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Anti-KIF20B autoantibodies are associated with cranial neuropathy in systemic lupus erythematosus

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ABSTRACT

Background Cranial neuropathies (CN) are a rare neuropsychiatric SLE (NPSLE) manifestation. Previous studies reported that antibodies to the kinesin family member 20B (KIF20B) (anti-KIF20B) protein were associated with idiopathic ataxia and CN. We assessed anti-KIF20B as a potential biomarker for NPSLE in an international SLE inception cohort.

Methods Individuals fulfilling the revised 1997 American College of Rheumatology (ACR) SLE classification criteria were enrolled from 31 centres from 1999 to 2011 and followed annually in the Systemic Lupus Erythematosus International Collaborating Clinics inception cohort. Anti-KIF20B testing was performed on baseline (within 15 months of diagnosis or first annual visit) samples using an addressable laser bead immunoassay. Logistic regression (penalised maximum likelihood and adjusting for confounding variables) examined the association between anti-KIF20B and NPSLE manifestations (1999 ACR case definitions), including CN, occurring over the first 5 years of follow-up.

Results Of the 1827 enrolled cohort members, baseline serum and 5 years of follow-up data were available on 795 patients who were included in this study: 29.8% were anti-KIF20B-positive, 88.7% female, and 52.1% White. The frequency of anti-KIF20B positivity differed only for those with CN (n=10) versus without CN (n=785) (70.0% vs 29.3%; OR 5.2, 95% CI 1.4, 18.5). Compared with patients without CN, patients with CN were more likely to fulfil the ACR haematological (90.0% vs 66.1%; difference 23.9%, 95% CI 5.0%, 42.8%) and ANA (100% vs 95.7%; difference 4.3%, 95% CI 2.9%, 5.8%) criteria. In the multivariate analysis adjusting for age at baseline, female, White race and ethnicity, and ACR haematological and ANA criteria, anti-KIF20B positivity remained associated with CN (OR 5.2, 95% CI 1.4, 19.1).

Conclusion Anti-KIF20B is a potential biomarker for SLE-related CN. Further studies are needed to examine how autoantibodies against KIF20B, which is variably expressed in a variety of neurological cells, contribute to disease pathogenesis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Antibodies to the kinesin family member 20B (anti-KIF20B) protein have been associated with idiopathic ataxia and peripheral neuropathies in previous studies.

WHAT THIS STUDY ADDS

⇒ The aim of this study was to investigate the associations between anti-KIF20B positivity and disease phenotype in a large international cohort of patients with SLE, with a specific focus on neuropsychiatric manifestations.

⇒ The results of this study show that anti-KIF20B autoantibodies are associated with cranial neuropathies (CN) in this SLE cohort.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study introduces anti-KIF20B as a potential novel biomarker for CN in SLE.

⇒ Future research should focus on how anti-KIF20B contributes to the development of CN in SLE, as well as the utility of these antibodies in clinical practice.

INTRODUCTION

SLE is a complex and heterogeneous autoimmune disease that can affect almost any organ system. Both the central nervous system (CNS) and the peripheral nervous system (PNS) can be involved in a clinical subset referred to as neuropsychiatric SLE (NPSLE). In 1999, the American College of Rheumatology (ACR) defined 19 NPSLE manifestations, which can be subdivided into central and peripheral manifestations, as well as focal and diffuse

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manifestations.[1] Despite these definitions, which help identify and characterise SLE-related NPSLE manifestations, our understanding of which patients develop these manifestations is still lacking.

Several serum and cerebrospinal fluid (CSF) biomarkers, including autoantibodies and cytokines, have been associated with central NPSLE manifestations. Antiphospholipid (aPL) antibodies, immune complex deposition and complement activation result in focal and diffuse ischaemia, while increased blood–brain barrier leakage, antibodies within the CSF and inflammatory mediator production result in tissue damage.[2] The aPL antibodies anti-beta-2-glycoprotein 1 (anti-β2GP1), anti-cardiolipin (aCL) and lupus anticoagulant have been associated with seizure and stroke in patients with SLE,[3 4] supporting the idea that CNS SLE manifestations are, at least in part, due to ischaemic events. Furthermore, anti-ribosomal P and anti-N-methyl-d-aspartate (NMDA) receptor antibodies have been shown to be associated with global CNS pathologies, particularly psychosis and depression.[5–7] Similarly, there is a reported association between SLE-related peripheral neuropathy and anti-Sjögren Syndrome antigen A (anti-SSA/Ro60) autoantibodies.[8 9]

Ascertaining whether neuropsychiatric pathologies are the cause or consequence of SLE disease activity or an unrelated disease mechanism is challenging. It is currently based on expert opinion and clinician judgement combined with radiographic, electrodiagnostic and serological testing. Further research is needed to clarify how and when these tests are best used in the clinical setting.[10–13] Identifying NPSLE-associated biomarkers may aid in the diagnosis of NPSLE and help us understand these complex disease processes.

