Systemic lupus erythematosus presenting with brainstem lesions

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INTRODUCTION

Systemic lupus erythematosus (SLE) is a multiorgan autoimmune disease. Owing to its varied presentation, it can be difficult to diagnose. This article reports two cases in which young women with features of brainstem dysfunction were diagnosed as having gliomas and treated accordingly, suffering severe side effects of treatment. In both cases, the subsequent course of events suggested that SLE, rather than glioma, was responsible for the original presentation.

CASE REPORT 1

In 1981, a 25-year-old woman developed Raynaud's phenomenon with positive antinuclear antibodies. She was otherwise healthy, and no further investigations were performed, nor was treatment given for Raynaud's phenomenon.

Onset of brainstem features

In 1985, she developed vomiting and nystagmus. Initial investigations did not reveal a cause. A computed tomography (CT) scan of her brain was normal. However, magnetic resonance imaging (MRI) scanning showed an abnormal signal in her brainstem without swelling.

Diagnosis of glioma made, radiotherapy given

A stereotactic biopsy was unsuccessful in obtaining a sample for histology. A presumptive diagnosis of glioma was made, and radiotherapy (total of 50 Gy in 25 fractions) with dexamethasone was given. The patient improved, although nystagmus and poor palatal movement with deviation to the right side persisted. Wasting of the right side of her tongue was also noted. Nasogastric feeding was commenced because of poor swallowing and continued for 1 month.

Diagnosis of systemic lupus erythematosus

In 1987, she presented with alopecia, joint stiffness (without pain) and a photosensitive rash on her back. Poor memory, impaired balance, diplopia and dysphagia were documented. Levels of anti-double-stranded DNA antibodies were raised. A diagnosis of systemic lupus erythematosus (SLE) with central nervous system (CNS) involvement was made.

Immunosuppression was commenced, initially with prednisolone and subsequently with varying regimens, including azathioprine and cyclophosphamide.

Progress

In 1989, the patient had a grand mal seizure, attributed to SLE. She continued to have flares of SLE, manifesting as urticarial vasculitis, arthritis and trigeminal neuralgia. In 1993, she described further weakness, unsteadiness and nasal speech. A neurology opinion was that she had progressive brainstem atrophy; a repeat MRI scan confirmed this.

A year later, she developed pulmonary fibrosis. Subsequently, velopharyngeal insufficiency, resulting from worsening brainstem atrophy, necessitated a palatal lift procedure. MRI scanning in 1996 showed post-radiation changes in the medulla oblongata, with high signal lesions in the cerebral white matter possibly as a result of small vessel disease in SLE. There was no swelling or mass effect. Brainstem atrophy was noted. MRI scans over the next 3 years showed persistent brainstem atrophy with no other significant changes.

In 1998, she developed sensorineural deafness, a result of either SLE or post-radiation sequelae. Dysphagia with regurgitation worsened. In 2000, a percutaneous gastrostomy (PEG) feeding tube was inserted.

Current state

Currently, the patient depends on PEG feeding for her nutrition. She needs help with daily activities and awaits an electric wheelchair. There is no possibility of returning to her previous occupation as a cabaret singer.

DISCUSSION

Causes of diplopia, nystagmus and vomiting in a young woman include labyrinthitis, demyelination, stroke, tumour and vasculitis. One cause of brainstem vasculitis is SLE. Useful discriminating details include previous medical history, speed of onset, associated features and relative incidence of each disease.

Gliomas: epidemiology, features, treatment and prognosis

Gliomas have an age-adjusted incidence rate of 3–7 per 100 000 (Brada and Thomas, 1995). Brainstem involvement is characteristically the result of astrocytoma, glioblastoma or ependymoma. Common initial manifestations are of unilateral abducens and facial nerve palsies (Levin et al, 1993). Long-tract signs (hemiplegia, gait and limb ataxia, paraplegia, gaze disorders and hemisensory loss) may follow. Less commonly, long-tract signs precede cranial nerve features.

MRI findings include swelling or abnormal signal without swelling. Histological confirmation is not considered mandatory for diagnosis. Treatment options are surgical resection, radiotherapy and chemotherapy. Prognosis of histologically proven gliomas is poor, with prolonged survival of less than 20% (Grigsby et al, 1989). Non-resectable brainstem tumours have a median survival of less than 1 year and a 2-year survival of 10–20% (Vecht, 1999).

