CASE REPORT

SLE presenting as demyelinating autoimmune visual loss

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SUMMARY

A healthy 38-year-old woman developed sudden unilateral vision loss due to retrobulbar optic neuritis in the wake of varicella-zoster virus infection. She had no further central nervous system (CNS) lesions. Antinuclear antibodies (ANA) and anti-aquaporin 4 antibodies were found, consistent with neuromyelitis optica (NMO). Later, serial MRIs showed dynamic short-segment and long-segment myelitis lesions, ANA titre increased and additional autoantibodies were found including anti-dsDNA, anti-chromatin/nucleosome and antiphospholipid antibodies. In that setting, NMO can be regarded a rare presenting manifestation of systemic lupus erythematosus (SLE). The relevant literature is reviewed and the implications of NMO spectrum disorder demyelinating syndromes as the first manifestation of SLE (with or without antiphospholipid syndrome) (APS) or their later development (in a patient diagnosed with SLE) as part of the spectrum of neuropsychiatric SLE are analysed in view of recent research developments in the field.

BACKGROUND

Diverse mechanisms may be involved in the pathogenesis of autoimmune visual loss and may operate at different levels such as compression of the optic nerve in thyroid ophthalmopathy, neoplastic autoimmune retinopathy or systemic rheumatic diseases with associated retinal artery occlusion, posterior scleritis or uveitis.

Sudden autoimmune visual loss, however, occurs primarily by one of two predominant pathological pathways—either an arteritic (vasculitic) ischaemic optic neuropathy as in giant cell arteritis,¹ or an active immune-mediated inflammatory demyelinating lesion as in either multiple sclerosis (MS) or the distinct neuromyelitis optica spectrum disorders (NMOSD).² This area of autoimmune optic neuropathy has been all but transformed due to recent research advances. New practical problems have emerged which are not well recognised by clinicians and are presented and discussed through our report of an unusual healthy patient who developed sudden severe vision loss due to NMO, later diagnosed as the initial manifestation of systemic lupus erythematosus (SLE) and antiphospholipid antibodies (APL). The literature is briefly reviewed, to highlight the impact and utilisation of recent research-based insights on diagnostic and management decisions.

CASE PRESENTATION

A 38-year-old woman was admitted with acute unilateral painless visual loss. She had been previously healthy, non-smoker, on no medications or oral contraceptives and her family history was unremarkable excepting a grandmother and sister diagnosed with hypothyroidism. She had three children with no miscarriages and a unremarkable review of systems but notably, a history of recent severe herpes zoster (VZV) infection 3 months prior to admission.

Examination was consistent with Rt. optic neuritis (ON) but was otherwise completely normal as were all basic laboratory tests, excluding C reactive protein (18.2 mg/dL, $n < 5$), WBC ($15.9 \times 10^3/\mu\text{L}$) and platelets ($413 \times 10^3/\mu\text{L}$). Marcus-Gunn sign (indicating an afferent defect at the level of the retina or optic nerve) was +2 positive on the Rt. with a visual acuity of 6/90 (6/6 in the Lt. eye). The fundus appeared normal, becoming pale on later examinations. Visual fields examination showed a central scotoma on the Rt. side. Pulse high-dose intravenous methylprednisolone (1000 mg/day, over 3 days) was given with some improvement followed by plasmapheresis and tapering prednisone to 10 mg/day with azathioprine 50 mg/day (a higher dose was refused). Work-up included head and spinal MRI with gadolinium which demonstrated isolated Rt. retrobulbar neuritis (figure 1). The spinal cord was entirely normal (not shown).

INVESTIGATIONS

An extensive autoantibody (AutoAb) profile revealed positive antinuclear antibodies (ANA) at a titre of 1:160 (cytoplasmic pattern) with negative anti-dsDNA antibodies, no APL, negative Coomb's test and normal complement. A specific marker for neuromyelitis optica (NMO-IgG) directed against the water channel aquaporin 4 antigen (AQP4)³ was positive over the first 2 months (by ELISA) but later tested repeatedly negative (1.8 U/mL, $n < 3.0$). The cerebrospinal fluid (CSF) was normal and no oligoclonal bands were found. Optical coherence tomography showed Rt. nerve fibre layer thinning around the optic nerve and macula (mean 71 μm). Visual evoked potentials demonstrated a demyelinating damage of the Rt. visual pathway (P100 prolonged to 120 ms, Lt. eye 103 ms, normal).