Kinesin family member 20B (KIF20B), previously referred to as M-phase phosphoprotein 1, is a plus-end-directed slow molecular motor that plays a role in cytokinesis.[14] KIF20B regulates cortical neural stem cell development,[15] and mutations in KIF20B have been associated with microcephaly in mouse models.[16] The role of KIF20B in the PNS is less well understood. Antibodies directed against KIF20B (anti-KIF20B) were first identified in patients with idiopathic ataxia[17] and then in a patient with longstanding acquired demyelinating polyneuropathy.[18] Anti-KIF20B titres were elevated in 40% (10/25) of patients with idiopathic ataxia, many of whom had concurrent peripheral neuropathies.[17] In a cohort of Japanese patients with systemic autoimmune rheumatic diseases, anti-KIF20B expression was increased in patients with SLE when compared with healthy controls and was associated with high disease activity (Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-2K) in patients with SLE.[19] In a local SLE cohort (Calgary, Canada), we identified an association between anti-KIF20B antibodies with both cranial neuropathy (CN) and peripheral mononeuropathy.[20] The aim of the current study was to evaluate the association between anti-KIF20B antibodies and NPSLE manifestations in a large international inception SLE cohort.

METHODS

Study population

Between 1999 and 2011, 1827 patients fulfilling the 1997 updated ACR classification criteria for definite SLE[21] within 15 months of diagnosis from 31 medical centres in 11 countries were enrolled into the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) inception cohort (https://sliccgroup.org).[22] Sera, clinical and demographic data were collected at enrolment and annually thereafter. NPSLE manifestations occurring were also recorded and were based on the ACR case definitions[1] using a previously published NPSLE attribution rule: onset up to 10 years before SLE diagnosis and still present at diagnosis, or occurred subsequently; no 'exclusions' as outlined in the ACR case definitions; not one of the NPSLE manifestations with high prevalence in the general population identified by Ainiala and colleagues (isolated headaches, anxiety, mild depression, mild cognitive impairment and peripheral neuropathy without electrophysiological confirmation).[23 24] Permission from the SLICC Biological Material and Data Utilisation Committee was obtained to access the required data and biobanked serum samples.

Anti-KIF20B autoantibody testing

Anti-KIF20B titres were determined on baseline biobanked serum samples defined as at enrolment or on first follow-up samples if enrolment samples were not available (707/795 (88.9%) tested at enrolment). Autoantibody testing was performed by addressable laser bead immunoassay using an in vitro expressed full-length human KIF20B cDNA construct inserted into a green fluorescent protein (GFP) vector (Clontech Laboratories, Saint-Germain-en-Laye, France). The recombinant protein was recovered from cell lysates and affinity purified as previously described.[25] The upper value of the reference range of 1–500 median fluorescence units was established at 2 SD above the mean of age-matched healthy controls, and followed the requirements for validation of laboratory tests in the accredited diagnostic laboratory that performed these tests (MitogenDx, Calgary, Canada). Other SLE-associated autoantibodies were also tested in all participants at enrolment or first visit using previously established protocols (online supplemental table 1).

Statistical analysis

t-Tests and two-sample tests of proportions were used to compare baseline demographic and clinical characteristics between participants who were anti-KIF20B positive (anti-KIF20B+) and negative (anti-KIF20B−). χ^2 tests and univariate logistic regression were used to compare each NPSLE manifestation occurring over the first 5 years of follow-up between participants who were anti-KIF20B+ and anti-KIF20B−. For NPSLE manifestations

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Table 1 Baseline demographic and clinical characteristics

