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# Cerebral infarct mimicking glioma in Sjogren's syndrome

## 在舍格倫綜合症中酷似神經膠質瘤的腦梗塞

A 50-year-old Chinese woman with a chronic 20-year history of ataxic gait associated with dry eyes and mouth, was admitted to hospital after a single episode of syncope. Magnetic resonance imaging scans showed a large left frontal hypodense lesion suggestive of a glioma. Craniotomy was performed and the lesion excised, with histology showing only infarcted tissue and no malignant cells. Further diagnostic evaluation revealed that the patient had primary Sjogren's syndrome, with demyelinating polyneuropathy. In the absence of risk factors for stroke, it was considered likely that the cerebral infarct was secondary to autoimmune-related vasculitis. Functional neuroimaging, such as magnetic resonance spectroscopy, should be considered in evaluating doubtful or unusual brain lesions in patients with autoimmune disease.

一名 50 歲華裔婦女在暈厥後入院，她有 20 年慢性步態共濟失調及眼嘴乾燥的病史。磁共振成像掃描顯示左前沿有大片低密度損傷，顯示有神經膠質瘤存在。受損部分在顱骨切開術中被切除，組織學檢查顯示只有梗塞組織，沒有惡性細胞。進一步的診斷評估顯示，患者患有初級舍格倫綜合症以及脫髓鞘多神經病。由於沒有中風的危險因素，腦梗塞很可能是與自體免疫有關的脈管炎繼發的。在評估自體免疫病患者的可疑或不尋常腦損傷時，應該考慮進行功能性神經成像，如磁共振光譜儀成像的檢查。

### Introduction

Sjogren's syndrome is a chronic, multisystem immunological disorder of unknown pathophysiology, characterised by destructive mononuclear infiltration of the lacrimal and salivary glands, and similar visceral organ involvement which gives rise to a wide variety of symptoms and signs. Although both the peripheral nervous system (PNS) and the central nervous system (CNS) may be involved with a reported prevalence of up to 30%, CNS involvement alone occurs less frequently.<sup>1-3</sup> Higher prevalence figures for Sjogren's syndrome in Asian patients highlight the possibility of different immunological mechanisms in different ethnic groups.<sup>3-6</sup>

We report the unusual case of a patient with primary Sjogren's syndrome, whose initial presentation was of a suspected frontal lobe tumour. The clinical features, radiological images, operative, and histological features are described, followed by a review of the reported neurological manifestations of Sjogren's syndrome and a discussion on the usefulness of magnetic resonance spectroscopy (MRS) in distinguishing neoplastic from non-neoplastic lesions in the brain.

### Case report

A 50-year-old Chinese woman was admitted to hospital after a single witnessed episode of syncope lasting 5 minutes, consistent with a convulsion. She had no history of hypertension, hypercholesterolaemia, or diabetes mellitus, and no other medical history of note. She was a non-smoker and non-drinker. The patient did, however, state that she had a 20-year history of unsteady gait, dry eyes and mouth, as well as a recent right corneal ulcer. In addition, she described a Raynaud's-type phenomena affecting both upper and lower limbs.

#### Key words:

Cerebral infarction;  
Glioma;  
Magnetic resonance spectroscopy;  
Sjogren's syndrome

#### 關鍵詞：

腦梗塞；  
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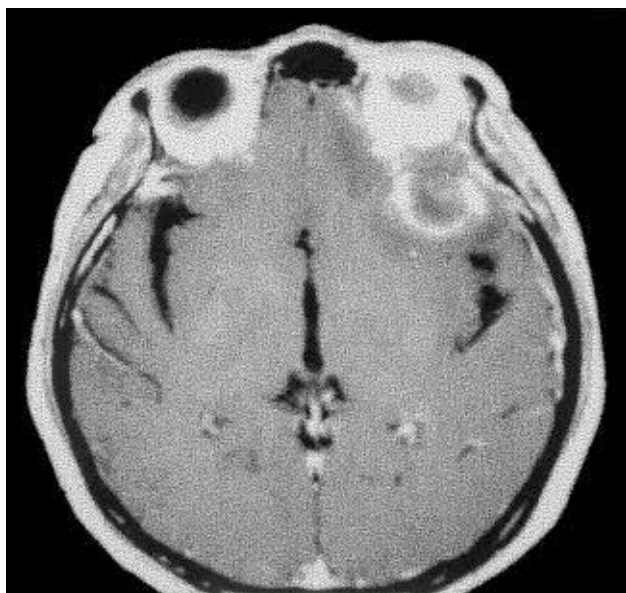
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**Fig.** Axial T1-weighted, contrast-enhanced magnetic resonance imaging scan of the brain showing the left frontal lesion, which has a heterogeneous appearance

On physical examination the patient was found to have an ataxic gait with loss of proprioception, vibration, and pain sensation in the lower limbs, as well as generalised areflexia. Muscle tone and motor strength were normal, with minimal muscle wasting. Plantar reflexes were down-going bilaterally. There was no facial rash, cutaneous vasculitis, livedo reticularis, telangiectasia, arthritis, subcutaneous nodules, sclerodactyly, calcinosis, mouth ulcers, or proximal myopathy to suggest the presence of an underlying connective tissue disorder. In addition, cardiovascular examination was normal with a regular heart rate and no cardiac murmurs evident.

