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SCIENTIFIC INVESTIGATIONS

Increased neutrophil-to-lymphocyte ratio as a possible marker to detect neuroinflammation in patients with narcolepsy type 1

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Study Objectives: Narcolepsy type 1 (NT1) is an autoimmune disease caused by the selective immune attack against orexin-producing neurons. However, the pathophysiology of narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) remains controversial. The neutrophil-to-lymphocyte ratio (NLR) is an easily calculated parameter from the white blood cell count, which has already been extensively used as an inflammatory marker in immunological disorders. In this study, we examined the white blood cell count of patients with NT1, NT2, and IH compared to healthy controls (HC) and evaluated the NLR to test the possibility of identifying an easy biofluid marker for detecting inflammation and distinguishing patients from HC.

Methods: White blood cell count and NLR were compared between 28 patients with NT1, 17 with NT2, 11 with IH, and 21 sex/age-matched HC. These parameters were correlated with cerebrospinal fluid levels of orexin-A, the cerebrospinal fluid/serum albumin ratio (as a marker of blood–brain barrier integrity), and polysomnographic parameters.

Results: Patients with NT1 (NLR 2.01 ± 0.44) showed significantly higher NLR than those with NT2 (NLR 1.59 ± 0.53) or IH (NLR 1.48 ± 0.37) and HC (NLR 1.48 ± 0.43). Correlation analysis did not document significant associations between NLR and the other biological markers in each group of patients. The receiver operating characteristic curve analysis detected an optimal cutoff value to discriminate patients with NT1 from those with NT2, IH, and HC for values of NLR ≥ 1.60, 1.62, and 1.59, respectively.

Conclusions: Patients with NT1 showed a higher NLR than those with NT2, IH, and HC, possibly reflecting lymphocyte migration within the central nervous system, supporting the hypothesis of a neuroinflammatory attack of lymphocytes against orexin-producing neurons. Considering its sensitivity, this easily obtainable biofluid marker could help to screen patients with NT1.

Keywords: NLR, WBC, NT1, NT2, IH, biomarker, biofluid

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BRIEF SUMMARY

Current Knowledge/Study Rationale: The search for biofluid markers to identify and characterize neuroinflammatory mechanisms in narcolepsy is currently ongoing, and different studies have suggested a role for lymphocytes in the pathophysiology of narcolepsy type 1. The neutrophil-to-lymphocyte ratio is a parameter indicating an inflammatory state that can be easily calculated from the white blood cell count.

Study Impact: The higher neutrophil-to-lymphocyte ratio detected in patients with narcolepsy type 1 than in those with narcolepsy type 2 or idiopathic hypersomnia and healthy controls may reflect a neuroinflammatory state that can sustain the hypothesis of a selective autoimmune attack against orexin-producing neurons. These findings may help to identify easily obtainable biomarkers for screening patients with narcolepsy type 1 and could lead to the development of new therapeutic targets for narcolepsy type 1, such as antagonism of lymphocyte migration across the blood–brain barrier.

INTRODUCTION

Narcolepsy is a chronic neurological disorder characterized by a decreased ability to regulate the sleep–wake cycle, resulting in excessive daytime sleepiness (EDS) and altered rapid eye movement (REM) sleep, which can cause sleep paralysis and hypnagogic/hypnopompic hallucinations.[1,2] EDS is defined as constant sleepiness, tiredness, or fatigue during the day. Furthermore, patients with narcolepsy experience difficulty remaining awake during daytime activities. Disturbed nighttime sleep is another symptom, described as a difficulty in maintaining continuous nocturnal sleep. It is further defined as a frequent awakening with a swift return to sleep. Narcolepsy affects young individuals, particularly adolescents. There are 2 types of narcolepsy: type 1 (NT1) and type 2 (NT2). NT1 is defined as the loss of orexinergic neurons with cataplexy, which is a sudden and transient episode of muscle weakness accompanied by awareness triggered by strong emotions. Most patients with NT1 carry the human leukocyte antigen HLADQB1*06:02 allele, linking NT1 to an autoimmune-based pathology. NT2 is characterized by the absence of cataplexy and comparable or minimally lower orexin-A cerebrospinal fluid (CSF) levels than those in healthy controls, and its pathophysiology currently remains unclear.[1,2]