One year later under the same treatment, ANA titre rose to 1:320 (homogenous and speckled pattern), anti-dsDNA were weakly positive ($> 1:20$) and anti-chromatin antibodies were positive at

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Figure 1 Head MRI, axial magnetic resonance images of the orbits. T1-weighted image (A) and T1-weighted image postgadolinium injection (B) demonstrating focal enhancement of the mid right optic nerve (broken arrow). No other pathology was found. Subsequent imaging revealed right optic nerve atrophy.

2.7 ($n < 0.2$) with neither anti-Sm or anti-RNP antibodies nor rheumatoid factors. In addition, IgG anticardiolipin antibodies (27.6 U/mL, later 116), IgG anti- β_2 glycoprotein (53.7 U/mL, later 96) and lupus anticoagulant (Russel Viper Venom Test - Lupus AntiCoagulant) ratio 1.6, $n < 1.3$) were all clearly positive. Thyroid stimulating hormone (TSH) was mildly increased (5.5 mIU/L, $n < 4.0$) and AutoAbs to thyroglobulin and thyroid peroxidase were detected. Repeat MRI revealed a new signal at the levels of C2–3 and D8–9 without enhancement—consistent with residual transverse myelitis (TM) (figure 2). The Rt. optic nerve demonstrated thinning and a positive signal with no enhancement.

DIFFERENTIAL DIAGNOSIS

Demyelinating syndromes (DSs) can occur either alone (isolated MS, ON or TM) or they can be associated with the subsequent development of another demyelinating syndrome (eg, MS and ON or TM; ON and TM). On our patient's presentation, MS could be ruled out since white matter lesions on brain MRI and

Figure 2 Sagittal magnetic resonance images of the cervical spine—T2 inversion recovery image (A) shows abnormal hyperintense signal of the spinal cord at C2–C3 level. T1 fat suppressed image postintravenous contrast administration (B) shows focal enhancing lesion within the spinal cord at C2–C3 level (arrow). A later MRI revealed a positive signal at the level of C2–C4 with enhancement after gadolinium. Note the incidental findings of posterior herniation of the intervertebral disc at C4–C5 level and bulging of the disc at C5–C6 level.

oligoclonal bands in the CSF were both negative—highly unusual for MS (sensitivity 98%).⁴ Also, optic nerve involvement in MS typically causes some pain, and improvement begins within 3 weeks—unlike our patient. Although low-titre ANA may occur in some patients with MS,⁴ the initially positive AQP4, development of extensive active myelitis lesions (see below) and multiple AutoAbs strongly suggest NMOSD and not MS.² Spinal cord sarcoidosis may sometimes mimic NMO TM but there are other suggestive features and AQP4 is not positive.⁵ NMOSD may be paraneoplastic and precede tumour detection in almost half of these rare cases (especially breast cancer).⁶ However, autoimmunity is its most important association.⁷ In our patient, the later development of high-titre ANA, anti-dsDNA antibodies, anti-chromatin antibodies and APL is strongly suggestive of SLE fulfilling 4 of the SLICC criteria.⁸ All these are not to be found in MS. Type I interferon signature was not examined here but could also be used to differentiate the two since it is typically high in SLE and also in NMO, but low in MS.⁴

TREATMENT

Azathioprine dose was increased to 2.5 mg/kg/day in addition to increased prednisone (0.5 mg/kg/day) until azathioprine will take full effect. Hydroxychloroquine (400 mg/day) and clopidogrel (75 mg/day) were added and a full immunisation and monitoring programme instituted.

OUTCOME AND FOLLOW-UP

Two years after the diagnosis she remains asymptomatic but MRI now reveals a positive signal at the level of C2–C4 with enhancement after gadolinium. AutoAb positivity persists with occasional upwards fluctuations in titres.

