Non-Hodgkin Lymphoma of The Head and Neck: A Literature Review on Its Etiology, Clinical Symptoms, and Treatment

Nur Afifah Naura Andika Putri[a], Muhtarum Yusuf[b], Dwi Hari Susilo[c]

[a] nur.afifah.naura-2020@fk.unair.ac.id
[a]Faculty of Medicine, Universitas Airlangga
[b]Department of Ear, Nose, Throat and Head and Neck Surgery, Faculty of Medicine/ Dr. Soetomo General Academic Hospital, Airlangga University, Surabaya, Indonesia
[c]Department of Surgery, Faculty of Medicine/ Dr. Soetomo General Academic Hospital, Airlangga University, Surabaya, Indonesia

Abstract

Non-Hodgkin Lymphoma (NHL) comprises around 90% of all lymphomas, presenting a diverse array of malignant tumors with distinct subtypes. The occurrence of lymphomas in the domain of head and neck malignancies fluctuates from 1% to 17%, contingent on the geographic location and the specific timeframe of the study. Due to the increasing number of NHL cases especially in the head and neck, this research aims to provide a better understanding of its etiology, clinical symptoms, and treatment.

Keywords: non-Hodgkin lymphoma, etiology, chief complaints, treatment, chemotherapy

1. Background

Lymphomas are distinguished into Hodgkin's Lymphoma (HL) and non-Hodgkin's Lymphoma (NHL). The latter, as reported by the Global Cancer Observatory in 2020, accounted for 544,352 cases, resulting in 259,793 fatalities [1]. The complex interplay of genetic and environmental factors contributes to NHL, with demographics, environmental variations, and lifestyle factors influencing its incidence. Prior research establishes a correlation between certain occupations and the risk of DLBCL [2], [3]. The choice of treatment for NHL is significantly influenced by the type of lymphoma, its stage, and its clinical profile [4]. Recognizing patients' chief complaints is crucial, with specific symptoms identified in studies focusing on distinct lymphoma locations. For instance, tonsil involvement often presents with difficulties in swallowing, a sore throat, and painless swelling [5]. The histopathological diagnosis and staging through biopsy, supported by immunohistochemistry examination, guide appropriate treatment choices. In the context of aggressive B-cell NHL, the gold standard treatment is the combination therapy R-CHOP [6].

2. Non-Hodgkin Lymphoma

2.1 Definition

Lymphomas, characterized by the malignant proliferation of immune system cells, represent a diverse group of neoplasms. Among them, non-Hodgkin lymphoma (NHL) constitutes approximately 90% of all lymphomas, encompassing a variety of malignant tumors with distinct subtypes [7]. The incidence of lymphomas within the realm of head and neck malignancies varies between 1% and 17%, depending on the geographical location and the specific time of the study [8]. NHL arises from abnormalities in B-cell and T-cell lymphocytes, manifesting with diverse clinical and pathological symptoms, therefore classified as B-cell and NK/T-cell lymphoma [9]. Notably, B-cell malignancies account for 80-85% of lymphoid malignancies, followed by T lymphocytes, and infrequently, natural killer (NK) cells. Extra-nodal predilections in NHL present challenges in early detection and prediction [10].

The World Health Organization (WHO) classification, until 2015, recognized 36 distinct disease entities falling under the umbrella of NHL [11]. Globally, non-Hodgkin lymphomas exhibit a higher prevalence in males

compared to females, and the incidence is steadily rising across various regions and nations, with a documented increase of up to 35% over the past two decades [12].

2.2 Etiology

The diverse nature of non-Hodgkin lymphoma (NHL) encompasses various clinical, histopathologic, and immunologic subtypes, with its definitive etiology remaining elusive. Multiple factors contribute to the development of NHL, including viral and bacterial infections, immunodeficiency, genetic susceptibility, and organ transplantations [4]Viral infections, particularly Epstein Barr Virus, infectious mononucleosis, and C-virus type viruses, with morphologies resembling RNA viruses, are frequently associated with NHL [10], [13]. Additionally, causative viruses such as HHV-8 and human T-cell lymphotropic virus 1 (HTLV-1) have been implicated [14]. Recent evidence also suggests a potential role of the hepatitis C virus (HCV), a single-strand RNA virus, in NHL development.