The first clue to indicate an autoimmune disease etiology of NT1 was the strong association found between NT1 and human leukocyte antigen haplotypes.[3] Following this observation, several other reports have documented the autoimmune etiology of narcolepsy, particular NT1, although these reports were replicated

infrequently and controversial results have been published. The other evidence presented in the literature included the following: (1) the association of narcolepsy diagnosis with variants within genes that regulate the immune system,[4–6] (2) the documentation that both H1N1 influenza and the associated Pandemrix vaccination triggered NT1 pathophysiology in several patients in China and in the Scandinavian region,[7,8] and (3) the role of humoral immune responses with the documentation of specific autoantibodies against epitopes present on the orexin neurons[9–11] or cellular immune response involving autoreactive CD4+ T cells possibly activating CD8+ T cells against the orexin cells in patients with narcolepsy.[12,13]

Idiopathic hypersomnia (IH) is a central disorder of hypersomnolence, primarily characterized by EDS that cannot be explained by other medical, neurological, or psychiatric conditions. Distinct from narcolepsy, IH does not present with REM sleep dysregulation.[2]

The neutrophil-to-lymphocyte ratio (NLR) is an easily measurable biofluid marker that reflects immune activation along two main branches (innate and adaptive immunity). Neutrophils are part of the innate immunity and represent the first line of defense against pathogens, enacting different mechanisms such as reactive oxygen species release, release of cytokines, and phagocytosis. They further act as a bridge between innate and adaptive immunity, because they are involved in the systemic inflammatory response. Lymphocytes are part of the adaptive immune response and provide an antigen-specific response mediated by the major histocompatibility complex class I. A lower NLR indicates an efficient immune system.[14,15] The NLR is now considered a meaningful biomarker for conditions accompanied by systemic inflammation due to various underlying causes. Although a specific cutoff value has not yet been established, an increase in the NLR has been associated with a systemic inflammatory state, infections, stroke, tissue damage, and an overall higher risk of mortality and morbidity in patients with cardiovascular disorders.[15] In particular, a high NLR may reflect the rearrangement of leukocyte populations due to proinflammatory activity.[15] Relative lymphopenia and a higher NLR have both been documented in neurological disorders indicative of lymphocyte migration within the central nervous system and in some cases associated with increased blood–brain barrier (BBB) permeability.[16,17]

In this context, the present study aimed to assess the peripheral immune profile, including the leukocyte subpopulation counts and the NLR, in patients with NT1, NT2, and IH compared to age- and sex-matched healthy controls (HC), and also examined the correlations between CSF orexin-A levels and the CSF/serum albumin ratio (indicative of BBB permeability) and the main clinical and polysomnographic parameters, in order to further investigate the dynamics of neuroimmunological activation triggering the pathophysiology of narcolepsy and to identify blood biomarkers for narcolepsy screening and diagnosis.

METHODS

Data collection and diagnosis

The present retrospective study enrolled patients with NT1, NT2, and IH who were followed up at the Sleep Medicine Center of the University Hospital of Rome Tor Vergata between January 2017 and December 2023. NT1, NT2, and IH were diagnosed according to the *International Classification of Sleep Disorders*, third edition.[18] All patients were compared with age- and sex-matched HC, who were all healthy individuals undergoing routine blood examinations for occupational surveillance. The exclusion criteria for the patients and controls were as follows: acute/chronic systemic/inflammatory/infectious diseases potentially affecting blood counts, including cold or subtle infections presenting with clinical symptoms; C-reactive protein > 0.1 mg/L; medical disorders; immunosuppressant/immunomodulatory therapies; and concomitant neurological or psychiatric diseases.

The demographic characteristics, medical histories, and blood counts of all participants were reviewed. Data reviewed for patients with NT1, NT2, and IH also included nocturnal polysomnography (PSG), Multiple Sleep Latency Test (MSLT),[19] Epworth Sleepiness Scale,[20,21] and biofluid markers (CSF and blood data) obtained at the time of diagnosis.

This retrospective study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the local ethics committee. All the participants signed an informed consent form.