DISCUSSION

Our patient had a genetic autoimmune diathesis (personal and family history of chronic autoimmune thyroiditis) and importantly, a superimposed environmental factor—acute viral infection (Varicella Zoster Virus) which preceded her autoimmune optic neuropathy and may have triggered it.^{9 10} An intriguing association between VZV and subsequent development of a DS has been previously noted. A literature review (1975–2009) identified 25 cases of parainfectious NMO and 11 of them were in association with viral infections, including VZV¹¹ in immunocompetent adults.¹² Also, VZV vaccination had been implicated in the pathogenesis of ON¹³ and responded to high-dose methylprednisolone. In contrast, although transient APL of doubtful clinical significance have been reported in children with varicella¹⁴ and isolated reports describe APS and venous thromboembolism associated with acute VZV infection in as many as 15% of 100 patients with APS associated with infections reported in the literature,¹⁵ our patient's APL first appeared 15 months after the infection and therefore is not very likely to be causally related.¹⁶ Thus, the preceding VZV infection in our susceptible patient may have triggered the NMSOD rather than being coincidental. Her clinical presentation and tests on admission are consistent with acute optic nerve inflammation and demyelination, and as discussed above, MS was considered and ruled out (no progressive clinical course, no CSF oligoclonal bands, no brain findings on MRI and so on). On the other hand, the initially positive AQP4, development of extensive active myelitis lesions and multiple AutoAbs strongly suggest NMOSD.² NMO (Devic's disease) is a rare, idiopathic, severe demyelinating disease that preferentially affects the optic nerve and/or spinal cord, so-called NMOSD. It manifests as acute attacks of ON or TM

with the potential of a commonly relapsing course and significant disability.¹⁷ A major advance in understanding its pathogenesis was the discovery of a disease-specific B-cell derived AutoAb marker identified in over two-thirds of the patients and highly specific for clinically diagnosed NMOSD.¹⁸ Termed NMO-IgG or aquaporin-4 AutoAb (AQP4-IgG), it is directed against the principal CNS water channel aquaporin-4 and has a direct role in the pathogenesis.² Thus, regions enriched for AQP4 are preferentially affected¹⁹; AQP-4 AutoAb titres correlate with the extent of the spinal lesions²⁰ and have been shown to target astrocyte-AQP4, activating complement and causing demyelination and necrosis.^{21 22} In 2006, AQP4-IgG was incorporated into the revised NMO diagnostic criteria.¹⁷

Our patient fulfils accepted criteria for NMOSD diagnosis.¹⁷ Her initially positive AQP-4 AutoAb may have converted to seronegative status as a result of immunosuppressive treatment.²³ Fortunately, her spinal cord involvement on imaging was clinically silent, allowing time for more effective treatment since MRI dynamics clearly indicated an ongoing active disease. Although longitudinally extensive spinal cord lesions (LETM) on T2-weighted MRI (extending for ≥ 3 vertebral segments) are typical of NMO, short TM is not uncommon²⁴ and was found in our patient before LETM developed. However, the subsequent course strongly suggests that the seemingly isolated NMOSD DS in our patient was in fact the presenting neuropsychiatric (N-P) feature of SLE.

There are few isolated but consistent publications about overlapping NMO and autoimmune disease (ATID).²⁴ Autoantibodies (AutoAbs) are commonly detected in patients with NMOSD but clinical autoimmune diseases (ATIDs) are very unusual.²⁵ For example, 43.8% of 153 NMOSD patients had ANA, 15.7% had Sjogren's syndrome A (SSA) antibodies, and rheumatoid factors (RF) and SSB have also been observed (3%–5%),⁷ but only five patients (3.2%) had coexisting ATID.²⁶ Nevertheless, a recent review of the literature identified 22 autoimmune conditions reported to be associated with NMO, including organ-specific ATID (eg, thyroid diseases) and non-organ-specific ATID (eg, SLE, APS).²⁷ Indeed, a specific rare subset of NMOSD includes ON or LETM associated with systemic ATID,² and these patients are briefly acknowledged by the International Panel for NMO diagnosis.¹⁷ In very few patients, NMOSD demyelination syndrome may be the presenting feature of a bona fide ATID such as SLE (with or without associated APS) or primary APS.^{28–30} Our patient had a strong serological proof of APS, including LAC positivity which shows best correlation with clinical events.³¹ However, actual clinical event is a requirement for the diagnosis of APS and qualifying events are either vascular (venous, arterial or small vessel) thromboses or unexplained fetal loss, not autoimmune demyelination at present. Nevertheless, although neither the Sapporo criteria nor their update have found enough evidence to include demyelination syndromes among the potential clinical criteria for APS,³² data from animal models³³ as well as a few case reports^{29 30} suggest that this novel possibility should be considered.