	Cohort (N=795), %	Anti-KIF20B+ (n=237), %	Anti-KIF20B– (n=558), %	Difference, % (95% CI)
Demographics				
Age at enrolment (years), mean (SD)*	35.5 (13.5)	32.9 (12.2)	36.7 (13.9)	**–3.8 (–5.9** to **–1.8)**
Age <18 years at diagnosis*	6.2	7.2	5.7	1.4 (–2.4 to 5.2)
Sex, % female*	88.7	85.2	90.1	**–4.9 (–10.1 to 0.0)**
Ethnicity, % White*	52.1	46.0	54.7	–8.7 (–16.2 to –1.1)
Clinical characteristics				
SLEDAI-2K at enrolment, mean (SD)†	5.7 (5.4)	6.4 (5.6)	5.3 (5.3)	**1.1 (0.3 to 1.9)**
ACR criteria*				
Malar rash	33.0	34.6	32.3	2.3 (–4.9 to 9.5)
Discoid rash	11.1	12.7	10.4	2.3 (–2.7 to 7.2)
Oral ulcers	35.4	30.4	37.5	–7.1 (–14.2 to 0.0)
Serositis	27.8	27.0	28.1	–1.1 (–7.9 to 5.6)
Arthritis	70.4	75.5	68.3	**7.2 (0.5 to 13.9)**
Photosensitivity	33.8	32.5	34.4	–1.9 (–9.1 to 5.2)
Renal disorder	26.7	27.4	26.3	1.1 (–5.7 to 7.8)
Neurological disorder	4.4	5.1	4.1	0.9 (–2.3 to 4.2)
Haematological disorder	66.4	69.6	65.1	4.6 (–2.5 to 11.6)
Immunological disorder	79.6	84.8	77.4	**7.4 (1.7 to 13.1)**
ANA	95.7	94.1	96.4	–2.3 (–5.7 to 1.1)
Hypocomplementaemia‡	42.8	50.2	39.7	**10.6 (2.7 to 18.4)**
Leucopenia§	8.8	7.6	9.3	–1.7 (–6.1 to 2.7)
Anticardiolipin IgG¶	16.7	19.4	15.7	3.7 (–2.6 to 10.1)
Anticardiolipin IgM¶	5.7	6.1	5.5	0.6 (–3.3 to 4.5)
Anti-ß2GP1 IgG¶	9.1	8.2	9.4	–1.2 (–5.8 to 3.4)
Anti-ß2GP1 IgM¶	11.5	6.6	13.3	**–6.7 (–11.2 to –2.1)**
Lupus anticoagulant**	35.8	33.3	37.3	–4.0 (–23.7 to 15.8)
Anti-dsDNA¶	73.3	81.1	70.3	**10.9 (4.1 to 17.6)**
Antihistone¶	31.1	39.3	28.0	**11.3 (3.4 to 19.2)**
Anti-Jo-1¶	1.7	2.0	1.6	0.5 (–1.8 to 2.7)
Anti-ribosomal P¶	25.9	36.2	21.9	**14.3 (6.7 to 21.9)**
Anti-Sm¶	23.5	32.1	20.2	**12.0 (4.6 to 19.4)**
Anti-U1RNP¶	28.6	36.2	25.6	**10.6 (2.9 to 18.3)**
Anti-PMScl¶	11.0	13.3	10.2	3.1 (–2.3 to 8.5)
Anti-CENP-B¶	3.1	3.6	2.9	0.6 (–2.3 to 3.6)
Anti-PCNA¶	17.8	21.9	16.2	5.7 (–0.9 to 12.3)
Anti-Ro52/TRIM21¶	39.2	33.2	41.5	**–8.3 (–16.2 to –0.5)**
Anti-SSA/Ro60¶	43.9	39.3	45.6	–6.3 (–14.4 to 1.8)
Anti-SSB/La¶	22.4	18.9	23.7	–4.8 (–11.4 to 1.8)
Medications				
Steroids, ever	81.8	81.4	81.9	–0.5 (–5.4 to 6.4)
Antimalarials, ever	76.5	75.1	77.1	–2.0 (–4.6 to 8.4)
Immunosuppressants, ever	44.2	44.7	43.9	0.8 (–8.4 to 6.7)

Bold indicates statistically significant results.
Medication use reflects current medications taken at the time of anti-KIF20B testing or ever exposed prior to testing.
*n=795.
†n=793.
‡n=741.
§n=714.
¶n=707.
**n=95.
ACR, American College of Rheumatology; CENP-B, centromere protein B; dsDNA, double-stranded DNA; ß2GP1, beta-2-glycoprotein 1; KIF20B, kinesin family member 20B; PCNA, proliferating cell nuclear antigen; PMScl, polymyositis/scleroderma overlap antigens of the human exosome; Ro52/TRIM21, tripartite motif containing-21 (Ro52); SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2K; Sm, Smith; SSA/Ro60, Sjögren Syndrome antigen A (Ro60); SSB/La, Sjögren Syndrome antigen B (La); U1RNP, U1 ribonucleoprotein.

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Table 2 Anti-KIF20B positivity and OR between patients with and without NPSLE manifestations* within 5 years of follow-up using attribution model B

	Any NPSLE manifestation (n=153)	No NPSLE manifestations (n=642)	OR (95% CI)
Anti-KIF20B+, n (%)	42 (27.5)	195 (30.4)	0.9 (0.6 to 1.3)
	Any CNS manifestation (n=127)	**No CNS manifestations (n=668)**	
Anti-KIF20B+, n (%)	34 (26.8)	203 (30.4)	0.9 (0.6 to 1.3)
	Any PNS manifestation (n=34)	**No PNS manifestations (n=761)**	
Anti-KIF20B+, n (%)	11 (32.4)	226 (29.7)	1.1 (0.5 to 2.4)
	Any CN† (n=10)	**No CN (n=785)**	
Anti-KIF20B+, n (%)	7 (70.0)	230 (29.3)	**5.2 (1.4 to 18.5)**

Bold indicates statistically significant results.
*ACR NPSLE manifestations with onset within 10 years of SLE diagnosis and still present within the enrolment window or occurred subsequently; no 'exclusions'; not one of the NPSLE manifestations with high prevalence in the general population identified by Ainiala *et al*.[23] Only the significant CNS and PNS subtypes are shown.
†Individual CN manifestations were trochlear, abducens, vestibulocochlear, facial, glossopharyngeal, optic and trigeminal.
ACR, American College of Rheumatology; CN, cranial neuropathy; CNS, central nervous system; KIF20B, kinesin family member 20B; NPSLE, neuropsychiatric SLE; PNS, peripheral nervous system.

associated with anti-KIF20B+ in the univariate analysis, baseline demographic, clinical characteristics, and medications were compared between participants with and without the neuropsychiatric manifestation using t-tests and two-sample tests of proportions. Multivariate logistic regression analysis using penalised maximum likelihood estimates was then performed to assess the association between these NPSLE manifestations and anti-KIF20B+, adjusting for age at baseline, female sex, White race and ethnicity, and variables that were statistically significant on univariate analysis. Kaplan-Meier survival curve analysis and Cox regression analysis were used to evaluate anti-KIF20B as a predictor of NPSLE manifestations at 5-year and all follow-up visits. There were 773 (97.2%) patients with follow-up past 5 years, 565 (71.1%) with at least 10 years of follow-up, and 2 (0.2%) with 20 years of follow-up. Primary analyses included NPSLE events that occurred within the first 5 years of follow-up as all patients had available data. Subsequent sensitivity analyses included all available follow-up data (up to 20 years). Only NPSLE manifestations that were statistically significant in the univariate analysis were included in the survival analysis, and events present at baseline were excluded.

Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Study population

Of the 1827 patients originally recruited, 805 patients had available clinical data with at least 5 years of follow-up. As described in a previous study, those 805 patients had similar clinical and demographic characteristics when compared with those who were excluded, except there was a higher proportion of Asian (difference 18.8%, 95% CI 15.3%, 22.2%) and lower proportion of Hispanic participants (difference −20.6%, 95% CI −24.5%, −16.8%) in the study cohort when compared with those who were excluded.[26] Of those 805 patients, 795 (98.8%) had anti-KIF20B testing and were therefore included in this study. The mean age at enrolment was 35.5±13.5 years, 88.7% (705/795) were female and 52.1% (414/795) were White (table 1). The mean SLEDAI-2K at baseline was 5.7±5.4. There were 10 cases of CN in the SLICC cohort within the first 5 years of follow-up.

Anti-KIF20B testing and associations

237 participants (29.8%) were anti-KIF20B+ at baseline (table 1). When compared with anti-KIF20B− patients, anti-KIF20B+ patients were younger at enrolment (32.9 years vs 36.7 years; difference −3.8 years, 95% CI −5.9, −1.8). Although both groups were predominantly female, there was a lower proportion of female patients in the anti-KIF20B+ group when compared with anti-KIF20B− (85.2% vs 90.1%; difference −4.9%, 95% CI −10.1%, 0.0%). Anti-KIF20B+ patients had a higher SLEDAI-2K at baseline when compared with anti-KIF20B− (6.4 vs 5.3; difference 1.1, 95% CI 0.3%, 1.9%); however, there was no difference in total 1997 updated ACR SLE classification criteria fulfilled between anti-KIF20B+ versus anti-KIF20B− group (4.9 vs 4.8; difference 0.1, 95% CI −0.024, 0.292). When individual 1997 updated ACR SLE classification criteria were compared between anti-KIF20B+ and anti-KIF20B− groups, there was a greater proportion of anti-KIF20B+ patients who had arthritis (75.5% vs 68.3%; difference 7.2%, 95% CI 0.5%, 13.9%), immunological disorder (84.8% vs 77.4%; difference 7.4%, 95% CI 1.7%, 13.1%), were hypocomplementaemic (50.2% vs 39.7%; difference 10.6%, 95% CI 2.7%, 18.4%) or positive for anti-double-stranded DNA (81.1% vs 70.3%; difference 10.9%, 95% CI 4.1%, 17.6%). When other SLE-related biomarkers were compared between groups at baseline, anti-KIF20B+ patients were more likely to express antihistone (39.3% vs 28.0%; difference 11.3%, 95% CI 3.4%, 19.2%), anti-ribosomal P (36.2% vs 21.9%; difference

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Table 3 Comparison of baseline demographic and clinical characteristics of SLE patients with and without cranial neuropathy within 5 years of follow-up

	Entire cohort (N=795)	With CN (n=10)	Without CN (n=785)	With vs without CN Difference (95% CI)
Demographics				
Age at baseline (years), mean (SD)*	35.7 (13.5)	37.0 (11.5)	35.6 (13.5)	1.4 (–7.1 to 9.8)
Age at diagnosis (years), mean (SD)*	35.1 (13.5)	36.4 (11.5)	35.1 (13.5)	1.4 (–7.1 to 9.8)
Sex, % female*	88.7	80.0	88.8	–8.8 (–33.7 to 16.1)
Ethnicity, % White*	52.1	60.0	52.0	8.0 (–22.5 to 38.6)
Clinical characteristics				
SLEDAI-2K at baseline, mean (SD)†	5.7 (5.4)	3.4 (5.7)	5.7 (5.4)	–2.3 (–5.7 to 1.1)
ACR criteria*				
Malar rash	33.0	40.0	32.9	7.1 (–23.4 to 37.7)
Discoid rash	11.1	0.0	11.2	**–11.2 (–13.4 to –9.0)**
Oral ulcers	35.4	20.0	35.5	–15.5 (–40.6 to 9.5)
Serositis	27.8	20.0	27.9	–7.9 (–32.9 to 17.1)
Arthritis	70.4	80.0	70.3	9.7 (–15.3 to 34.7)
Photosensitivity	33.8	30.0	33.9	–3.9 (–32.5 to 24.7)
Renal disorder	26.7	20.0	26.8	–6.8 (–31.7 to 18.2)
Neurological disorder	4.4	0.0	4.5	**–4.5 (–5.9 to –3.0)**
Haematological disorder	66.4	90.0	66.1	**23.9 (5.0 to 42.8)**
Immunological disorder	79.6	80.0	79.6	0.4 (–24.6 to 25.3)
ANA	95.7	100.0	95.7	**4.3 (2.9 to 5.8)**
Hypocomplementaemia‡	42.8	37.5	42.8	–5.3 (–39.1 to 28.4)
Leucopenia§	8.8	0.0	8.9	**–8.9 (–11.0 to –6.8)**
Other serological markers				
Anticardiolipin IgG¶	16.7	11.1	16.8	–5.7 (–26.4 to 15.1)
Anticardiolipin IgM¶	5.7	0.0	5.7	**–5.7 (–7.5 to –4.0)**
Anti-ß2GP1 IgG¶	9.1	0.0	9.2	**–9.2 (–11.3 to –7.0)**
Anti-ß2GP1 IgM¶	11.5	11.1	11.5	–0.4 (–21.0 to 20.3)
Lupus anticoagulant**	35.8	50.0	35.5	14.5 (–55.5 to 84.5)
Anti-dsDNA¶	73.3	88.9	73.1	15.8 (–5.0 to 36.6)
Antihistone¶	31.1	33.3	31.1	2.2 (–28.7 to 33.2)
Anti-ribosomal P¶	25.9	55.6	25.5	30.1 (–2.6 to 62.7)
Anti-Sm¶	23.5	22.2	23.5	–1.3 (–28.6 to 26.1)
Anti-U1RNP¶	28.6	22.2	28.7	–6.4 (–33.8 to 20.9)
Anti-PCNA¶	17.8	33.3	17.6	15.7 (–15.2 to 46.6)
Anti-Ro52/TRIM21¶	39.2	22.2	39.4	–17.2 (–44.6 to 10.2)
Anti-SSA/Ro60¶	43.9	22.2	44.1	–21.9 (–49.3 to 5.5)
Anti-SSB/La¶	22.4	22.2	22.4	–0.1 (–27.5 to 27.2)