Magnetic resonance imaging (MRI) scans of the brain revealed a large irregular lesion in the left frontal lobe. It measured 4x2x2 cm and was heterogenous in appearance, with patchy contrast enhancement and surrounding oedema (Fig). The lesion demonstrated high T1-signal intensity and low signal intensity on T2-weighted sequences, with mild mass effect. Magnetic resonance angiography of the Circle of Willis showed normal vessel calibre with no stenosis or vessel irregularity. Electroencephalography (EEG) was normal.

Since the MRI pictures were suggestive of a frontal lobe glioma, the patient underwent craniotomy and gross total resection of the lesion. Histological examination revealed only infarcted tissue and very occasional macrophages, with no malignant cells. Postoperative recovery was uneventful.

Subsequent investigations revealed a mild normochromic, normocytic anaemia with normal platelet and white blood cell counts. There were positive antinuclear antibodies of 1/800 of the speckled and nucleolar type, a rheumatoid factor of 175, an anti-Ro of 80 units/mL, and an anti-La of 35 units/mL. Schirmer's test was positive (<5 mm

**Table.** Classification criteria for Sjogren's syndrome<sup>7</sup>

|     |   |
|-----|---|
| I   | Ocular symptoms (dry eyes)  |
| II  | Oral symptoms (dry mouth)   |
| III | Evidence of keratoconjunctivitis sicca (positive Schirmer's test) |
| IV  | Presence of autoantibodies (anti-Ro and anti-La)                  |
| V   | Focal sialoadenitis by minor salivary gland biopsy                |
| VI  | Instrumental evidence of salivary gland involvement               |

in 5 minutes). Antidouble stranded DNA testing, complement level, coagulation profile, and urine microscopy were normal, however. The presence of four of the six criteria for primary Sjogren's syndrome (Table<sup>7</sup>) in this patient confirmed the diagnosis. In addition, electromyography and nerve conduction studies revealed absent sensory nerve action potential in the lower limbs and absent potentials of both median and tibial nerves. These findings indicated severe sensory and motor demyelinating polyneuropathy of the lower limbs and the presence of abnormal somato-sensory conduction.

Further investigations into the possible cause of the infarct were performed, including prothrombotic screening for protein C and S, antithrombin III, Leiden Factor V, homocysteine and cryoglobulin levels, anticardiolipin antibodies and lupus anticoagulant, two-dimensional echocardiography, and ultrasound of both carotid arteries, all of which were normal. In view of the underlying autoimmune disorder and the absence of risk factors for stroke, it seemed likely that the aetiology of the cerebral infarct in this patient was autoimmune-related vasculitis.<sup>8,9</sup> The patient was therefore commenced on aspirin 300 mg daily, and prednisolone 30 mg daily on a gradually reducing dose. On review 18 months after the event, she remained well with no recurrence of neurological symptoms.

## Discussion

The neurological manifestations of Sjogren's syndrome embrace a wide spectrum of clinical features involving both the PNS and CNS. Peripheral nervous system involvement is characterised by predominantly sensory or occasionally mixed neuropathies, carpal tunnel syndrome, and mononeuritis multiplex.<sup>3</sup> Although CNS involvement occurs less frequently, both neurological and vascular manifestations have been described. These include cortical atrophy, stroke, aseptic meningitis, trigeminal neuropathy, isolated third nerve palsy, multiple sclerosis-like lesions, migraine and neuropsychiatric disease, vasculitis, and multiple cerebral artery occlusions.<sup>2,3,8-10</sup>

This case is interesting from several aspects. Firstly, the patient had a long-standing demyelinating polyneuropathy, which was predominantly sensory, affecting the lower limbs more than the upper limbs. This preceded the diagnosis of Sjogren's syndrome by 20 years. While some reports suggest that the aetiology of pure sensory neuropathy may be direct lymphocytic infiltration of the dorsal root ganglia, the exact aetiology of demyelination remains unknown. A

systemic ischaemic process, such as vasculitis, could account for the presence of both PNS and CNS involvement as seen in this patient, however.<sup>1,11</sup>

Secondly, the patient presented with a syncopal episode suggesting a convulsion, but EEG detected no abnormalities. While the MRI findings were suggestive of a glioma, other differential diagnoses considered included lymphoma, metastatic tumour, and amelanotic melanoma. Acute infarctions have been described as appearing hypointense on T2-weighted MRI,<sup>12</sup> but are more commonly hyperintense on MRI studies.<sup>12</sup> Subacute infarctions can be associated with a further increase in T2-weighted sequence intensity, and in 20% of cases, regions of increased T1-weighted sequence intensity may occur when there is a haemorrhagic component.<sup>12</sup> Histological findings after surgical resection of the lesion revealed only infarcted tissue with no malignant glioma cells and only very occasional macrophages. These features were suggestive rather than confirmatory of an inflammatory process. Vasculitis was not demonstrated in the histologic specimen. It has been postulated, however, that the possible mechanism of stroke in patients with Sjogren's syndrome is mononuclear cell-dependent ischaemic damage caused by infiltration of vessel walls. In addition, the presence of extractable nuclear antigen (Ro/La) in these patients has been associated with vasculitis.<sup>2,9,10,13</sup> In this setting therefore, it appears reasonable to hypothesise in this case that the underlying aetiology is autoimmune-related vasculitis.

