Recurrent acute ischaemic strokes as the primary presentation of Sjögren’s syndrome

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Abstract
Sjögren’s syndrome (SS) is a multi-systemic autoimmune disease. Central nervous system (CNS) involvement is rare. We report a case of large-vessel vasculitis and cerebral infarction as an initial presentation of SS. Neurological complications in SS is often due to peripheral neuropathy through small-vessel vasculitis. In rare cases, CNS involvement can occur, including acute ischaemic strokes (AIS), linked to both accelerated atherosclerosis and large-vessel vasculitis. Management of SS-related AIS remains complex due to the scarcity of evidence, although a role for immunomodulation and biologics remains promising. Clinicians should remain vigilant in identifying SS as a cause for stroke, especially in the young.

Keywords
Stroke, autoimmune, vasculitis, Sjögren’s syndrome, case report

Introduction
Sjögren’s syndrome (SS) is an autoimmune disease, often involving exocrine glands via lymphocytic infiltration, with possible multi-systemic sequelae. Extra-glandular complications occur in 70% of patients, often involving the joints, lung, skin and peripheral nervous system (PNS). Rarely, there can be central nervous system (CNS) involvement. We report a rare case of large-vessel vasculitis and subsequent cerebral infarction as the sole initial presentation of SS.

Case report
A 34-year-old woman was admitted following an episode of right-sided numbness and weakness affecting the face and upper arm lasting for four hours. Her vitals were stable on arrival, and clinical examination revealed no residual neurology and absent carotid bruits bilaterally. In view of symptom resolution, she was diagnosed as having a transient ischaemic attack following a normal computed tomography (CT) imaging of the brain. She was started on antiplatelets and admitted for inpatient observation.

Unfortunately, the following day, the patient suffered from further episodes of similar-natured right-sided weakness (Medical Research Council (MRC) 4/5), numbness and expressive aphasia. Repeat CT imaging was performed, revealing a new left-sided frontal lobe infarct, which was later confirmed on MRI (magnetic resonance imaging) and magnetic resonance angiography (MRA) of the brain (Figure 1). The MRA revealed M1 segment narrowing of the left middle cerebral artery (MCA), with beaded appearance, and small calibre anterior cerebral arteries (ACAs) bilaterally, with similar beaded appearance worst at A1 segments. Diagnostic cerebral angiography was subsequently performed, confirming the above earlier findings on MRI with no evidence of the ‘puff of smoke’ appearance to suggest Moya–Moya disease.

Further work-up for young stroke was performed (Table 1). The results showed possible evidence of vasculitis-related pathology, most likely SS. However, upon taking further history details, the patient denied any glandular and extra-glandular related symptoms prior to this presentation.

The patient was started on a three-day course of intravenous methylprednisolone, followed by oral prednisolone. Unfortunately, despite completing her course of methylprednisolone, the patient suffered from worsening clinical symptoms, including severe right-sided upper- and lower-limb numbness, weakness (MRC 0/5) and persistent expressive aphasia.

A repeat MRI of the brain revealed large areas of hyper-intensities, with sulci effacement and restricted diffusion (Figure 2) seen at the left-sided frontal, parietal, anterior temporal lobe, caudate nucleus and basal ganglia in keeping
with a new left MCA infarction. Following the severe neurological sequelae, the patient was started on fortnightly intravenous cyclophosphamide, of which she had six cycles, and is concurrently undergoing intensive inpatient rehabilitation whilst on high-dose prednisolone as maintenance therapy. Unfortunately, the patient declined a labial salivary gland biopsy, but Schirmer’s test was positive, allowing a diagnosis of primary SS to be made.

Discussion

The prevalence of neurological complications in SS ranges between 10% and 60%, and is often due to peripheral neuropathy through small-vessel vasculitis. Rarely, CNS involvement can occur, manifesting as psychiatric illnesses, cognitive deficits, meningoencephalitis, demyelinating disease and transverse myelitis amongst others. Even more uncommonly, acute ischaemic strokes (AIS), driven primarily by accelerated atherosclerosis and vasculitis, can develop.