Polysomnographic monitoring

All patients with NT1, NT2, and IH underwent PSG to evaluate nocturnal sleep (SOMNOscreen; SOMNOmedics GmbH, Randersacker, Germany), following the procedure described in previous studies.[22] In brief, the electrodes were positioned according to the 10–20 International System. The montage consisted of 2 oculographic channels, 3 electromyographic channels (mental and anterior tibialis muscles), and 8 electroencephalographic channels (F4, C4, O2, A2, F3, C3, O1, A1). Respiration was assessed by recording the oronasal flow, thoracic and abdominal movements (plethysmography), pulse oximetry, and electrocardiography. Patients and their caregivers were instructed to maintain their usual sleep schedule during the week preceding the evaluation. The first-night sleep study was considered an adaptation period. Sleep analysis was performed during the second PSG monitoring according to the standard criteria. The following standard parameters were computed: time in bed (time spent in bed between lights off and lights on), total sleep time, sleep efficiency (the ratio between total sleep time and time in bed), sleep onset latency (the time interval between lights off and sleep onset), REM sleep latency (the time interval between sleep onset and the first epoch of REM sleep), stage 1 of non-REM sleep, stage 2 of non-REM sleep, stage 3 of non-REM sleep, REM sleep, and wakefulness after sleep onset. Sleep stage percentages were calculated using the total sleep time. PSG scorers (C.L., F.P., and F.I.) identified apnea/hypopnea events and leg movements according to standard criteria.[23]

The MSLT,[19] which consisted of 5 trials performed at 2-hour intervals, was performed to objectively test daytime sleepiness, as previously reported.[23] In brief, the test started the morning after the second PSG recording, was stopped at habitual awakening of the patients, and was checked by analyzing the sleep diary completed 15 days before the neurophysiological examinations. Before starting the test, clinical researchers (C.L., F.P., and F.I.)

monitored whether the patient was asleep following the usual schedule reported in the sleep diary and for at least 6 hours during the PSG recording and also scored the PSG.

Biofluid markers measurements

CSF samples were collected by lumbar puncture the day after the MSLT recording. The CSF levels of orexin-A, immunoglobulin G count, link index, and CSF/serum albumin ratio were evaluated and measured as previously described.[24,25] In brief, hypocretin-1/orexin-A CSF levels were detected using a commercially available enzyme-linked immunoassay kit (Orexin A/Hypocretin-1 EIA Kit; Phoenix Pharmaceuticals Inc., Belmont, CA, USA) as previously described.[26–28] The immunoglobulin G count, link index, and CSF/serum albumin ratio were measured using a flex reagent cartridge (Dimension Vista System; Siemens Healthcare Diagnostics GmbH, Munich, Germany) as previously described.[29,30] A blood sample drawn on the day of lumbar puncture from patients with NT1, NT2, and IH was also analyzed. Blood was withdrawn within 30 minutes of the lumbar puncture in a fasting state. In the control group, blood samples were collected in the morning after fasting. All samples were analyzed in a local laboratory using an automated hematological analyzer (Dasit-Sysmex, Milan, Italy). Leukocyte counts (neutrophils, lymphocytes, monocytes, eosinophils, and basophils) were recorded. From these, the neutrophil and lymphocyte counts were used to calculate the NLR as previously reported.[16]

Statistical analysis

Descriptive statistics were used to describe the demographic and clinical characteristics of the HC, NT1, NT2, and IH groups. Because the Kolmogorov–Smirnov test revealed a normal distribution for all the quantitative variables, parametric tests were used. One-way analysis of variance was used to compare the quantitative variables between the HC, NT1, NT2, and IH groups. Differences between each pair of groups were analyzed using Bonferroni post hoc analysis. The chi-square test was applied to compare qualitative variables between groups. Correlations between quantitative variables were analyzed using Spearman's correlation. Receiver operating characteristic (ROC) curve analyses were performed to evaluate the accuracy of NLR in discriminating patients with NT1 from those with NT2 and IH and HC. The optimal cutoff value (threshold) was determined according to the Youden index. The area under the curve, sensitivity, and specificity are provided along with their 95% confidence intervals (CI), which were computed with 2,000 bootstrap replicates. In all analyses, 2-sided P values < .05 were considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics 26 (IBM, Armonk, New York) and R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

This study included 45 patients with narcolepsy (28 NT1 and 17 NT2), 11 with IH, and 21 HC. The groups were similar in terms of age and sex. The demographic, clinical, and biofluid marker data (both CSF and blood data) of the study population are summarized in **Table 1**.