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SLE: epidemiology, features, treatment and prognosis

SLE has an incidence of 4–8 per 100 000, with a prevalence up to 65 per 100 000 (Snaith and Isenberg, 1996). Of cases, 90% present in women of child-bearing age (Hahn, 2001). It is most common in Afro-Caribbean, Chinese, Asian and South American Indian groups (Snaith and Isenberg, 1996). It can affect multiple organs, including the skin, kidneys, cardiovascular system, bone marrow, gastrointestinal system and CNS.

Up to half of SLE patients have neurological features, usually caused by a small vessel vasculitis (Harrison, 1996). There may be depression, malaise, fits, psychosis, hemiplegia or cranial nerve palsies. Less than 5% of patients will develop cranial nerve lesions during the course of their disease. Diagnosis depends on clinical features (American College of Rheumatology criteria; *Table 1*) and autoantibodies (including antinuclear antibodies (ANA), antidouble-stranded DNA antibodies, anti-Sm and

CASE REPORT 2

In 1987, a previously healthy 29-year-old woman returned from a holiday in Nigeria with headache and dizziness. She was 12 weeks pregnant.

Onset of brainstem features

Soon afterwards, she described 1 year's worsening diplopia, dysarthria and falling to her left side. In clinic, she exhibited a right lateral rectus palsy, left upper motor neurone facial nerve palsy and poor coordination on the left side. Computed tomography (CT) and magnetic resonance imaging (MRI) showed an extremely bulky swelling of the medulla and right dorsolateral pons encroaching on the fourth ventricle. No blood tests were documented.

Diagnosis of glioma made, radio- and chemotherapy given

A stereotactic biopsy was carried out, but there were no conclusive histological features. A presumptive diagnosis of glioma was made on the basis of the clinical findings and imaging. After the biopsy, the patient's incoordination worsened with a new left-sided oculomotor cranial nerve palsy. After an induced abortion, radiotherapy, at a curative dose of 50 Gy, was given. High-dose corticosteroids were also administered. These were well tolerated, and the patient's diplopia and incoordination improved greatly. She continued on dexamethasone at an initial dose of 2 mg three times a day, which was gradually reduced. She became cushingoid.

Progress

Two months later, a repeat CT scan with contrast showed low attenuation in the pons, a dilated fourth ventricle, slight dilatation of the lateral ventricles, but no swelling. These features were consistent with post-radiation changes.

The patient continued to take low-dose oral steroids, but in 1993 the prescription was changed from dexamethasone to hydrocortisone. She again developed dysarthria and dysphasia. MRI showed recurrence of brainstem swelling (*Figures 1* and *2*). She was believed to have a recurrence of her glioma. Further radiotherapy was considered inadvisable, and palliative chemotherapy (10 courses of procarbazine, lomustine and vincristine, with dexamethasone and metoclopramide as antiemetics) was administered. The patient developed ovarian failure, and hormone replacement therapy was commenced. Despite chemotherapy, her dysarthria and dysphasia persisted. She continued to take a maintenance dose of dexamethasone 1 mg per day.

In 1998, the patient presented with 3 months' dyspnoea, pleuritic chest pain, arthralgia, myalgia, alopecia and a dry mouth. A chest X-ray showed a left-sided pleural effusion. A ventilation perfusion scan was not suggestive of pulmonary embolism. Erythrocyte sedimentation rate was raised. Anti-nuclear antibodies (ANA) were positive (1:640, diffuse), antibodies to double-stranded DNA (dsDNA) were slightly raised (1:20) and there was a slight normochromic normocytic anaemia. All other autoantibodies were negative.

Diagnosis of systemic lupus erythematosus

Systemic lupus erythematosus was diagnosed on the basis of the clinical picture of symptoms in the scalp, chest, joints and muscles with typical autoantibody profile. There was no evidence of involvement of the kidneys, and an increase in oral steroids was not required. Her chest pain settled, and the effusion did not recur.

Current state

Currently, the patient continues to have dysarthria, nystagmus, titubation and truncal ataxia. She also has poor balance with falls, fracturing an ankle in 1998. Osteoporosis, presumably secondary to long-term use of oral corticosteroids, was confirmed on dual energy X-ray absorptiometry scanning in 1999, and she has sustained a thoracic vertebral crush fracture.

She was reviewed by the neurologists in 1999. The persistent neurological dysfunction was felt to be the result of chronic brainstem damage, with no evidence of active CNS lupus and no likelihood of improvement. She is now wheelchair-bound and has difficulty mobilizing as a result of obesity, ataxia and previous fractures. She requires a great deal of help from her carers.

