

From acute inflammatory demyelinating polyradiculoneuropathy to non-Hodgkin's lymphoma - a challenge for diagnosis and treatment

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Abstract: Paraneoplastic neurological syndromes (PNS), such as Guillain-Barre syndrome (GBS) are rarely associated with non-Hodgkin's lymphoma (NHL), so far only isolated cases have been reported. This study aimed to assess scientific activity regarding non-Hodgkin's lymphoma and Guillain-Barré syndrome related research. We retrieved publications from Web of Science (WoS) and the VOSviewer tool was used to perform bibliometric analysis and visualization. In order to (1) provide an overview of the research in the field and (2) examine linkages/gaps/frontiers between/of researches, network diagrams based on authors, keywords, sources, references, citations were created. Key-concepts and relevant terminology of the topic are also identified. Paraneoplastic sensory-motor neuropathies that precede the diagnosis of lymphomas are mainly demyelinating neuropathies that may meet the diagnostic criteria for Guillain-Barré syndrome. The diagnosis, but especially the treatment of patients with GBS and NHL is a challenge, which requires a good collaboration between neurologists and hematologists as well as the evaluation of specialized studies, in order to choose the optimal therapeutic scheme. Also, using the VOSviewer tool we were allowed to find that more patients develop GBS after instituting chemotherapy for the NHL (17 studies) and in only 7 cases Guillain-Barré syndrome preceded the diagnosis of non-Hodgkin's lymphoma. Hematological malignancies can be aggravated by neurological disorders, each condition requiring separate treatment. Also, most of the time, the treatment of hematological disease induces the onset of Guillain-Barré syndrome. This association of diseases, even if it is rare, must be known by specialists to allow a rapid therapeutic intervention. In addition, the use of the VOSviewer tool allowed us to evaluate publications in the Web of Science (WoS), providing easy access to published studies related to this topic, so that the therapeutic scheme of this category of patients can be facilitated.

Keywords: Non-Hodgkin's lymphoma; Guillain-Barré syndrome; acute inflammatory demyelinating polyradiculoneuropathy; chemotherapy; VOSviewer; bibliometric analysis; network maps; visualization

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1. Introduction

Guillain-Barre syndrome (GBS) or acute demyelinating inflammatory polyneuropathy, is the most common and severe form of acute inflammatory demyelinating polyradiculoneuritis. It is a neurological syndrome characterized by decreased muscle strength, acute and ascending, associated with loss of osteotendinous

reflexes, due to damage to the peripheral nervous system. It is considered one of the most common causes of acute flaccid muscle paralysis [1], and can affect people of all ages.

Triggering etiopathogenic factors can be identified over a variable period of time before the onset of the first symptoms of acute polyradiculoneuritis, but sometimes further investigation is needed to establish the etiology of this condition. Usually GBS is precipitated by an underlying infection, but has been well described in the presence of malignant tumors, especially lymphomas [2,3].

The neurological manifestations associated with non-Hodgkin's lymphomas (NHL) are unusual, often present only in the advanced stages of the disease. Guillain-Barré paraneoplastic syndrome (GBS) has been described in association with several hematological neoplasms, but especially in association with Hodgkin's lymphoma (HL) [4]. GBS as an initial manifestation of the NHL is very unusual [5] and there is little data in the literature on this association, so far only isolated cases have been reported.

This study aimed to assess scientific activity regarding non-Hodgkin's lymphoma and Guillain-Barré syndrome related research, in order to (1) provide an overview of the research in the field and (2) examine linkages/gaps/frontiers between/of researches, using bibliometric analysis and visualization with VOSviewer.

2. Material and methods

We searched the WOS (Web of science Core Collection) online database, in March 2020, for high quality relevant articles focusing on our specific topic: non-Hodgkin's lymphoma (keyword group: non-Hodgkin / non Hodgkin's lymphoma, B-cell lymphoma, NHL) and Guillain-Barré syndrome (keyword group: Guillain-Barré / Guillain Barré's syndrome, GBS). Search keywords included the combination of the two terms using the Boolean operator AND, without date ore language limits. The search yielded an initial number of 31 articles. This initial pool of studies was screened (title, abstract and/or full text) and those studies reporting data on patients with non-Hodgkin's lymphoma and Guillain-Barré syndrome were included for further analysis. Duplicates (2), literature reviews (3), studies not reporting necessary data on patients (12), were excluded. Ten additional studies were identified from the screening of the reference list of the initial pool of documents and from Google Scholar search.