Bold indicates statistically significant results.
Covariates with zero cells not included in the analysis.
Data presented as per cent positive unless otherwise specified.
*n=795.
†n=793.
‡n=741.
§n=714.
¶n=707.
**n=95.
ACR, American College of Rheumatology; CN, cranial neuropathy; dsDNA, double-stranded DNA; ß2GP1, beta-2-glycoprotein 1; KIF20B, kinesin family member 20B; PCNA, proliferating cell nuclear antigen; Ro52/TRIM21, tripartite motif containing-21 (Ro52); SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2K; Sm, Smith; SSA/Ro60, Sjögren Syndrome antigen A (Ro60); SSB/La, Sjögren Syndrome antigen B (La); U1RNP, U1 ribonucleoprotein.

14.3%, 95% CI 6.7%, 21.9%), anti-Smith (anti-Sm) (32.1% vs 20.2%; difference 12.0%, 95% CI 4.6%, 19.4%) or anti-U1 Ribonucleoprotein (anti-U1RNP) antibodies (36.2% vs 25.6%; difference 10.6%, 95% CI 2.9%, 18.3%). At baseline, a lower proportion of anti-KIF20B+ patients were positive for anti-β2GP1 IgM (6.6% vs 13.3%; difference –6.7%, 95% CI –11.2%, –2.1%) or anti-Ro52/tripartite motif-containing protein 21 (anti-Ro52/TRIM21) (33.2% vs 41.5%; difference –8.3%, 95% CI –16.2%, –0.5%). There were 15 anti-KIF20B+ patients who were

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Table 4 Multivariate analysis examining the association between anti-KIF20B positivity and cranial neuropathy within 5 years of follow-up

Covariates*	Cranial neuropathy positivity OR (95% CI)
Anti-KIF20B+ at baseline	**5.2 (1.4 to 19.1)**
Age at baseline	1.0 (0.9 to 1.1)
Female	0.6 (0.1 to 2.5)
White race and ethnicity	1.4 (0.4 to 5.1)
Haematological disorder	3.0 (0.5 to 17.1)
ANA	1.2 (0.1 to 21.0)

Bold indicates statistically significant result.
*Model covariates include anti-KIF20B positivity, adjusting for age at baseline (enrolment or first follow-up visit), female, White race and ethnicity, and significantly different clinical characteristics at baseline.
KIF20B, kinesin family member 20B.

negative for other SLE-associated antibodies that also had available ANA pattern descriptions as defined by the International Consensus on ANA Patterns (ICAP).[27] In total, there were 18 different ICAP ANA patterns observed (some sera had more than one pattern): AC1 (homogenous nuclear, n=3), AC2 (nuclear-dense fine-speckled, n=1), AC4 (nuclear fine-speckled, n=6), AC5 (nuclear large-speckled, n=5), AC7 (nuclear few discrete nuclear dots, n=1), AC10 (punctate nucleolar, n=1), AC20 (cytoplasmic fine-speckled, n=2) and AC nuclear matrix (not a recognised ICAP pattern, n=1). Of note, none had an AC27 intracellular bridge pattern. There were no significant differences between anti-KIF20B+ and anti-KIF20B– when medication use was compared at baseline (table 1).