Figure 1. Cross-sectional magnetic resonance image showing abnormally high signal in the medulla.

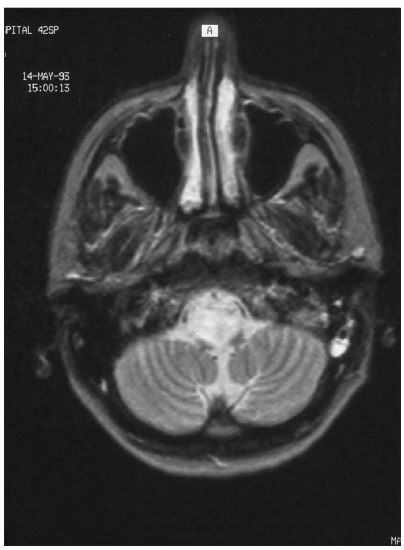
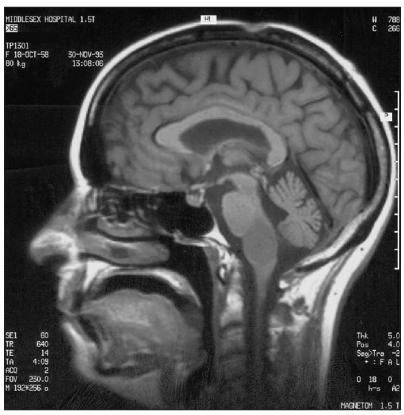


Figure 2. Sagittal magnetic resonance image showing swelling in the medulla.



antiphospholipid). Treatment consists primarily of corticosteroids and other immunosuppressants (Snaith and Isenberg, 1996). Despite improved mortality, it remains a serious and sometimes fatal disease that can be difficult to diagnose.

Review of literature

The authors have found no previous reports of undiagnosed SLE presenting with brainstem features and corresponding swelling on MRI. There are two documented cases of vertebrobasilar artery infarction (without swelling of the brainstem) as the initial manifestation of SLE (Kwon et al, 1999). Cerebellar and brainstem signs in patients already known to have SLE are documented (Smith et al, 1994; Vaille and Davis, 1998; Yaginuma et al, 1999). One case featured bilateral internuclear ophthalmoplegia, more commonly found in multiple sclerosis (Cogan et al, 1987).

In retrospect

This article has reported two cases in which young, healthy women presented with brainstem features which were presumed to be gliomas despite lack of histological confirmation. In each case, treatment of these lesions with radiotherapy and/or chemotherapy has led to severe and disabling side effects which are irreversible. Despite this, both patients are alive 15 years after their initial presentation. Such survival times are unlikely to be consistent with a diagnosis of glioma. This suggests that the original brainstem dysfunction in both cases was not caused by glioma. An alternative cause must be postulated.

In case 1, it seems highly likely that SLE caused the initial brainstem presentation. The patient had previously been known to have positive ANA and subsequently developed SLE with confirmed neurological involvement. Consideration of the diagnosis of SLE at the time of the original presentation might have prevented the need for brainstem biopsy and radiotherapy.

In case 2, SLE was not diagnosed until 11 years after the initial presentation, and it is harder to be sure that this disease caused the original brainstem impairment. Brainstem vasculitis secondary to SLE, although rare, would account for the presenting features. This would have responded to the dexamethasone given with radiotherapy. The symptoms recurred after changing to low-dose hydrocortisone – inadequate immunosuppression could have caused a flare of SLE. The chemotherapy she received for this recurrence also included dexamethasone (albeit meant as an antiemetic), which could have contributed to the subsequent partial remission.

TABLE 1.
American College of Rheumatology criteria for classification of systemic lupus erythematosus

Malar rash
Discoid rash
Photosensitivity
Oral ulcers
Arthritis
Serositis
Renal disease
Neurological disease
Haematological disease
Immunological disease
Antinuclear antibodies

From Tan et al (1982). Four of these eleven features occurring at the same time are needed for diagnosis, although patients with less than four criteria may still have lupus (Snaith and Isenberg, 1996)

CONCLUSIONS

These two cases highlight the importance of excluding SLE in young women presenting with brainstem or other CNS lesions. A screening test for ANA should be carried out – this is positive in 95% of patients with SLE. If the ANA test is positive, levels of anti-dsDNA should be measured. High anti-dsDNA levels are very specific for SLE and tend to vary with disease activity. Failure to diagnose SLE in such cases could result in unnecessary and tragic treatment sequelae. HM

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