The case is more complex for SLE. The mere inclusion of either seizures or psychosis in the long-standing ACR criteria was expanded in 1999 by an American College of Rheumatology (ACR) expert committee to include 19 potential neuropsychiatric (N-P) syndromes including diffuse CNS (eg, seizure, acute confusional state), focal CNS (eg, stroke) and peripheral nervous system syndromes (eg, polyneuropathy).³⁴ At the diagnosis of SLE, 28% of 572 patients in an international inception cohort study experienced a N-P event.³⁵ However, many were minor/non-specific (eg, headache) and only 19%–38% could

be attributed to SLE.³⁶ None had a demyelination syndrome.³⁵ A prospective analysis of N-P events in a larger cohort of over 1200 patients followed for 1.9 ± 1.2 years confirmed these findings and identified a frequency of 0.7%–1.2% for DSs.³⁷ A recent prospective 3-year study of 370 patients with SLE with no previous history of CNS involvement found that only 16 patients developed a major CNS event (4.3%). Two of them had NMOSD and were NMO-IgG-positive.³⁸ Thus, CNS demyelination syndrome is a rare but well-established lupus-associated neuropsychiatric event. It can be the presenting feature of SLE in 43% or develop in patients already diagnosed and consists either of an isolated demyelination syndrome (TM more prevalent than ON) or a combination of the two.³⁹

In our patient, the NMO/TM syndrome in combination with high-titre ANA (homogenous), anti-dsDNA, APL and anti-chromatin antibodies is highly suggestive of SLE.⁸ Anti-chromatin (antinucleosome) antibodies, a ubiquitous feature of murine SLE,⁴⁰ are directed against the native intranuclear histone-DNA complex and considered quite specific for SLE and a more sensitive marker than anti-dsDNA.^{30 41} In one study of 100 patients with SLE, positive levels were detected in 69% versus <10% of patients with other ATID and none of healthy controls.⁴² Moreover, patients with anti-chromatin AutoAb had a twofold higher prevalence of lupus nephropathy and their levels correlated with SLE disease activity scores.⁴² Among 36 patients with primary APS studied, only one (2.8%) had anti-chromatin AutoAb and this patient later developed features of SLE including ON.⁴³

We believe that our patient's NMOSD constituted the presenting symptom of central nervous system involvement in

Patient's perspective

It is unbelievable how 1 min you are healthy and the next, you find yourself in the hospital with endless tests and infusions. When I suddenly completely lost my vision in one eye and all treatments could not reverse it, I thought that was bad enough, but I could live with it. Then I gradually understood that this was just the tip of the iceberg. And that new damage can still develop in my nervous system or in my body. It is something which I try to forget.

Learning points

- Sudden visual loss may be due to autoimmune mechanisms by either ischaemic optic neuropathy due to vasculitis (such as giant cell arteritis) or an inflammatory demyelinating lesion (such as in multiple sclerosis or neuromyelitis optica (NMO)).
- The absence of intracerebral lesions on MRI, cerebrospinal fluid which is negative for oligoclonal bands, positive specific anti-aquaporin 4 antibodies (often other autoantibodies as well) and additional extensive active lesions of spinal demyelination on MRI (myelitis) strongly suggest NMO spectrum disorder (NMOSD).
- NMOSD can be the tip of the iceberg, heralding a diagnosis of frank systemic lupus erythematosus (SLE).
- Patients should be monitored for new symptoms, laboratory markers or new myelitis lesions on imaging, since NMOSD demyelinating syndromes constitute an organ-threatening CNS event (neuropsychiatric SLE) mandating appropriate immunosuppressive treatment.

SLE, with secondary antiphospholipid antibodies, a rare presentation. Accordingly, she may be regarded as having ‘organ-threatening’ disease—especially as dynamic TM lesions and rising AutoAb titres were demonstrated despite (low intensity) treatment. Several treatment options exist, including intravenous cyclophosphamide⁴⁴ but shared decision-making led to the choice of increasing azathioprine dose with temporary increase of oral steroid therapy⁴⁵ and the addition of hydroxychloroquine and an antiaggregant. Other long-term immunosuppressive treatment options exist (eg, rituximab) or are being developed,⁴⁶ but no evidence-based treatment recommendations exist due to the rarity of these patients.^{45 47}

In conclusion, a patient with isolated optic neuritis revealed clinically silent dynamic transverse myelitis and multiple AutoAbs including anti-chromatin antibodies and antiphospholipid antibodies strongly suggesting that her optic neuritis and later - NMOSD were the presenting CNS features of SLE.