NPSLE manifestations

During the first 5 years of follow-up, the frequency of anti-KIF20B+ was higher in those with CN when compared with those without CN (70.0% vs 29.3%; OR 5.2, 95% CI 1.4, 18.5) (table 2), but the frequency of anti-KIF20B+ did not differ between patients with and without the other 18 individual NPSLE manifestations (online supplemental table 2). During the 5-year follow-up period, there were no significant differences in the proportion of anti-KIF20B+ when patients with any NPSLE manifestation were compared with those without (27.5% vs 30.4%; OR 0.9, 95% CI 0.6, 1.3), any CNS NPSLE manifestation versus those without (26.8% vs 30.4%; OR 0.9, 95% CI 0.6, 1.3), and any PNS NPSLE manifestation versus those without (32.4% vs 29.7%; OR 1.1, 95% CI 0.5, 2.4).

Cranial neuropathy

Of the 10 patients with CN at baseline or within the first 5 years of follow-up, 3 of the CN occurred at baseline, while the remaining 7 occurred during the 5-year follow-up. Compared with those without CN, patients with CN were more likely to fulfil the 1997 ACR haematological (90.0% vs 66.1%; difference 23.9%, 95% CI 5.0%, 42.8%) and ANA (100.0% vs 95.7%; difference 4.3%, 95% CI 2.9%, 5.8%) criteria (table 3). Several 1997 updated ACR classification criteria and autoantibodies were only present in patients without CN and showed a significant difference (discoid rash, neurological disorder, leucopenia, aCL IgM, anti-β2GP1 IgG); however, these variables were not included in the multivariate analysis as they were automatically removed from the model due to their imbalanced distribution.

In the multivariate analysis, anti-KIF20B+ remained associated with CN development within the first 5 years of follow-up (OR 5.2, 95% CI 1.4, 19.1) after adjusting for age at baseline, female, White race and ethnicity, and ACR criteria for haematological disorder and ANA (table 4). The majority of patients with CN had other NPSLE manifestations (7/10, 70%) (online supplemental table 3), although these varied between patients.

To perform the Kaplan-Meier survival analysis and Cox proportional hazard regression analysis, three CN events were removed because they occurred at baseline. All three patients with CN at baseline were also anti-KIF20B+ (3/3, 100%), while four of the seven patients with later CN events were anti-KIF20B+ (4/7, 57.1%). With the limited number of CN events (n=7), there was a non-significant association between anti-KIF20B+ and CN when adjusting for age at baseline, female, White race and ethnicity, and ACR criteria for haematological disorder and ANA (HR 3.2, 95% CI 0.7, 14.4) (online supplemental figure 1).

In order to capture all possible events, a secondary Cox proportional hazard regression analysis was performed using all available follow-up data (up to 20 years). When all available follow-up data were assessed, there were 11 CN events, 3 of which occurred at baseline and were excluded. Once again, there was a non-significant association between anti-KIF20B+ and CN when adjusting for age at baseline, female, White race and ethnicity, and ACR criteria for haematological disorder and ANA (HR 2.2, 95% CI 0.7, 7.5) (online supplemental figure 2).

DISCUSSION

In SLE, NPSLE manifestations are a significant source of morbidity and mortality and are challenging from both a diagnostic and therapeutic perspective.[9 28] When compared with central NPSLE events, peripheral NPSLE events are rarer and account for less than 10% of all NPSLE events[9]; however, these manifestations are associated with significant functional impairment and reduced quality of life.[9] Compared with CNS manifestations, there is a paucity of literature and research on peripheral NPSLE; therefore, research into biomarkers for peripheral NPSLE would help provide clarity in this difficult diagnostic and clinical management area. A previous study suggested that anti-KIF20B is associated with peripheral neuropathies, specifically mononeuropathies and CN, in patients with SLE from a single-centre cohort.[20] The results of the present study involving a multicentre international SLE inception cohort suggest an association of anti-KIF20B antibodies with CN in cross-sectional analyses, but we could not identify anti-KIF20B as a clear marker for CN in longitudinal analyses due to the limited number of events.

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The pathogenic mechanisms in NPSLE are multifactorial and likely differ between the different manifestations. Ischaemic events, immune complex deposition and complement activation can manifest as strokes and seizures,[3] while inflammation and subsequent tissue damage have been associated with anti-ribosomal P autoantibodies and may result in psychosis and depression,[5] although there are conflicting studies that have shown no association.[29] Patients with SLE can develop overlap syndromes with other autoimmune neurological diseases like neuromyelitis optica spectrum disorder (NMOSD), as well as express autoantibodies directed to the NMDA receptor type I[30 31] and type II.[32] Although NMOSD can affect the optic nerve, this is traditionally thought of as a centrally manifested neurological disease. Some studies have shown an association between anti-SSA/Ro60, anti-Ro52/TRIM21 and anti-SSB/La autoantibodies and peripheral neuropathy in SLE and Sjögren disease[8 33]; however, other studies did not find an association of peripheral NPSLE manifestations with any of the antibodies tested.[9] To our knowledge, the association between anti-KIF20B antibodies and CN reported here is the first autoantibody specifically associated with CN in SLE.

CN is a rare manifestation of SLE but is a significant source of morbidity in affected patients.[9 28] A reduced health-related quality of life (HRQoL) has been reported in SLE patients with CN, polyneuropathies and mononeuropathies. As expected, HRQoL scores improved in patients with polyneuropathy and mononeuropathy following resolution of their pathology; however, scores remained low for patients with CN even after resolution of their symptoms.[9] In this study, we have shown that anti-KIF20B antibodies are a potential biomarker for SLE-associated CN, and further study into anti-KIF20B-associated CN may help us understand the mechanisms that underlie this significant cause of morbidity.