The VOSViewer tool was used to construct bibliometric networks and their visualization for the studies identified from WOS [6-8]. Bibliometric approach using this tool was applied in studies from various area of research [9-13].

3. Results

A final corpus of 24 articles were considered for further analysis. The fact that Guillain-Barre syndrome (GBS) is rarely associated with non-Hodgkin's lymphoma (NHL) is sustained by the small number of studies published so far (Table 1, Figure 1).

Table 1. List of analyzed documents.

Studies	References
Web of science Core Collection	2, 14 - 26
Other sources	5, 27 - 35

The most cited document is that of Vallat – 1995 [14] published in Brain journal, with 122 citations and 5 links (cited by Re – 2000 [16], Zuk – 2001 [21], Wanschitz – 2006 [26], Bahl – 2010 [20], Polo – Romero – 2012 [2]), followed by Re – 2000 [16] published in Annals of Oncology, with 39 citations and the highest number of links (9). Wanschitz – 2006 [26] and Bashir – 1992 [24] are on the third position in the citation hierarchy with 16 citations and six respectively zero links. The network of authors and the network of journals are detailed in Figure 1 and Figure 2.

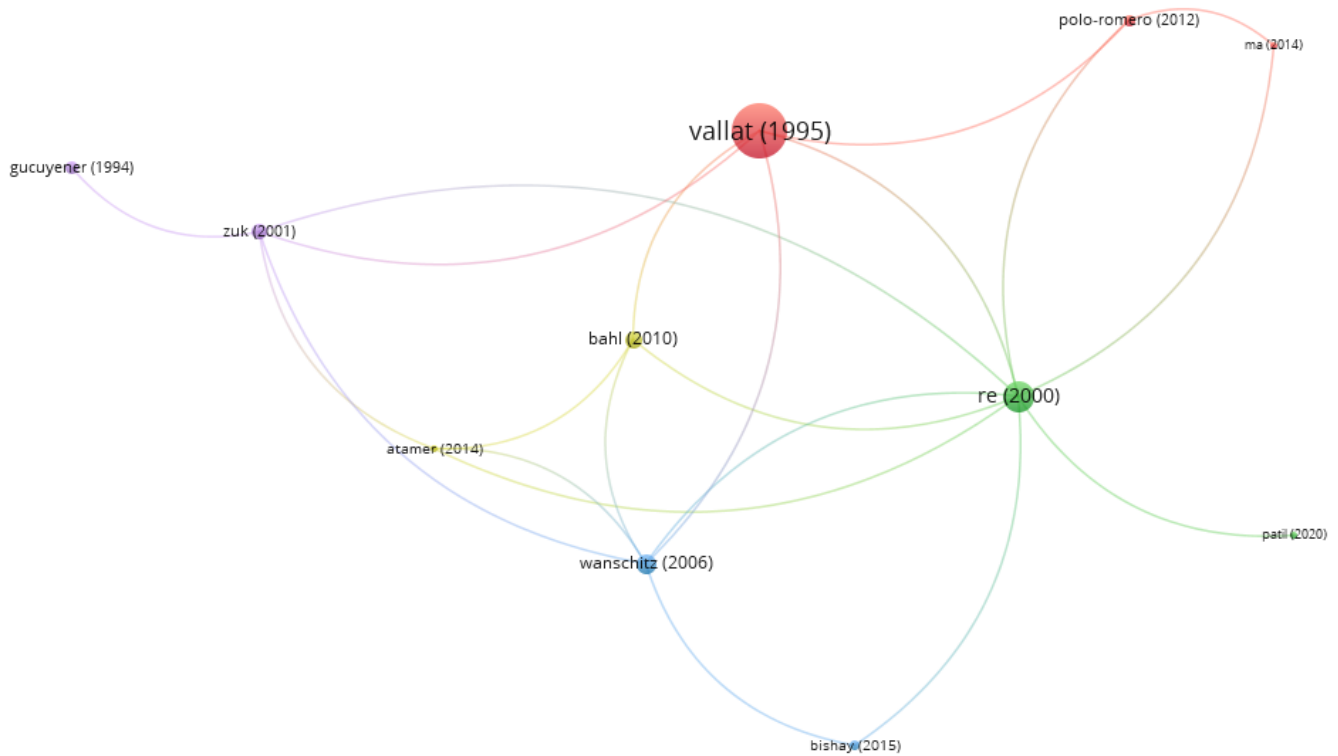


Figure 1. VOSviewer network visualization map (type of analysis: citations, weights— citations) of documents. Of 14 items, 3 are not connected with the others and are not presented in the network.