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REFERENCES

- Singh AG, Kermani TA, Crowson CS, *et al.* Visual manifestations in giant cell arteritis: trend over 5 decades in a population-based cohort. *J Rheumatol* 2015;42:309–15.
- Wingerchuk DM, Lennon VA, Lucchinetti CF, *et al.* The spectrum of neuromyelitis optica. *Lancet Neurol* 2007;6:805–15.
- Popescu BF, Guo Y, Jentoft ME, *et al.* Diagnostic utility of aquaporin-4 in the analysis of active demyelinating lesions. *Neurology* 2015;84:148–58.
- Magro Checa C, Cohen D, Bollen EL, *et al.* Demyelinating disease in SLE: is it multiple sclerosis or lupus? *Best Pract Res Clin Rheumatol* 2013;27:405–24.
- Flanagan EP, Kaufmann TJ, Krecke KN, *et al.* Discriminating long myelitis of neuromyelitis optica from sarcoidosis. *Ann Neurol* 2016;79:437–47.
- Cai G, He D, Chu L, *et al.* Paraneoplastic neuromyelitis optica spectrum disorders: three new cases and a review of the literature. *Int J Neurosci* 2016;126:660–8.
- Pittock SJ, Lucchinetti CF. Neuromyelitis optica and the evolving spectrum of autoimmune aquaporin-4 channelopathies: a decade later. *Ann N Y Acad Sci* 2016;1366:20–39.
- Petri M, Orbai AM, Alarcón GS, *et al.* Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012;64:2677–86.
- Schattner A, Rager-Zisman B. Virus-induced autoimmunity. *Rev Infect Dis* 1990;12:204–22.
- Fujinami RS. Can virus infections trigger Autoimmune Disease? *J Autoimmun* 2001;16:229–34.
- Sellner J, Hemmer B, Mührlau M. The clinical spectrum and immunobiology of parainfectious neuromyelitis optica (Devic) syndromes. *J Autoimmun* 2010;34:371–9.
- Galbusera A, Tagliabue E, Frigo M, *et al.* Isolated bilateral anterior optic neuritis following chickenpox in an immunocompetent adult. *Neurol Sci* 2006;27:278–80.
- Han SB, Hwang JM, Kim JS, *et al.* Optic neuritis following Varicella zoster vaccination: report of two cases. *Vaccine* 2014;32:4881–4.
- Josephson C, Nuss R, Jacobson L, *et al.* The Varicella-autoantibody syndrome. *Pediatr Res* 2001;50:345–52.
- Cervera R, Asherson RA, Acevedo ML, *et al.* Antiphospholipid syndrome associated with infections: clinical and microbiological characteristics of 100 patients. *Ann Rheum Dis* 2004;63:1312–7.
- Schattner A. Consequence or coincidence? The occurrence, pathogenesis and significance of autoimmune manifestations after viral vaccines. *Vaccine* 2005;23:3876–86.
- Wingerchuk DM, Banwell B, Bennett JL, *et al.* International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015;85:177–89.
- Jiao Y, Fryer JP, Lennon VA, *et al.* Aquaporin 4 IgG serostatus and outcome in recurrent longitudinally extensive transverse myelitis. *JAMA Neurol* 2014;71:48–54.
- Pittock SJ, Weinshenker BG, Lucchinetti CF, *et al.* Neuromyelitis optica brain lesions localized at sites of high aquaporin 4 expression. *Arch Neurol* 2006;63:964–8.
- Jarius S, Aboul-Enein F, Waters P, *et al.* Antibody to aquaporin-4 in the long-term course of neuromyelitis optica. *Brain* 2008;131:3072–80.
- Lennon VA, Kryzer TJ, Pittock SJ, *et al.* IgG marker of optic-spinal multiple sclerosis binds to the aquaporin-4 water channel. *J Exp Med* 2005;202:473–7.
- Hokari M, Yokoseki A, Arakawa M, *et al.* Clinicopathological features in anterior visual pathway in neuromyelitis optica. *Ann Neurol* 2016;79:605–24.
- Jiao Y, Fryer JP, Lennon VA, *et al.* Updated estimate of AQP4-IgG serostatus and disability outcome in neuromyelitis optica. *Neurology* 2013;81:1197–204.
- Flanagan EP, Weinshenker BG, Krecke KN, *et al.* Short myelitis lesions in aquaporin-4-IgG-positive neuromyelitis optica spectrum disorders. *JAMA Neurol* 2015;72:81–7.
- Polgár A, Rózsa C, Müller V, *et al.* Devic’s syndrome and SLE: challenges in diagnosis and therapeutic possibilities based on two overlapping cases. *Autoimmun Rev* 2011;10:171–4.
