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CASE REPORT

"Exploring Diverse Presentations of extra nodal Non-Hodgkin's Lymphoma: A Comprehensive Study of Clinical Staging, Treatment, and Controversies.

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ABSTRACT

Lymphoma involves abnormal lymphoid cell growth, often originating in lymphatic tissue, but in this case series non-Hodking's lymphoma is visible in the extra-nodal region. This research explores different lymphoma cases, focusing on diverse presentations and utilizing modern imaging for evaluation. Four cases are detailed, involving an 18-year-old woman with tonsillar lymphoma, a 69-year-old man with ocular lymphoma, a 38-year-old lady with abdominal lymphoma, and a 30-year-old man with gastric lymphoma. All cases received adjuvant chemotherapy (RCHOP), leading to significant symptom relief after four cycles.

The discussion highlights the debate surrounding the classification of primary extranodal non-Hodgkin's lymphoma (NHL), challenging the existing Ann Arbor classification's applicability.

A major challenge in managing primary extranodal lymphomas is the absence of specific treatment guidelines. Evaluation criteria, defining complete response as the disappearance of all evidence of the disease, guided the study. In conclusion, this case series underscores the importance of a multidisciplinary approach in diagnosing, staging, and managing non-Hodgkin's lymphoma. Despite challenges in defining and treating primary extranodal non-Hodgkin's lymphoma, the study demonstrates the effectiveness of adjuvant chemotherapy in providing relief, as all the cases revealed recovery after 4 continuous cycles of chemotherapy.

Keywords: non-Hodgkin's lymphoma, extranodal Non-Hodgkin's lymphoma, case series, oncology, chemotherapy.

Introduction

Lymphoma is the seventh most common type of cancer in both men and women[1]. It involves the abnormal growth of lymphoid cells and can affect various parts of the body, including lymph nodes, bone marrow, spleen, and thymus. While lymphomas usually start in the lymph nodes, they can also occur outside these nodes[1,2].

Non-Hodgkin's lymphoma (NHL) is a diverse group of cancers marked by the abnormal clonal proliferation of T-cells, B-cells, or both. The majority of adult NHL cases are of B-cell origin, and these malignancies have been recognized as a distinct group of diseases since the 1950s. NHLs span a spectrum from slow-growing and less aggressive tumors, known as indolent malignancies with low-grade histology, to rapidly growing and highly aggressive tumors with high-grade histologies[3].

The typical age of presentation for NHL is around 42 years, with a median age of 58 years for low-grade cases, and the incidence tends to increase with advancing age. B-cell origin is predominant, with over 90% of patients expressing the CD20 antigen. Generally, low-grade or follicular NHL is considered to have a less aggressive course when compared to intermediate- and high-grade NHL. This diversity underscores the complexity of NHL, requiring a nuanced understanding to tailor effective treatment strategies[4,5].

Milder types of non-Hodgkin's lymphoma (NHL) include follicular lymphoma (FL), marginal zone lymphoma (MZL), cutaneous T-cell lymphoma (CTCL), small-cell lymphocytic lymphoma/chronic lymphocytic leukemia (SLL/CLL), and lymphoblastic lymphoma. These makeup about 30% of all NHL cases in the United States. More severe types, known as aggressive subtypes, include diffuse large B-cell lymphoma (DLBCL)[6], peripheral T-cell lymphoma (PTCL), and mantle-cell lymphoma (MCL). Among the aggressive subtypes, DLBCL is the most common, accounting for approximately 30% of all NHL diagnoses in adults. Despite progress in treatment over the past thirty years, where combination immunotherapy has been used, a significant number of patients still experience relapse or are unresponsive to these treatments[7].

Modern imaging techniques, such as [18F] fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT), play a crucial role in assessing lymphomas, especially in tracking treatment responses[7].

The present study defines 4 different extra-nodal non-Hodgkin's lymphoma. Usually, non-Hodgkin's lymphoma (NHL) is seen in lymphatic tissues, but in the present case series, NHL is reported in the extranodal region. All the cases reveal better recovery after four cycles of chemotherapies.

Case Summaries:

CASE I: A young woman of 18 years visited the cancer clinic with complaints of difficulty swallowing and a lump in her throat persisting for six months. During an examination of her mouth, a visible mass was identified on her right tonsils, extending into the throat and affecting a fold in the throat. She was then referred to the Ear, Nose, and Throat (ENT) department, where a biopsy revealed non-Hodgkin's Lymphoma (NHL).

CASE II: A 69-year-old man was referred from the Ophthalmology department due to a

painless swelling in his left eye. Despite the absence of pain, the swelling, measuring 7x8 cm, led to facial disfigurement. Pulling the eyeball resulted in proptosis, redness, and tearing. A biopsy conducted by ophthalmologists confirmed the presence of NHL based on histopathological examinations.

