Are patients with CLL at higher risk of suffering non-hematological autoimmune? Prevalence, characteristics, and clinical correlates. Results from a single-center general CLL population

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BACKGROUND

- Chronic lymphocytic leukemia (CLL) is marked by severe immune dysfunction, and an increased risk of autoimmune disorders (AID).
- The association of autoimmune cytopenia (AIC) with CLL has been extensively studied. However. there is little information about its relationship with other non-hematologic autoimmune complications.

OBJETIVES

1. Main objective: to describe the prevalence and characteristics of patients with CLL spectrum (CLL. small lymphocytic lymphoma. and monoclonal B-cell lymphocytosis) and non-hematologic AID.
2. Secondary objective: to ascertain differences in clinical and prognostic features between AIC and non-hematologic AID groups.

PATIENTS AND METHODS

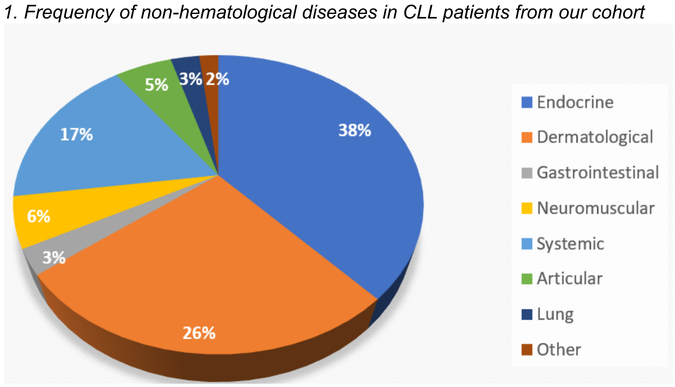
- We included 712 patients with CLL from the historical database of our center.
- AID were categorized based on the American Autoimmune Related Diseases Association classification. Those patients with both AIC and non-hematologic AID were included into the AIC group.

RESULTS (I)

- After a median follow-up of 6.4 years (0.1-36.4). 87/712 (12.2%) presented non-hematologic AID. and 45/712 (6.3%) showed AIC; 11/712 (1.5%) had both AIC and a non-hematologic AID.
- In the non-hematologic AID group (Figure 1). endocrine disorders were the most frequent (48.3%; 42/87). followed by dermatological AID (33.3%; 29/87; including 5 patients with paraneoplastic pemphigus). and other AID such as rheumatoid arthritis (6.9%; 6/87). vasculitis (5.7%; 5/87). and neuromuscular syndromes (6.9%; 6/87).
- As diseases, most observed non-hematologic AID were autoimmune hypothyroidism (n=41). psoriasis (n=17). rheumatic polymyalgia (n=7). rheumatoid arthritis (n=6). and pemphigus (n=5).

RESULTS (II)

Figure 1. Frequency of non-hematological diseases in CLL patients from our cohort



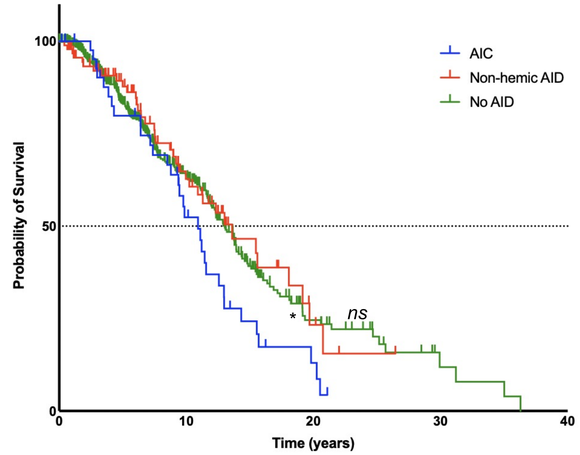
- Most patients (51/87; 58.6%) presented the non-hematologic AID before CLL diagnosis. with a median time of - 1.3 years (-45.8 – 15.9).
- We found a significant association between AIC and the presence of poor biological variables (e.g.. unmutated IGHV). and anti-CLL therapy. Female gender was the only variable significantly associated with non-hematologic AID (Table 1).

Table 1. Characteritics of CLL in patients with autoimmune diseases and CLL
*ns = not significative; *= significant differences*

	AIC (n=45)	Non-hematologic AID (n=87)	p
Age at CLL diagnosis. years	67 (47.3-93.9)	69.5 (43.8-95.8)	ns
Age at AID diagnosis. years	71.4 (54.2-93.6)	68 (15.2-97.5)	ns
Sex. male	31 (55.4%)	34 (39.1%)	*
CLL diagnosis (vs SLL. MBL)	48 (85.7%)	72 (82.8%)	ns
Binet at diagnosis			Ns
A	40 (71.4%)	74 (72.4%)	
B	9 (16.1%)	6 (6.9%)	
C	7 (12.5%)	7 (8%)	
IGHV unmutated	25/45 (55.6%)	22/61 (36.1%)	*
FISH alterations			ns
del(11)q	7/49 (14.3%)	6/71 (6.9%)	
+12	13/49 (26.5%)	16/71 (18.4%)	
del(13q)	18/49 (36.7%)	29/72 (33.3%)	
del(17p)	6/49 (12.2%)	9/72 (12.5%)	
Complex karyotype	5/23 (21.7%)	11/50 (22%)	ns
***TP53* mutated**	1/21 (4.8%)	1/46 (1.1%)	ns
Need therapy for AID	56/56 (100%)	66/87 (75.9%)	*
Treatment for CLL. type			ns
Alkylating agents	10/40 (25%)	14/32 (43.8%)	
Purine analogues	7/40 (17.5%)	13/32 (40.6%)	
Chemoimmunotherapy	13/40 (32.5%)	23/32 (71.9%)	
Targeted therapies	13/40 (32.5%)	12/32 (37.5%)	

- Patients with CLL and AIC had shorter OS than those with non-hematologic AID (median 10.9 vs. 13.9 years; p=0.002) (Figure 2) and without autoimmune disorders.

Figure 2. OS according to the presence or not of autoimmune disorders



CONCLUSIONS

- 12.2% of patients with CLL presented non-hematologic AID. the endocrine disorders being the most frequent.
- The presence of non-hematologic AID was not associated with CLL adverse features and these patients had the same prognosis as those with CLL without autoimmunity.
- AIC was linked to the presence of poor biological features and had a negative impact on patients' outcomes.
- Non-hematologic autoimmune disorders do not appear to be more frequent in CLL than in the general population. albeit the challenges in the management of patients with CLL should not be dismissed.

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