Leukocyte counts and NLR

A significant difference in the NLR was observed between the HC, NT1, NT2, and IH groups ($F = 7.25$, $P < .001$). Bonferroni post hoc analyses revealed a significantly higher NLR in patients with NT1 than in those with NT2 ($P = .02$) and IH ($P = .009$) and HC ($P = .001$) (**Figure 1**). No other significant differences in leukocyte counts were observed between groups.

Correlations between NLR and CSF, PSG, and MSLT parameters in patient groups

The NLR was correlated with PSG and MSLT parameters in the NT1, NT2, and IH groups. Only a negative correlation was observed between NLR and sleep efficiency in the NT1 group ($r = –0.55$, $P = .007$). No other significant correlations were observed. Furthermore, no significant correlations were observed between the NLR and CSF levels of orexin-A, immunoglobulin G count, CSF/serum albumin ratio, or link index in all groups of patients evaluated.

ROC curves

Finally, ROC curves were computed to determine the optimal cutoff score to distinguish patients with NT1 from those with NT2 and IH and HC using NLR (**Figure 2**).

Using the ROC curve (area under the curve = 0.74 [95% CI, 0.58–0.91]), we identified NLR ≥ 1.60 as the optimal cutoff value to distinguish patients with NT1 from patients with NT2 (sensitivity 0.89 [95% CI, 0.79–1.00]; specificity 0.65 [95% CI, 0.41–0.88]). Moreover, using the ROC curve (area under the curve = 0.81; 95% CI, 0.65–0.97), we identified NLR ≥ 1.62 as an optimal cutoff value to distinguish patients with NT1 from those with IH (sensitivity 0.86 [95% CI, 0.71–0.96]; specificity 0.82 [95% CI, 0.55–1.00]). Finally, using the ROC analysis (area under the curve = 0.81 [95% CI, 0.68–0.94]), we identified an optimal cutoff value of NLR ≥ 1.59 to differentiate patients with NT1 from those with HC (sensitivity 0.89 [95% CI, 0.79–1.00]; specificity 0.67 [95% CI, 0.48–0.86]).

DISCUSSION

The present study confirmed the alteration in innate and adaptive immune responses in patients with NT1 by showing the significant increase of the NLR, which was higher than that of the other groups of patients and controls. The present study also aimed to explore the clinical potential of using the NLR as a biofluid marker to identify patients with EDS at risk for narcolepsy diagnosis in clinical practice, suggesting the potential role of the NLR as an inflammatory marker to screen NT1 with high sensitivity. In particular, we found that a cutoff NLR of ≥ 1.60 could discriminate patients with NT1 from those with NT2 (89% sensitivity), ≥ 1.62 could distinguish patients with NT1 from those with IH (86% sensitivity), and ≥ 1.59 could differentiate patients with NT1 from HC (89% sensitivity).

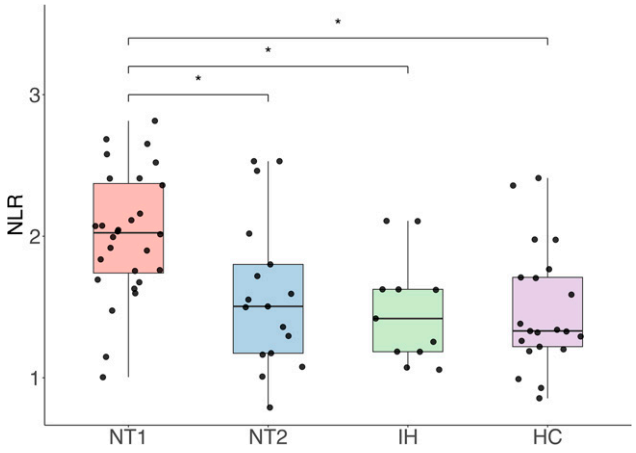
Relative lymphopenia (which also accounts for the higher NLR) in patients with NT1 may follow lymphocyte migration within the central nervous system in response to a neuroinflammatory state, as previously described for narcolepsy.[31] This

Table 1—Study population demographic and biofluid data.