There are studies proving subclinical atherosclerosis in cases of SS via measurement of carotid intimal media thickness, pulse wave velocity and aortic distensibility as surrogate markers. However, the role of atherosclerosis remains debatable. A nationwide Taiwanese study revealed no increased risk of atherosclerosis-related AIS amongst primary SS patients, which has since been similarly echoed by several other studies.

There are, however, a handful of case reports detailing the development of AIS felt to be primarily due to vasculitis. The overall prevalence of vasculitis in young stroke patients, based on a single-centre Korean study, was approximately 2%. Changes seen in the cerebral angiography performed led us to belief that a more prominent vasculitic pathophysiological process had taken place.

Unfortunately, management in case of vasculitis-related cerebral infarcts, including that of SS, are often difficult due to the scarcity of evidence and guidelines. There may be a role for immunomodulation, through corticosteroid, steroid-sparing agent (e.g. azathioprine and cyclophosphamide) and intravenous immunoglobulin therapy, although evidence at present is limited, even more so for CNS involvement, as it is much rarer. Outcomes from trials using biologic agents including rituximab remain debatable, and the general consensus seems to suggest their use should be limited to those with severe disease or complications.

Conclusion

CNS involvement in SS is a possible complication that remains difficult to manage, despite advances in therapy. To our knowledge, there has only been one similar case of SS presenting solely with AIS due to large-vessel vasculitis reported in the

Table 1. Blood and cerebrospinal fluid investigations performed.

| Test                          | Result | Test                          | Result |
|-------------------------------|--------|-------------------------------|--------|
| Haemoglobin (g/L)             | 107    | Erythrocyte sedimentation rate (mm/h) | 43     |
| Mean corpuscular volume (fl)  | 77     | C-reactive protein (mg/L)     | 3.13   |
| White cell count (10⁹/L)      | 12.1   | Complements C3 (mg/dL)        | 116    |
| Platelets (10⁹/L)             | 408    | Complements C4 (mg/dL)        | 21     |
| Rheumatoid factor (IU/mL) (0–20) | 8      | Lupus anticoagulant           | Negative |
| ANF titre                     | Positive 1:640 | Hepatitis B serology          | Negative |
| ANF pattern                   | Speckled SS-A/Ro pattern seen | Hepatitis C serology          | Negative |
| Ro52                          | Strongly positive 1:2560 | Cardiolipin antibody          | Negative |
| SS-A                          | Positive 1:1280 | Protein C activity            | Negative |
| SS-B                          | Negative | Protein S activity            | Negative |
| RNP                           | Negative | Factor V activity             | Negative |
| Sm                            | Negative | Cerebrospinal fluid           |        |
| Sci-70                        | Negative | Protein (g/L) (0.18–0.40)     | 0.43   |
| Jo-1                          | Negative | Glucose (mmol/L) (2.5–3.5)    | 2.9    |
| Serum immunoglobulin A (g/L) (0.8–3.0) | 1.4     | Leucocyte (per μL) (0–3)     | 2      |
| Serum immunoglobulin G (g/L) (6.0–16.0) | 9.2     | Erythrocyte (per μL) (0–10)  | 0      |
| Serum immunoglobulin M (g/L) (0.4–2.5) | 2.0     | Appearance                    | Clear  |
literature. Although rare, clinicians should remain vigilant in identifying SS as a cause for stroke, especially in the young.

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Authors’ contributions

R.E.F. R.S. was responsible for the data collection and analysis and for drafting the manuscript. S.K. was responsible for the drafting and revision of the manuscript.

Availability of data and materials

The data that support the findings of this study are available from UiTM Sungai Buloh, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of UiTM Sungai Buloh.

Ethical approval

Ethical approval to report this case was obtained from the Universiti Teknologi MARA (UiTM) Ethics Committee (approval ID UiTM 01/2020).

Informed consent

Written informed consent was obtained from the patient for their anonymised information to be published in this article.

Declaration of conflicting interests

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