KIF20B is a plus-end-directed kinesin-related protein that is expressed during interphase.[25 34] KIF20B plays a role in CNS development in mice[15 16]; however, the role of KIF20B in cranial nerve development and regeneration is not reported. In a cohort of Japanese patients with SLE, systemic sclerosis, mixed connective tissue disease, Sjögren's disease and idiopathic inflammatory myositis, anti-KIF20B expression was significantly increased only in patients with SLE (18/89, 20.2%) when compared with healthy controls (3/46, 6.5%) and was associated with increased disease activity (SLEDAI-2K). In this Japanese SLE cohort, there was no association between anti-KIF20B expression and any NPSLE manifestations; however, the power to detect an effect was limited by their relatively small sample size (n=89).[19] In the Japanese cohort, 71.4% (30/42) anti-KIF20B+ sera demonstrated staining of the intercellular bridge and midbody in telophase cells; however, we were unable to find a consistent HEp-2 staining pattern in our anti-KIF20B+ patients. At this time, it is unknown if anti-KIF20B antibodies are a bystander biomarker for SLE-related CN or directly contribute to disease pathogenesis. Given that anti-KIF20B autoantibodies are expressed in both SLE and non-SLE patients with peripheral nerve disease,[17 18] further research is needed to better understand the role of KIF20B in the PNS.[35]

A strength of this study is that we included an international inception SLE cohort, representative of a global SLE population with diverse ethnicities. By using an SLE inception cohort, all 19 ACR-defined NPSLE manifestations were recorded prospectively using a standardised data collection protocol. A limitation of this study is that, although we were able to analyse the 19 ACR-defined NPSLE manifestations, any neurological events that were not part of these predefined criteria may have been missed. In our study, anti-KIF20B status was not predictive of future CN. However, our models were limited by the small number of CN events. A larger study including more CN events is needed; however, CN is a rare NPSLE manifestation. We only had 10 CN events in the 5-year follow-up period, 3 of which occurred at baseline. Since autoantibodies are known to fluctuate over time, patients may seroconvert.[36] We could only test baseline samples for anti-KIF20B antibodies due to sample availability, but studies to assess anti-KIF20B expression at later time points are underway.

In conclusion, anti-KIF20B antibodies detected early in disease were associated with CN in SLE in cross-sectional analyses, but not in longitudinal analyses. Further studies are needed to examine anti-KIF20B antibodies over the disease course and to determine whether anti-KIF20B antibodies are predictive of CN development and contribute to disease pathogenesis in SLE.

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Contributors EK contributed to study design and drafted the manuscript. MYC was the principal investigator of this study, contributed to study design, reviewed the manuscript, and is the guarantor. AEC and JGH contributed to study design, reviewed the manuscript, recruited patients and collected data. MJF and KAB contributed to study design and reviewed the manuscript. RC performed the statistical analysis and reviewed the manuscript. The remaining authors were involved in patient recruitment, data collection and review of the manuscript.