	NT1 (n = 28)	NT2 (n = 17)	IH (n = 11)	HC (n = 21)	*P*	Post Hoc Analysis					
						NT1 vs NT2	NT1 vs IH	NT2 vs IH	NT1 vs HC	NT2 vs HC	IH vs HC
Demographic and clinical data											
Age (years)	42.00 ± 16.43	33.28 ± 13.84	32.38 ± 12.59	41.10 ± 13.33	n.s.						
Sex (M/F)	13/15	8/9	6/5	12/9	n.s.						
ESS	16.68 ± 2.58	17.00 ± 2.65	15.78 ± 4.35	/	n.s.						
Leukocites parameters											
WBC ($10^3/\mu l$)	6.47 ± 1.38	5.72 ± 1.11	5.61 ± 0.90	6.21 ± 0.86	n.s.						
Neutrophils ($10^3/\mu l$)	3.50 ± 0.79	3.09 ± 0.85	2.85 ± 0.69	3.24 ± 0.55	n.s.						
Lymphocytes ($10^3/\mu l$)	2.22 ± 0.74	2.09 ± 0.51	1.96 ± 0.32	2.30 ± 0.48	n.s.						
Monocytes ($10^3/\mu l$)	0.53 ± 0.20	0.49 ± 0.15	0.40 ± 0.09	0.44 ± 0.12	n.s.						
Eosinophils ($10^3/\mu l$)	0.29 ± 0.60	0.14 ± 0.08	0.20 ± 0.16	0.18 ± 0.11	n.s.						
Basophils ($10^3/\mu l$)	0.04 ± 0.05	0.02 ± 0.02	0.04 ± 0.02	0.04 ± 0.02	n.s.						
NLR	2.01 ± 0.44	1.59 ± 0.53	1.48 ± 0.37	1.48 ± 0.43	<.001	.02	.009	n.s.	.001	n.s.	n.s.
PSG data											
TST (minutes)	412.50 ± 63.74	397.40 ± 54.73	383.53 ± 57.69		n.s						
SE (%)	86.08 ± 9.11	88.70 ± 9.38	85.26 ± 9.81		n.s.						
SL (minutes)	7.76 ± 8.51	10.67 ± 15.77	7.94 ± 6.84		n.s.						
Wake after sleep onset (%)	13.89 ± 9.74	10.40 ± 9.75	12.65 ± 9.41		n.s.						
REM (%)	17.47 ± 6.05	17.68 ± 7.55	19.31 ± 8.79		n.s.						
N1 (%)	8.04 ± 5.25	13.67 ± 21.71	12.71 ± 12.68		n.s.						
N2 (%)	42.98 ± 10.64	39.75 ± 15.68	39.58 ± 15.39		n.s.						
N3 (%)	18.10 ± 8.71	22.92 ± 12.42	19.14 ± 10.86		n.s.						
MSLT data											
MSL (minutes)	3.68 ± 1.82	6.56 ± 3.31	6.20 ± 4.34		.003	.005	.009	n.s.			
No. of SOREMPs	2.71 ± 1.36	2.12 ± 1.17	0.64 ± 0.51		<.001	n.s.	<.001	.006			
CSF data											
Orexin-A (pg/ml)	58.23 ± 22.44	184.34 ± 43.35	246.94 ± 80.98		<.001	<.001	<.001	.01			
IgG (mg/dl)	2.39 ± 0.52	2.85 ± 1.18	2.54 ± 0.94		n.s						
Link index	0.50 ± 0.07	0.47 ± 0.03	0.56 ± 0.04		n.s						
CSF/serum albumin ratio	4.48 ± 1.66	5.32 ± 1.68	4.04 ± 1.06		n.s.						