Bacterial infections, notably Helicobacter pylori (H. pylori), are linked to an increased risk of gastric mucosa-associated lymphoid tissue (MALT), while Borrelia burgdorferi infection is considered a plausible factor [15]. Some congenital abnormalities are associated with lymphoma, and immune mechanisms play a crucial role, particularly in cases involving immunosuppressants [13]. Ultraviolet exposure is proposed as a potential risk factor for NHL occurrence [16]. Prior research also highlights the correlation between the increasing incidence of NHL and rising annual rates of skin cancer in the US [8], [14].

2.3 Clinical symptoms

An extensive comprehension of the chief complaints related to non-Hodgkin lymphoma (NHL) of the head and neck emerges from various studies. In an investigation spanning from 2003 to 2011, identified indolent lymphadenopathy, fatigue, and occasional B-symptoms such as elevated body temperature, night sweats, and weight loss as common clinical manifestations [5]. Susceptibility to infections and alterations in the haemogram were also observed. Notably, odynophagia or dysphagia was reported by 49 patients, and in five cases, occult lymphoma without clinical signs was incidentally discovered during sonographic scans for unrelated conditions.

Another research also supplemented these findings, highlighting swelling as the most prevalent symptom followed by pain, ulcers, paresthesia, redness, and difficulty swallowing [8]. Persistent, painless lymphadenopathy emerged as a recurrent feature in NHL patients, accompanied by constitutional symptoms such as night sweats, unexplained weight loss, and persistent fevers [4], [17].

The spectrum of symptoms observed in 2015 underscored the diverse clinical presentations of NHL, with swelling being the predominant complaint in 97% of cases. Pain, ulcers, paresthesia, redness, and difficulties swallowing were also reported variably [8]. Research in 2019 emphasized cervical masses as a prevalent symptom, with odynophagia occurring significantly. Furthermore, specific symptomatology emerged based on the site of lymphoma involvement. For instance, palatine tonsil involvement led to complaints of dysphagia, sore throat, and asymptomatic tonsil enlargement, while rhinopharyngeal lymphoma manifested with symptoms such as enlarged neck nodes, increased nasal obstruction, and hearing loss [5].

Another finding in 2022 further contributes to this understanding by indicating that the most common presenting symptoms in NHL were swelling, along with pain and dysphagia[18]. This aligns with the observations from other studies, emphasizing the significance of these symptoms in the clinical presentation of NHL. Analyzing these findings collectively provides a nuanced understanding of the diverse chief complaints associated with NHL of the head and neck.

2.4 Treatment

The management of non-Hodgkin lymphoma (NHL) in the head and neck region involves a nuanced approach that considers factors such as the histological type, stage, tumor nature, patient age, and general condition. Patients failing to achieve remission with initial treatment, typically R-CHOP administered for a median of five cycles, may undergo salvage radiotherapy if the affected area is not extensive. The choice of therapy varies, and radiation and/or chemotherapy are generally employed. The stage and grade of lymphoma, categorized as low-grade, intermediate-grade, or high-grade malignancies by the IWF, influence the appropriateness and scope of chemotherapy [4].

In advanced-stage diffuse large B-cell lymphoma, R-CHOP chemotherapy stands as a standard approach, supported by evidence from randomized controlled trials[19]–[21]. Despite advancements, the addition of maintenance rituximab following chemoimmunotherapy has not demonstrated substantial benefits [22], [23].

Noteworthy is the local preference for CHOP chemotherapy in the head and neck region, as evidenced by studies in Surabaya and Denpasar, which report higher utilization and complete response rates with CHOP compared to R-CHOP [24], [25]. This treatment landscape reflects the evolving understanding and context-specific choices in managing NHL of the head and neck.

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