or even years, while in high-grade lymphoma, it can happen much more quickly. Around a third of patients might have lymphoma outside of the lymph nodes, which can affect almost any organ or tissue. When lymphoma appears as a solid tumor in other parts of the body, it may look like another type of cancer at first until the biopsy results come in [5]. When present with non-Hodgkin's lymphoma, to confirm the illness diagnosis, a biopsy is necessary.. A biopsy is a medical procedure where a sample of tissue or cell is removed to be examined under a microscope to determine a diagnosis. When conducting a biopsy, the best approach is an excisional lymph node biopsy, but if the lymph node's location makes it difficult to reach, a radiologically guided core biopsy can be an alternative. Fine needle aspiration generally is not enough for a proper diagnosis. While bone marrow biopsy is occasionally done for staging, it is not typically used to diagnose lymphoma. Even if the bone marrow biopsy appears normal, it does not rule out lymphoma [5]. After the biopsy is taken, immunophenotyping is done to figure out whether the lymphoma comes from B-cells or T-cells. This process uses antibodies to detect certain markers on the surface of the cells that are specific to NHL. This step is important for classifying the type of lymphoma and helps guide the treatment plan. Additional genetic and molecular tests may be done to look for specific mutations or chromosomal changes that are often found in NHL. Methods like fluorescence in situ hybridization (FISH) and polymerase chain reaction (PCR) can identify these genetic alterations in lymphoma cells. These tests offer important information about the kind of NHL and can help estimate the trajectory of the disease [6].

4. Treatment of non-Hodgkin's lymphoma

Before the 1980s, high-dose radiation therapy was the primary treatment for Hodgkin lymphoma. This approach often involved mantle field radiation, targeting lymph nodes in the neck, chest, and armpits [7], yet people treated with only radiotherapy, were reported with cure rates varied from 25% to 75% but averaged less than 50%, and since no trials have been published as of yet, it is unclear if radiation improves the overall result [8].

4.1. Chemotherapy drugs

So regularly, chemotherapy has been the predominant treatment for non-Hodgkin's, and all other types of cancer. In more severe Hodgkin's disease (stages IIIB-IV), it is easier to evaluate how well chemotherapy is working compared to localized cases, since chemotherapy is the primary treatment and relapses are more common. Three primary chemotherapy regimens have been employed: ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine), MOPP (mustine, vincristine, procarbazine, and prednisolone), and a mixture of the two. MOPP, which has been the standard treatment, involves alternating two-week intervals of oral and intravenous medication with rest periods to allow the body to recover [9]. Chemotherapy has also been faced with complications, as side effects that can go long-term can include peripheral neuropathy, which in some cases may be severe enough to cause disability. Cardiomyopathy is a studied risk related to the anthracycline component of R-CHOP chemotherapy.

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4.2. Chemotherapy drugs 2

Treatment with rituximab often leads to low immunoglobulin levels (hypogammaglobulinemia), though it rarely results in serious infections. Kidney damage may be induced by nephrotoxic chemotherapy agents, such as platinum compounds, or as a tumor lysis syndrome complication that can occur during treatment for certain aggressive lymphomas. To meet these challenges, advances in the biology of the molecular and genetic processes underlying lymphoma have made targeted therapy available for specific genetic subtypes of the disease. Phase I and II clinical trials are showing early positive results—e.g., ibrutinib has been effective against mantle cell lymphoma. However, the emergence of drug resistance and novel toxicities remains a serious problem, and further research will be needed to optimize the use of these drugs. Success of any salvage chemotherapy regimen is only measured in relation to patient characteristics, namely time to relapse and chemotherapy treatment history. The most successful outcomes to date, 20% five-year progression-free survival, in patients whose therapy with MOPP or its analogues has been unsuccessful have been obtained using ABVD. In contrast, MOPP has had limited success in those resistant to ABVD. Following in line or different orders of MOPP/ABVD regimens, most traditional-dose salvage treatments have proven of little benefit. The optimum response has come from the CEP regimen (Prednimustine, etoposide, and CCNU), which has yielded a 47% complete remission rate and a 20% five-year survival rate. For those patients not responding to salvage chemotherapy, but not a candidate for high-dose chemotherapy, single-agent chemotherapy remains capable of affecting effective symptom control [10].

4.3. Bone marrow transplant

Bone marrow transplants have also been used with high doses of chemotherapy, yet in a study previously done from results of breast cancer, bone marrow transplant paired with chemotherapy found no extra benefit. In this study, researchers randomly assigned almost up to 200 patients, who were 15 to 65, with stage I-IV non-Hodgkin's lymphoma to either undergo a correspondent bone marrow transplant or be part of the control group. All participants had already completed three cycles of the CHVmP/BV regimen, which includes Prednisone, doxorubicin, teniposide, cyclophosphamide, bleomycin, and vincristine added midway through each cycle. Of the 194 patients, 140 were classified as low or intermediate risk based on the global prognostic index. Patients who participated in the bone marrow transplant arm were administered three additional cycles of CHVmP/BV, as well as the BEAC regimen of carmustine, etoposide, cytarabine, and cyclophosphamide. Control patients, meanwhile, continued on five additional cycles of CHVmP/BV. At 53 months of follow-up, 61% of patients with a bone marrow transplant had no evidence of disease relapse, and 68% survived. 56% remained progression-free and 77% were alive in the control arm. The differences between the two groups were not statistically significant, indicating that the combination therapy and bone marrow transplant did not provide a clear survival advantage [11].