Data are presented as mean ± standard deviation. CSF = cerebrospinal fluid, ESS = Epworth Sleepiness Scale, F = female, HC = healthy controls, IgG = immunoglobulin G, IH = idiopathic hypersomnia, M = male, MSL = mean sleep latency, MSLT = Multiple Sleep Latency Test, n.s. = not statistically significant, N1 = stage 1 of non-REM sleep, N2 = stage 2 of non-REM sleep, N3 = stage 3 of non-REM sleep, NLR = neutrophil-to-lymphocyte ratio, NT1 = narcolepsy type 1, NT2 = narcolepsy type 2, PSG = polysomnography, REM = rapid eye movement, SE = sleep efficiency, SL = sleep latency, SOREMP = sleep onset REM period, TST = total sleep time, WBC = white blood cell count.

Figure 1—Box and scatter plot of NLR in the NT1, NT2, IH, and HC groups.

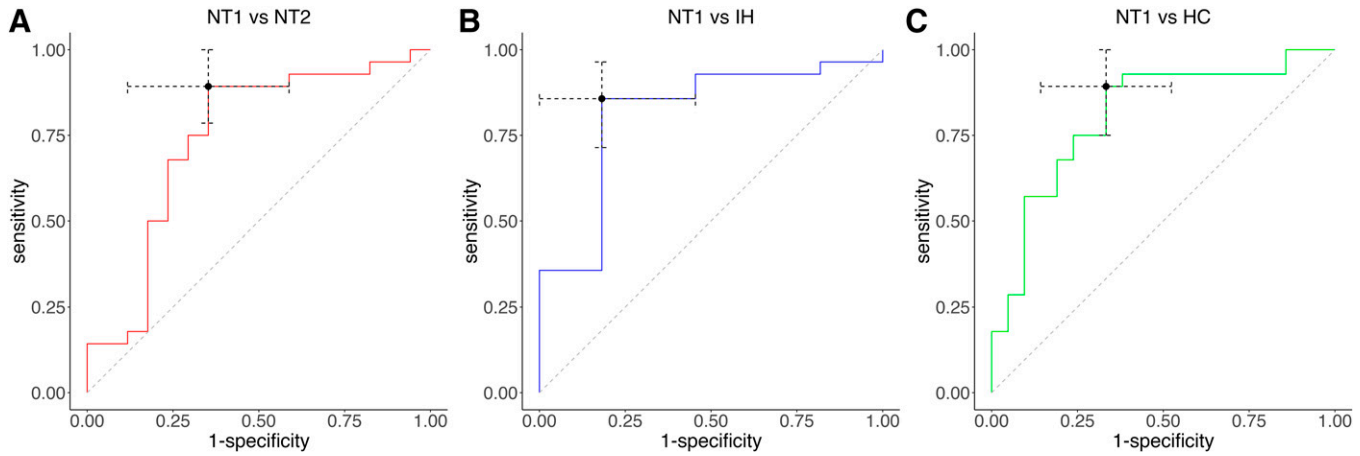


*Significant difference between groups (P < .05). HC = healthy controls, IH = idiopathic hypersomnia, NLR = neutrophil-to-lymphocyte ratio, NT1 = narcolepsy type 1, NT2 = narcolepsy type 2.