The final issue for consideration is the role of MRI findings which may be suggestive but not pathognomic of tumour or infarction. In doubtful cases, we suggest that additional information be obtained from functional studies, such as MRS or positron emission tomography (PET). Magnetic resonance spectroscopy analyses the metabolic activity of specifically targeted areas of the brain. Thus, it can distinguish infarct from tumour, in that during an acute cerebral ischaemic event metabolic acidosis causes significant increases in inorganic phosphate and lactate levels but a reduction in choline-containing compounds such as N-acetyl aspartate due to neuronal loss. This is in contrast with brain tumour, which is generally associated with lower lactate and higher choline peaks.<sup>13</sup> Positron emission tomography studies also allow quantitative assessment of the biochemistry of specified areas of the brain, as well as the state of perfusion or hypoxia.<sup>14</sup> The advantages of MRS over PET studies, however, are that costs are lower, multiparametric data are obtained, tracers are not required, and it can be performed at the same time as other MRI

studies. In this patient, such functional studies could have contributed to the differential diagnosis of infarct as opposed to tumour, and precluded unnecessary surgery.

## Conclusion

Autoimmune disease can present with a myriad of clinical features. Consequently, we would recommend that patients such as this case presenting with an intracranial lesion are carefully evaluated with a combination of imaging modalities, including MRI and functional studies as appropriate. This may avoid unnecessary craniotomy and the accompanying risks of open surgery.

## References

1. Font J, Valls J, Cervera R, Pou A, Ingelmo M, Graus F. Pure sensory neuropathy in patients with primary Sjogren's syndrome: clinical, immunological, and electromyographic findings. *Ann Rheum Dis* 1990; 49:775-8.
2. Bragoni M, Di Piero V, Priori R, Valesini G, Lenzi GL. Sjogren's syndrome presenting as ischemic stroke. *Stroke* 1994;25:2276-9.
3. Andonopoulos AP, Lagos G, Drosos AA, Moutsopoulos HM. The spectrum of neurological involvement in Sjogren's syndrome. *Br J Rheumatol* 1990;29:21-3.
4. Tajima Y, Mito Y, Owada Y, Tsukishima E, Moriwaka F, Tashiro K. Neurological manifestations of primary Sjogren's syndrome in Japanese patients. *Intern Med* 1997;36:690-3.
5. Govoni M, Bajocchi G, Rizzo N, et al. Neurological involvement in primary Sjogren's syndrome: clinical and instrumental evaluation in a cohort of Italian patients. *Clin Rheumatol* 1999;18:299-303.
6. Niemela RK, Hakala M. Primary Sjogren's syndrome with severe central nervous system disease. *Semin Arthritis Rheum* 1999;29: 4-13.
7. Vitali C, Bombardieri S, Moutsopoulos HM, et al. Assessment of the European classification criteria for Sjogren's syndrome in a series of clinically defined cases: results of a prospective multicentre study. The European Study Group on Diagnostic Criteria for Sjogren's Syndrome. *Ann Rheum Dis* 1996;55:116-21.
8. Pou Serradell A, Vinas Gaya J. 3 cases of rare peripheral neuropathies associated with primary Gougerot-Sjogren syndrome [in French]. *Rev Neurol (Paris)* 1993;149:481-4.
9. Mauch E, Volk C, Kratzsch G, et al. Neurological and neuropsychiatric dysfunction in primary Sjogren's syndrome. *Acta Neurol Scand* 1994;89:31-5.
10. Nagahiro S, Mantani A, Yamada K, Ushio Y. Multiple cerebral arterial occlusions in a young patient with Sjogren's syndrome: case report. *Neurosurgery* 1996;38:592-5.
11. Binder A, Snaith ML, Isenberg D. Sjogren's syndrome: a study of its neurological complications. *Br J Rheumatol* 1988;27:275-80.
12. Mathews VP, Whitlow WD, Bryan RN. Cerebral ischaemia and infarction. In: Atlas SW. *Magnetic resonance imaging of the brain and spine*. 2nd ed. Philadelphia: Lippincott-Raven; 1996:559-62.
13. Lee PL, Gonzalez RG. Magnetic resonance spectroscopy of brain tumors. *Curr Opin Oncol* 2000;12:199-204.
14. Roelcke U, Leenders KL. PET in neuro-oncology. *J Cancer Res Clin Oncol* 2001;127:2-8.