5. Conclusion

The primary methods for diagnosing NHL are biopsy and immunophenotyping, which establishes whether the cancer starts in T-cells or B-cells. Fluorescence in situ hybridization (FISH) and polymerase chain reaction (PCR) are two more genetic and molecular diagnostics that shed light on the prognosis and classification of diseases. From high-dose radiation therapy to chemotherapy regimens including MOPP, ABVD, and R-CHOP, treatment approaches have changed over time.

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Chemotherapy is still the most common treatment, however it can have negative side effects such immunosuppression, cardiomyopathy, and neuropathy. New targeted treatments, including ibrutinib for mantle cell lymphoma, have shown promise but need more study because of their unpredictable effects and acquired resistance. Although bone marrow transplantation has been investigated as a therapeutic option, clinical research has produced conflicting findings about how well it improves survival. However, the molecular processes of tumor progression have not been thoroughly explored throughout the study, the discussion of environmental risk factors is not specific enough with regard to exposure levels and their direct role in NHL development, and the efficacy of more recent targeted therapies is still uncertain because of a lack of long-term clinical data. Future studies should concentrate on a few crucial areas to improve our comprehension and handling of NHL. Immunotherapy and molecular oncology developments should be incorporated into treatment plans, especially when it comes to customizing medications to each patient's unique genetic profile. Clear causal relationships must be established by additional investigation of environmental risk factors, particularly thorough epidemiological research on pesticide exposure and NHL incidence. It is still imperative to create more potent targeted treatments with fewer adverse effects, and continuous clinical trials are needed to confirm their safety and effectiveness.

References

[1] Tatham, L., Tolbert, P., & Kjeldsberg, C. (1997). Occupational Risk Factors for Subgroups of Non-Hodgkin's Lymphoma. Epidemiology, 8(5), 551–558. http: //www.jstor.org/stable/3702687
[2] Pearce, N., & McLean, D. (2005). Agricultural exposures and non-Hodgkin's lymphoma. Scandinavian Journal of Work, Environment & Health, 31, 18–25. http: //www.jstor.org/stable/40967432
[3] Gu, Y., Shore, R. E., Arslan, A. A., Koenig, K. L., Liu, M., Ibrahim, S., Lokshin, A. E., & Zeleniuch-Jacquotte, A. (2010). Circulating cytokines and risk of B-cell non-Hodgkin lymphoma: a prospective study. Cancer Causes & Control, 21(8), 1323–1333. http: //www.jstor.org/stable/40792978
[4] Rêgo, M. A. V., Sousa, C. S. C., Kato, M., de Carvalho, A. B., Loomis, D., & Carvalho, F. M. (2002). Non-Hodgkin's Lymphomas and Organic Solvents. Journal of Occupational and Environmental Medicine, 44(9), 874–881. http: //www.jstor.org/stable/44996356
[5] Al-Naeeb, A. B., Ajithkumar, T., Behan, S., & Hodson, D. J. (2018). Non-Hodgkin lymphoma. BMJ: British Medical Journal, 362. https: //www.jstor.org/stable/26963387
[6] McCunney, R. J. (1999). Hodgkin's Disease, Work, and the Environment: A Review. Journal of Occupational and Environmental Medicine, 41(1), 36–46. http: //www.jstor.org/stable/44994912
[7] Lin, X., & Corcoran, S. (2019). ORIGINAL RESEARCH: Caring for Survivors of Hodgkin Lymphoma. The American Journal of Nursing, 119(2), 32–41. https: //www.jstor.org/stable/26665991
[8] O'Reilly, S. E., & Connors, J. M. (1992). Non-Hodgkin's Lymphoma. I: Characterisation And Treatment. BMJ: British Medical Journal, 304(6843), 1682–1686. http: //www.jstor.org/stable/29716095
[9] Carde, P. (1992). Hodgkin's Disease: I: Identification And Classification. BMJ: British Medical Journal, 305(6845), 99–102. http: //www.jstor.org/stable/29716264
[10] Carde, P. (1992). Hodgkin's Lymphoma. II: Treatment And Delayed Morbidity. BMJ: British Medical Journal, 305(6846), 173–176. http: //www.jstor.org/stable/29716339
[11] Gottlieb, S. (2001). Bone Marrow Transplants Show No Benefit For Non-Hodgkin's Lymphoma. BMJ: British Medical Journal, 322(7279), 127–127. http: //www.jstor.org/stable/25466007