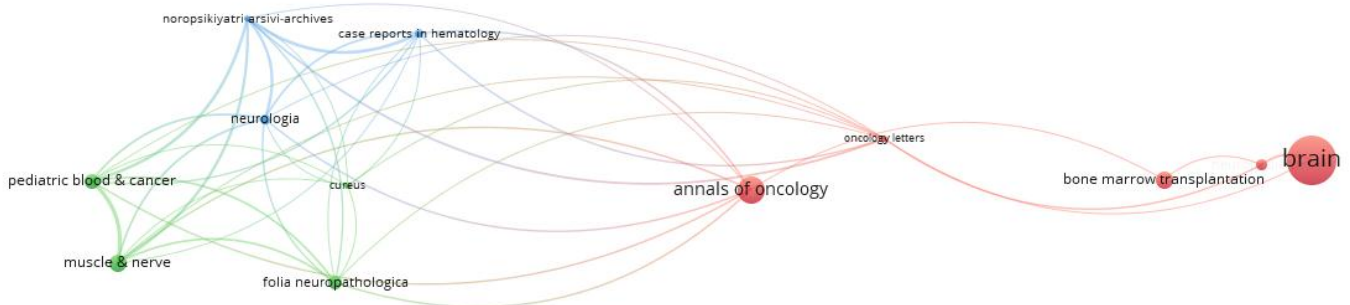


Figure 2. VOSviewer network visualization map (type of analysis: bibliographic coupling, weights— citations) of sources. Of 14 items, 2 are not connected with the others and are not presented in the network.

Network map by co-citation sources is presented in Figure 3. The most cited sources (with at least 10 citations) are Neurology with 18 citations (links 84, total link strength 355), Annals of neurology with 13 citations (links 69, total link strength 248), Muscle Nerve and Brain with 12 citations (links 58, total link strength 222 respectively links 68, total link strength 215) and Journal of Neurology and Bone Marrow Transplantation with 10 citations (links 67, total link strength 212 respectively links 69, total link strength 176).

The analysis of the 24 studies revealed various ideas related to the time of GBS onset, therapeutic behavior and the evolution of patients with NHL and associated GBS, but also regarding the epidemiological data of NHL. The incidence of NHL increases with age (50% of patients over the age of 50) and more frequently affected are male patients (50% of patients were male, 29.17% were female, and in 5 cases the sex of the patients in the study was not specified).

Malignant tumors may act as sources of antigenic factors that are responsible for initiating an immune response in the nervous system, which may later manifest as GBS, thus explaining the onset of GBS prior to NHL diagnosis. On the other hand, the toxicity of hematological medication is probably the most common cause that triggers GBS in these cases [27], this aspect being supported by the results of our analysis.

The diagnosis of Guillain-Barre syndrome was based on the clinical aspect (acute motor deficit areflexive with varying degrees of sensitivity), the biochemical examination of the CSF and the study of nerve conduction. The time interval until the onset of GBS after the introduction of chemotherapy for lymphoma varied from 2 days to 12 months. It should be noted that GBS recurrence was mentioned only in patients who developed GBS after the introduction of chemotherapy.

Regarding the treatment administered, 50% of patients received treatment with intravenous immunoglobulins (0.4g/kgc/day). Of the 12 patients treated with immunoglobulins, 3 patients relapsed, 2 of them receiving a new immunoglobulin cure, and one patient benefited from 2 immunoglobulin cures and associated plasmapheresis. Plasmapheresis, as the only therapy, was used in only 2 patients with GBS. Corticosteroid therapy was mentioned only in two cases, one of which showed an unfavorable evolution.

The diagnosis and treatment of patients with GBS and NHL requires a multidisciplinary approach, an aspect that also emerges from the field of journals where the mentioned articles are published: neurology, hematology, oncology (Figure 3).

4. Conclusions

Hematological malignancies can be aggravated by neurological disorders, each condition requiring separate treatment. Also, most of the time, the treatment of hematological disease induces the onset of Guillain-Barré syndrome. This association of diseases, even if it is rare, must be known by specialists to allow a rapid therapeutic intervention. In addition, the use of the VOSview tool allowed us to evaluate publications in the Web of Science (WOS), providing easy access to published studies related to this topic, so that the therapeutic scheme of this category of patients can be facilitated. Researchers could also combine different bibliometric, review and meta-analysis tools [36-39] for their literature mining research in order to achieve a wide / comprehensive overview on their research field.

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