- Pittock SJ, Lennon VA, de Seze J, *et al.* Neuromyelitis optica and non organ-specific autoimmunity. *Arch Neurol* 2008;65:78–83.
- Iyer A, Elson L, Appleton R, *et al.* A review of the current literature and a guide to the early diagnosis of autoimmune disorders associated with neuromyelitis optica. *Autoimmunity* 2014;47:154–61.
- Frigui M, Frikha F, Sellemi D, *et al.* Optic neuropathy as a presenting feature of systemic lupus erythematosus: two case reports and literature review. *Lupus* 2011;20:1214–8.
- D’Cruz DP, Mellor-Pita S, Joven B, *et al.* Transverse myelitis as the first manifestation of systemic lupus erythematosus or lupus-like disease: good functional outcome and relevance of antiphospholipid antibodies. *J Rheumatol* 2004;31:280–5.
- Marie I, Hervé F, Borg JY, *et al.* Retrobulbar optic neuritis revealing primary antiphospholipid antibody syndrome. *Scand J Rheumatol* 2007;36:156–7.
- Pengo V, Testa S, Martinelli I, *et al.* Incidence of a first thromboembolic event in carriers of isolated lupus anticoagulant. *Thromb Res* 2015;135:46–9.
- Miyakis S, Lockshin MD, Atsumi T, *et al.* International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006;4:295–306.
- Katzav A, Chapman J, Shoenfeld Y. CNS dysfunction in the antiphospholipid syndrome. *Lupus* 2003;12:903–7.
- The American college of rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum* 1999;42:599–608.
- Hanly JG, Urowitz MB, Sanchez-Guerrero J, *et al.* Neuropsychiatric events at the time of diagnosis of systemic lupus erythematosus. *Arthritis Rheum* 2007;56:265–73.
- Hanly JG. The neuropsychiatric SLE SLICC inception cohort study. *Lupus* 2008;17:1059–63.
- Hanly JG, Urowitz MB, Su L, *et al.* Prospective analysis of neuropsychiatric events in an international disease inception cohort of SLE patients. *Ann Rheum Dis* 2011;69:529–35.
- Kampylafka EI, Alexopoulos H, Kosmidis ML, *et al.* Incidence and prevalence of major central nervous system involvement in systemic lupus erythematosus: a 3-year prospective study of 370 patients. *PLoS One* 2013;8:e55843.
- Piga M, Chessa E, Peltz MT, *et al.* Demyelinating syndrome in SLE encompasses different subtypes: do we need new classification criteria? Pooled results from systematic literature review and monocentric cohort analysis. *Autoimmun Rev* 2017;16:244–52.
- Burlingame RW, Rubin RL, Balderas RS, *et al.* Genesis and evolution of antichromatin autoantibodies in murine lupus implicates T-dependent immunization with self antigen. *J Clin Invest* 1993;91:1687–96.
- Mehra S, Fritzel MJ. The spectrum of anti-chromatin/nucleosome autoantibodies: independent and interdependent biomarkers of disease. *J Immunol Res* 2014;2014:1–15.
- Cervera R, Vñas O, Ramos-Casals M, *et al.* Anti-chromatin antibodies in systemic lupus erythematosus: a useful marker for lupus nephropathy. *Ann Rheum Dis* 2003;62:431–4.
- de Souza AW, Keusseyan SP, da Silva NP, *et al.* Antinucleosome antibodies and primary antiphospholipid syndrome: an observational study. *Rev Bras Reumatol* 2012;52:357–65.
- Barile-Fabris L, Ariza-Andraca R, Olguin-Ortega L, *et al.* Controlled clinical trial of IV cyclophosphamide versus IV methylprednisolone in severe neurological manifestations in systemic lupus erythematosus. *Ann Rheum Dis* 2005;64:620–5.
- Trebst C, Jarius S, Berthele A, *et al.* Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). *J Neurol* 2014;261:1–16.
- Akashi T, Nakashima I. Efficiency of antibody therapy in demyelinating diseases. *Int Immunol* 2017;29:327–35.
- Kivity S, Agmon-Levin N, Zandman-Goddard G, *et al.* Neuropsychiatric lupus: a mosaic of clinical presentations. *BMC Med* 2015;13:43.

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