migration could occur independently of BBB impairment, because the CSF/serum albumin ratio, measured as the expression of BBB integrity, did not correlate with the NLR in the different groups of patients included in this analysis. Lymphocyte trafficking across the BBB is consistently observed under physiological conditions when the BBB is preserved. Accordingly, because immunosurveillance exists in the central nervous system under physiological conditions with the infiltration of activated leukocytes (particularly T cells) across the cerebral endothelium, the former concept that the central nervous system is an immune-privileged site has been tempered, with research indicating that the migration of T cells can also be present when the BBB is undamaged.[32,33] Existing literature supporting the idea that NT1 is an autoimmune disorder characterized by a selective attack on orexin-producing neurons by activated lymphocytes reinforces the results of the present study. Conversely, the pathophysiology of NT2 remains controversial and evidence for a selective neuroinflammatory attack is less evident. The central mechanisms underlying the pathophysiology of IH remain unknown. However, reactive T cells have been detected in the biofluid of patients with NT1 and NT2, particularly when they were tested near disease onset, indicating a possible role for these lymphocytes in the pathophysiology of the disease itself.[13] Consistently, the higher NLR documented in patients with NT1 compared to those with NT2 and IH and HC could reflect the activation of lymphocytes involved in the neuroinflammatory brain attack and may be responsible for orexin-producing neuronal loss. However, the NLR was not correlated with CSF orexin-A levels in this study, and none of the patients with narcolepsy included in this study were evaluated near disease onset. A further hypothesis supporting the present results could be drawn from the evidence that NLR increases in response to a systemic inflammatory state, which is also evident in other neurological diseases characterized by autoimmune and inflammatory mechanisms based on their pathophysiology.[34] In particular, it may reflect abundant cytokine and chemokine release and the rearrangement of leukocyte subpopulations toward proinflammatory activation.[13,16] Moreover, an increase in the NLR has been documented in obstructive sleep apnea syndrome, a sleep disorder characterized by EDS and presenting with increased systemic inflammation.[35,36] Notably, considering that patients with NT1 were compared both to patients with NT2 and those with IH who presented similar levels of EDS but lower NLR in this study, the hypothesis of a sustained inflammatory state more than EDS that can cause increased NLR in patients with NT1 can be better hypothesized.

Considering that NLR has also been investigated as a cost-effective and easily identifiable circulating clinical marker of

Figure 2—Receiver operating curve and optimal cutoff point with 95% confidence interval for neutrophil-to-lymphocyte ratio as a diagnostic marker of NT1.



(A) NT1 vs NT2. **(B)** NT1 vs IH. **(C)** NT1 vs HC. HC = healthy controls, IH = idiopathic hypersomnia, NT1 = narcolepsy type 1, NT2 = narcolepsy type 2.

chronic, low-grade inflammation in neurological diseases and multiple sclerosis,[37] we tested the clinical potential of using NLR as a screening biofluid marker to support NT1 diagnosis during the diagnostic setup. The significant sensitivity documented here could indeed help to reinforce the diagnosis in cases where NT1 seems to be evident and can help clinicians in following the diagnosis when the other criteria have been nearly met and need only to be boosted.

Consistently, in patients with NT1, the presence of disturbed nighttime sleep, as documented by low sleep efficiency, also correlated with a high NLR. These results, although apparent in contrast, reflect the prolonged but inefficient sleep duration evident in the case of a proinflammatory state,[38] which could also be evident in patients with NT1. However, this evidence is preliminary and should be further evaluated in other studies, possibly prospective and including more patients with narcolepsy, focused primarily on investigating this finding. Another limitation of this study that should be acknowledged is that the NLR was not longitudinally measured, thus limiting the possibility of correlating the ratio to disease progression or time from disease onset. Further, the possible influence of subtle infections without evident symptomatology at the time of NLR analysis cannot be excluded, because only infections presenting with clinical symptoms were considered as exclusion criteria for this study. Further, controls were considered healthy according to their medical charts, but no objective investigations of sleep, other blood, or CSF biomarkers were performed.

In conclusion, the present study documented a significant increase in the NLR in patients with NT1 compared to that in patients with NT2, IH or HC. This finding may be due to the pathophysiological mechanisms underlying NT1, further reinforcing the hypothesis of a lymphocyte attack on orexinergic neurons. However, the lack of evidence of increased NLR in patients with NT2 and IH requires further research to understand the mechanisms underlying these disorders, because the inflammatory or autoimmune drive does not seem to explain the pathophysiology of the diseases. Further studies are needed to understand the clinical potential of using the NLR as a biomarker to support the diagnosis of NT1 as well as other sleep disorders characterized by EDS, such as NT2 and IH.

ABBREVIATIONS

BBB, blood–brain barrier
CI, confidence interval
CSF, cerebrospinal fluid
EDS, excessive daytime sleepiness
HC, healthy controls
IH, idiopathic hypersomnia
MSLT, Multiple Sleep Latency Test
NLR, neutrophil-to-lymphocyte ratio
NT1, narcolepsy type 1
NT2, narcolepsy type 2
PSG, polysomnography
REM, rapid eye movement
ROC, receiver operating characteristic

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