CASE III: A 38-year-old lady reported to the clinic with abdominal pain, yellowish discoloration, loss of appetite, weakness, and indigestion. Upon abdominal examination, a poorly defined mass was palpable on her right upper abdomen. Abdominal sonography revealed a mass lesion on the gall bladder, measuring 9x10 cm and infiltrating nearby hepatic structures. A CT-guided Fine Needle Aspiration Cytology (FNAC) confirmed NHL upon histopathological examination.

CASE IV: A 30-year-old man was referred from the surgical department with a post-laparoscopic biopsy report indicating NHL in the stomach. He had been feeling well for six months before gradually developing abdominal pain. Over time, his symptoms worsened, and new issues such as vomiting, hematemesis, constipation, and bloating emerged.

Clinical Staging and Treatment:

The clinical stage of each case was determined using the Ann Arbor classification. This involved a thorough assessment, including a patient's history, examination of peripheral lymph nodes, examination of Waldeyer's ring by an ENT specialist, chest X-ray for mediastinal lymph nodes, and abdominal CT scans for lymph nodes, liver, and spleen. The International Prognostic Index (IPI) was calculated based on the criteria outlined by the International Non-Hodgkin's Prognostic Factors Project.

All cases underwent adjuvant chemotherapy consisting of Rituximab, cyclophosphamide, Vincristine, Doxorubicin, and prednisolone (RCHOP). Following four cycles of chemotherapy, patients were evaluated for symptom relief, and almost all patients experienced significant improvement in their symptoms. These findings emphasize the effectiveness of the chosen treatment regimen in providing relief to individuals diagnosed with non-Hodgkin's lymphoma.

Discussion:

The classification of primary extranodal non-Hodgkin's lymphoma (NHL) remains a topic of debate within the medical community. The Ann Arbor classification, a widely used system for staging lymphomas, does not distinguish between primary nodal and primary extranodal lymphomas[8]. This lack of differentiation is primarily due to the rarity of primary extranodal involvement in patients originally considered in the development of this classification, specifically those with Hodgkin's disease[9].

Critiques of the Ann Arbor classification's applicability to NHL patients have been established by Rosenberg, highlighting its limited validity in certain cases. Notably, observations by Muss Hoff and others have suggested that primary extranodal NHL should be recognized as a distinct clinical entity, presenting with a relatively favorable prognosis. In response to these concerns, a proposal was made to modify the Ann Arbor classification for NHL, separating primary nodal and extranodal NHL[10]. However, this

modification has not gained widespread acceptance within the medical community.

A notable challenge in the management of primary extranodal lymphomas is the absence of specific treatment guidelines. In evaluating treatment responses, a complete response (CR) is defined as the disappearance of all clinical, radiological, or other evidence of the disease[11]. To facilitate this study, comprehensive reviews of patient records were conducted, focusing on the results of staging investigations.

For categorization purposes, the International Classification of Disease for Oncology (ICD-O, 1976) was employed. Sites clinically involved in NHL, apart from the presenting site where the diagnostic biopsy was performed, were meticulously coded[12]. According to the Ann Arbor classification, lymphomas predominantly presenting in the lymph node, Waldeyer's ring, spleen, or thymus with minimal extra nodal involvement after staging were designated as primary nodal NHL. Conversely, cases with presentations at other sites showing no or only regional lymph node involvement after staging were considered of extranodal origin. This delineation is crucial for refining our understanding of NHL subtypes and tailoring appropriate management strategies based on the distinct characteristics of these cases.

Conclusion:

In this case series, we examined various presentations of non-Hodgkin's lymphoma (NHL) involving different anatomical sites. The cases illustrated the diverse manifestations of NHL, ranging from tonsillar involvement and ophthalmic manifestations to abdominal masses and gastric lymphoma. The use of modern imaging techniques, such as [18F] fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT), proved essential in the evaluation and tracking of treatment responses.

The study also highlighted the challenges in defining primary extranodal NHL, emphasizing the ongoing debate regarding the classification of lymphomas based on their primary site of involvement. The proposed modification to distinguish between primary nodal and extranodal NHL, while supported by some, has not gained widespread acceptance.

Despite the lack of specific treatment guidelines for primary extranodal lymphomas, the cases were managed with adjuvant chemotherapy, specifically Rituximab, cyclophosphamide, Vincristine, Doxorubicin, and prednisolone (RCHOP). Encouragingly, significant relief from symptoms was observed in almost all patients after completing four cycles of chemotherapy.

This case series underscores the importance of a multidisciplinary approach involving oncologists, ENT specialists, ophthalmologists, and other relevant medical professionals in the diagnosis, staging, and management of NHL. Further research and consensus in the classification and treatment of primary extranodal NHL are needed to enhance the understanding and improve patient outcomes in these diverse clinical scenarios.

Conflicts of Interest Statement:

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