Clinical Challenges and Management of Indolent Non-Hodgkin Lymphomas in Patients with Autoimmune Diseases: Integrating Hematologic and Immunologic Considerations

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Introduction

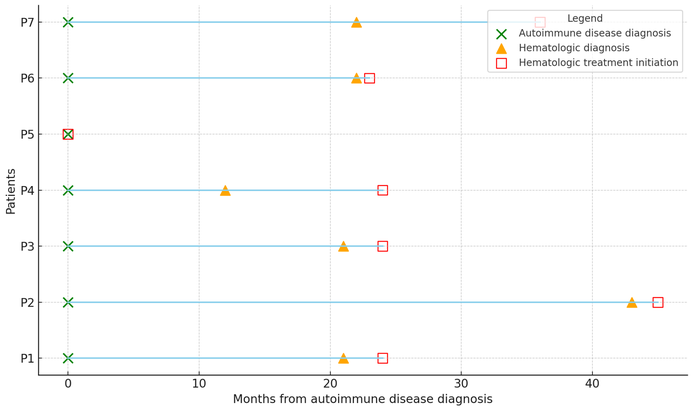
Indolent non-Hodgkin lymphomas (iNHL) progress slowly and have a generally favorable prognosis. In autoimmune diseases (AID), persistent inflammation and antigenic stimulation may contribute to malignant lymphoproliferation. Diagnosis can be delayed due to nonspecific symptoms shared with autoimmune activity.

Aim

To highlight the diagnostic and therapeutic challenges, and to compare clinical features, diagnostic approaches and treatment responses in patients with indolent non-Hodgkin lymphoma associated with an underlying autoimmune disease.

Methods

- We analysed 7 patients with concomitant indolent NHL and autoimmune diseases treated at Colentina Clinical Hospital, Bucharest, Romania, between 2019-2025.
- Data on the time between AID diagnosis to iNHL diagnosis, treatment and complications were retrospectively collected.



Results

- All patients were female (7/7) and the median age was 52 yo (42-62). The majority had follicular lymphoma (Figure 1).
- The AID preceded the iNHL diagnosis in all cases with a median time of 21,5 months for MALT lymphoma and 12 months for Follicular Lymphoma (Figure 2). MALT lymphoma was frequently diagnosed incidentally.
- At iNHL diagnosis, the median hemoglobin value was 12.3 g/dl (7.7-13.5), platelet value was 240000/mmc (111000-436000), median white blood cell value was 5370/mmc (2100-6300/mmc), while 2/7 were lymphopenic.
- Watch and wait strategies were more common and time to treatment was longer in MALT lymphoma than in Follicular Lymphoma. 4/7 patients received immunosuppresive therapy and all patients required immunochemotherapy for iNHL., which led to responses in AID as well.
- 4/7 patients experienced infectious complications (viral/bacterial/fungal), while no patients experienced progression/relapse or transformation of the iNHL during follow-up.

Figure 1. *Lymphoma Subtype Distribution*

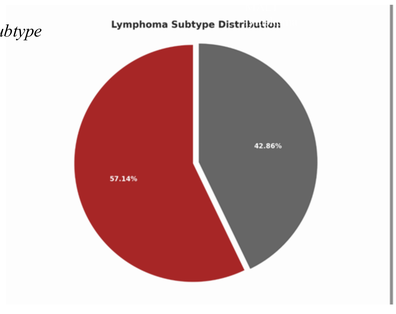


Figure 2*. Stratified Diagnostic-Treatment Timeline*

Case no.	Age	Sex	Indolent NHL type	Autoimmune disease	Immunosuppressive therapy	Immunochemotherapy	Complications
1.	52	F	MALT lymphoma (parotid gland)	Sjogren syndrome	MTX	R-CVPx6	Encephalitis probably infectious
2.	62	F	MALT lymphoma (gastric)	Rheumatoid arthritis	CTS	R-CVPx8 and R-M	Pulmonary aspergillosis
3.	49	F	Follicular lymphoma	Hashimoto disease	No	R-CVPx8 and R-M	Enterococcus spp sepsis, SARS-COV-2 infection
4.	57	F	Follicular lymphoma	Rheumatoid arthritis	No	R-CVPx8 and R-M	
5.	60	F	Follicular lymphoma	Rheumatoid arthritis	MTX	R-CHOPx6 and R-M	
6.	45	F	Follicular lymphoma	Rheumatoid arthritis	CTS	O-CHOPx6 and O-M	
7.	42	F	MALT lymphoma (gastric)	Hashimoto disease	No	R-CHOPx6 and R-M	SARS-COV-2 infection

Table 1. *Pathological, environmental and disease-related characteristics of the patient cohort. CTS = corticosteroids, MTX = methotrexate, R=Rituximab, C=cyclophosphamide, P=prednison, H= Doxorubicin, O=Obinutuzumab, O (in CHOP) and V=Vincristine, M=maintenance*

Discussion and Conclusions

- Although advances in pathobiology knowledge have confirmed an AID role in the development of lymphoproliferative diseases, results about AID influence on the prognosis of lymphoma are discordant. In our cohort, no patients experienced relapse/progression of iNHL.
- AID usually precedes the iNHL diagnosis, which confirms their role in pathogenesis. Autoimmune symptoms can mimic or mask lymphoma features which delays the iNHL diagnosis.
- The most common complications were infections. The range of etiological agents, including viral, fungal, and bacterial, underscores the complex consequences of autoimmune disease, lymphoma, and their associated therapies on immune system function.
- The role of autoimmunity on lymphoma development needs to be better defined. Such efforts will help to improve lymphoma management, and maybe prevent lymphogenesis with autoimmune drugs.

References

No external references were used

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