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REFERENCES

1 Liang MH, Corzillius M, Bae SC, *et al*. The American college of rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 1999;42:599–608.
2 Hanly JG, Kozora E, Beyea SD, *et al*. Review: nervous system disease in systemic lupus erythematosus: current status and future directions. *Arthritis Rheumatol* 2019;71:33–42.
3 Hawro T, Bogucki A, Krupińska-Kun M, *et al*. Intractable headaches, ischemic stroke, and seizures are linked to the presence of anti-B2GPI antibodies in patients with systemic lupus erythematosus. *PLoS One* 2015;10:e0119911.
4 Inzelberg R, Korczyn AD. Lupus anticoagulant and late onset seizures. *Acta Neurol Scand* 1989;79:114–8.
5 Choi MY, FitzPatrick RD, Buhler K, *et al*. A review and meta-analysis of anti-ribosomal P autoantibodies in systemic lupus erythematosus. *Autoimmun Rev* 2020;19:102463.
6 Omdal R, Brokstad K, Waterloo K, *et al*. Neuropsychiatric disturbances in SLE are associated with antibodies against NMDA receptors. *Eur J Neurol* 2005;12:392–8.
7 Aranow C, Diamond B, Mackay M. Glutamate receptor biology and its clinical significance in neuropsychiatric systemic lupus erythematosus. *Rheum Dis Clin North Am* 2010;36:187–201.
8 Su Y-J, Huang C-R, Chang W-N, *et al*. The association between autoantibodies and peripheral neuropathy in lupus nephritis. *Biomed Res Int* 2014;2014:524940.
9 Hanly JG, Li Q, Su L, *et al*. Peripheral nervous system disease in systemic lupus erythematosus: results from an international inception cohort study. *Arthritis Rheumatol* 2020;72:67–77.
10 Mok CC, Lau CS, Wong RW. Neuropsychiatric manifestations and their clinical associations in Southern Chinese patients with systemic lupus erythematosus. *J Rheumatol* 2001;28:766–71.
11 Sanna G, Bertolaccini ML, Cuadrado MJ, *et al*. Neuropsychiatric manifestations in systemic lupus erythematosus: prevalence and association with antiphospholipid antibodies. *J Rheumatol* 2003;30:985–92.
12 Hanly JG, Urowitz MB, Su L, *et al*. Autoantibodies as biomarkers for the prediction of neuropsychiatric events in systemic lupus erythematosus. *Ann Rheum Dis* 2011;70:1726–32.
13 Peretti C-S, Peretti CR, Kozora E, *et al*. Cognitive impairment in systemic lupus erythematosus women with elevated autoantibodies and normal single photon emission computerized tomography. *Psychother Psychosom* 2012;81:276–85.
14 Abaza A, Soleilhac J-M, Westendorf J, *et al*. M phase phosphoprotein 1 is a human plus-end-directed kinesin-related protein required for cytokinesis. *J Biol Chem* 2003;278:27844–52.
15 McNeely KC, Dwyer ND. Cytokinesis and postabscission midbody remnants are regulated during mammalian brain development. *Proc Natl Acad Sci U S A* 2020;117:9584–93.
16 Janisch KM, Vock VM, Fleming MS, *et al*. The vertebrate-specific Kinesin-6, Kif20B, is required for normal cytokinesis of polarized cortical stem cells and cerebral cortex size. *Development* 2013;140:4672–82.
17 Fritzler MJ, Kerfoot SM, Feasby TE, *et al*. Autoantibodies from patients with idiopathic ataxia bind to M-phase phosphoprotein-1 (MPP1). *J Investig Med* 2000;48:28–39.
18 Zochodne DW, Auer R, Fritzler MJ. Longstanding ataxic demyelinating polyneuronopathy with a novel autoantibody. *Neurology* 2003;60:127–9.
19 Koizumi H, Muro Y, Yamashita Y, *et al*. Anti-Kif20B autoantibodies in systemic autoimmune rheumatic diseases: their high prevalence in systemic lupus erythematosus. *J Dermatol* 2023;50:990–8.
20 Krustev E, Buhler K, Cardwell F, *et al*. Anti-MPP-1 autoantibodies in systemic lupus erythematosus: a potential biomarker for neuropsychiatric manifestations - ACR meeting abstracts. *Arthritis Rheumatol* 2021;73.
21 Hochberg MC. Updating the American college of rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997;40:1725.
22 Isenberg DA, Ramsey-Goldman R, Gladman D, *et al*. The systemic lupus International collaborating clinics (SLICC) group-it was 20 years ago today. *Lupus* 2011;20:1426–32.
23 Ainiala H, Hietaharju A, Loukkola J, *et al*. Validity of the new American college of rheumatology criteria for neuropsychiatric lupus syndromes: a population-based evaluation. *Arthritis Rheum* 2001;45:419–23.
24 Hanly JG, Urowitz MB, Gordon C, *et al*. Neuropsychiatric events in systemic lupus erythematosus: a longitudinal analysis of outcomes in an international inception cohort using a Multistate model approach. *Ann Rheum Dis* 2020;79:356–62.
25 Fritzler MJ, Brown RD, Zhang M. A monoclonal antibody to M-phase phosphoprotein 1/kinesin-like protein KIF20B. *Monoclon Antib Immunodiagn Immunother* 2019;38:162–70.
26 Choi MY, Clarke AE, Urowitz MB, *et al*. Longitudinal Analysis of ANA in the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort. Ann Rheum Dis.2022;81:1143–1150.
27 Chan EKL, Damoiseaux J, Carballo OG, *et al*. Report of the first international consensus on standardized nomenclature of antinuclear antibody HEp-2 cell patterns (ICAP) 2014-2015. *Front Immunol* 2015;6:412.
28 Bertsias GK, Ioannidis JPA, Aringer M, *et al*. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis* 2010;69:2074–82.
29 Teh LS, Isenberg DA. Antiribosomal P protein antibodies in systemic lupus erythematosus. *Arthritis Rheum* 1994;37:307–15.
30 Wang J, Xu J, Yang P. Neuropsychiatric lupus erythematosus: focusing on autoantibodies. *J Autoimmun* 2022;132:102892.
31 Mader S, Jeganathan V, Arinuma Y, *et al*. Understanding the antibody repertoire in neuropsychiatric systemic lupus erythematosus and neuromyelitis optica spectrum disorder *Arthritis Rheumatol* 2018;70:277–86.
32 Lapteva L, Nowak M, Yarboro CH, *et al*. Anti-N-methyl-D-aspartate receptor antibodies, cognitive dysfunction, and depression in systemic lupus erythematosus. *Arthritis Rheum* 2006;54:2505–14.
33 Scofield AK, Radfar L, Ice JA, *et al*. Relation of sensory peripheral neuropathy in Sjögren syndrome to anti-Ro/SSA. *J Clin Rheumatol* 2012;18:290–3.
34 Matsumoto-Taniura N, Pirollet F, Monroe R, *et al*. Identification of novel M phase phosphoproteins by expression cloning. *Mol Biol Cell* 1996;7:1455–69.
35 Zochodne DW. Sensory ganglionopathy. *N Engl J Med* 2021;384:192–3.
36 Faria AC, Barcellos KSA, Andrade LEC. Longitudinal fluctuation of antibodies to extractable nuclear antigens in systemic lupus erythematosus. *J Rheumatol* 2005;32:1267–72.

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