

Central Nervous System Sjögren's Syndrome in a Child: Case Report and Review of the Literature

ABSTRACT

We describe a case of pediatric Sjögren's syndrome with progressive neurologic involvement. At age 4 years, she had been diagnosed with Melkersson-Rosenthal syndrome. After being stable with facial diplegia and swelling for 5 years, she acutely presented with diplopia, vertigo, and ataxia. Cranial magnetic resonance imaging (MRI) showed a left dorsal midbrain lesion. Serologic and histopathologic findings confirmed primary Sjögren's syndrome. She responded well to intravenous methylprednisolone, with subsequent clinical improvement and MRI resolution. This report reviews the pediatric literature and underscores the importance of considering Sjögren's syndrome in a child with unexplained facial weakness and in the differential diagnosis of pediatric stroke. (*J Child Neurol* 2001;16:683–685).

Sjögren's syndrome is an autoimmune exocrinopathy marked by progressive lymphocytic infiltration of the lacrimal and salivary glands. Its hallmark symptoms are keratoconjunctivitis sicca and xerostomia. Typically a disease of adults,^{1,2} Sjögren's syndrome occasionally occurs in children,³ but central nervous system complications are distinctly unusual. In this study, we present a case of primary Sjögren's syndrome in a 9-year-old girl with a biphasic course, who at age 4 years had been initially diagnosed with Melkersson-Rosenthal syndrome. We emphasize that the onset of Sjögren's syndrome in children can be insidious, and correct diagnosis is critical when acute central nervous system symptoms present.

Case Report

A healthy 4-year-old girl developed left orofacial swelling, fever, conjunctivitis, and cervical lymphadenopathy. Laboratory studies were notable only for mild anemia and an antinuclear antibody (ANA) titer of 1:2560. Cultures and human immunodeficiency virus serology were negative. Antibiotics were ineffective. Within 6 months, bilateral facial swelling and dense facial diplegia had become fixed. Craniocervical computed tomography (CT)

demonstrated enlarged submandibular nodes and parotid glands. Serial lip biopsies revealed nonspecific inflammation without evidence of tumor. Lumbar puncture and two bone marrow biopsies were normal. In the absence of other findings, she was presumptively diagnosed with Melkersson-Rosenthal syndrome, an idiopathic disorder defined by the triad of orofacial swelling, peripheral facial palsy, and lingua plicata.^{4,5}

At age 9 years, she presented to our institution complaining of 5 days of bifrontal headache, dizziness, vertical diplopia, and "walking sideways." Drooping of the eyelids, left greater than right, then occurred. Medical review was notable for dry eyes, vaginal dryness and irritation, and multiple caries despite regular dental care. Her family history was notable for a paternal grandmother with "lupus and rash," although she denied photosensitivity, Raynaud's phenomenon, skin lesions, arthralgia, or hair loss. She was admitted for evaluation and appeared well nourished and alert, with normal vital signs. She had bilateral conjunctival injection and ptosis, left greater than right. There was lip and cheek swelling, right parotid gland enlargement, and dry eyes and mouth. No rash, arthritis, or alopecia was present. Her mental status was normal and language was intact, apart from mild dysarthria. Fundoscopic and pupillary examinations were normal. She had transient limitation of adduction and depression of the left eye, consistent with a partial left oculomotor palsy, but then developed a new right superior oblique palsy. Chronic facial diplegia, more prominent in the lower face, was unchanged. Testing of remaining cranial nerves, motor examination, muscle stretch reflexes, and extremity sensation were normal. Her stance was wide based and the gait ataxic with swaying to the left.

The following studies were normal or negative: routine chemistries, complete blood count, urine analysis, chest radiography, angiotensin converting enzyme level, erythrocyte sedimentation rate, rapid plasma reagin test, serum complement levels, Lyme titers, purified protein derivative test for tuberculosis, gallium scan, unenhanced cranial CT, cerebrospinal fluid chemistries, cell count, oligoclonal bands, and cultures for bacterial, viral, and fungal pathogens. ANA titer was elevated at 1:1280, and the anti-Ro/Sjögren's syndrome A antibody was positive at 607 (0-149). Anti-La/Sjögren's syndrome B antibody, rheumatoid factor; anti-double-stranded DNA, anti-Smith, and antiribonucleoprotein antibodies were negative. A hypercoagulable panel was normal, including anticardiolipin antibody, protein C, protein S, factor V Leiden, and antithrombin III.

Magnetic resonance imaging (MRI) of the brain (Figure 1) performed on day 2 of admission revealed a 1-cm rim-enhancing lesion in the dorsal left midbrain in the area of the oculomotor and trochlear nuclei and extending into the superior cerebellar peduncle, which correlated well with the clinical findings. A smaller, less distinct abnormality was seen in the left posterior periventricular white matter (not illustrated). Neither lesion showed evidence for acute ischemia or infarction on diffusion-weighted imaging and was instead consistent with vasogenic edema. Magnetic resonance angiography was normal.

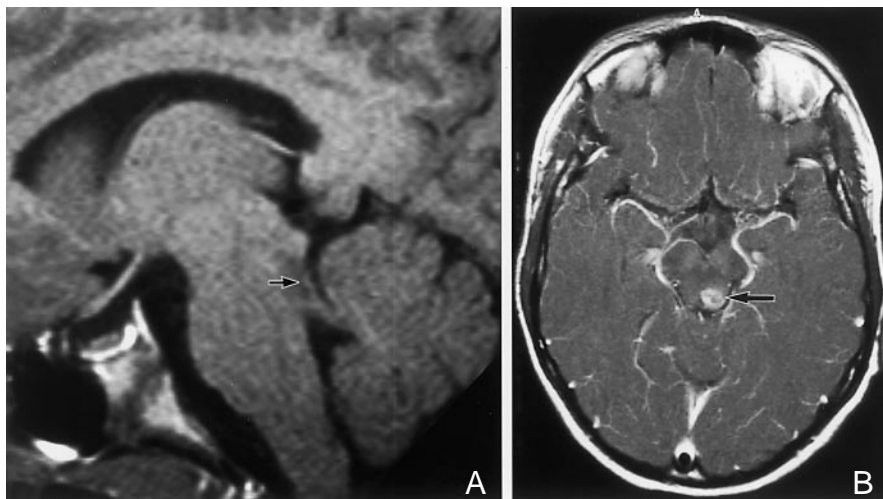


Figure 1. Cranial MRI scan (Siemens Vision, Erlangen, Germany) on hospital week 2. A, Midsagittal T₁-weighted image (TR: 650 msec; TE: 14 msec) reveals an area of low signal intensity in the dorsal midbrain with extension into the left superior cerebellar peduncle (arrow). B, Postgadolinium axial T₁-weighted image (TR: 820 msec; TE: 20 msec) demonstrates focal enhancement in the left dorsal midbrain (arrow) without significant mass effect.

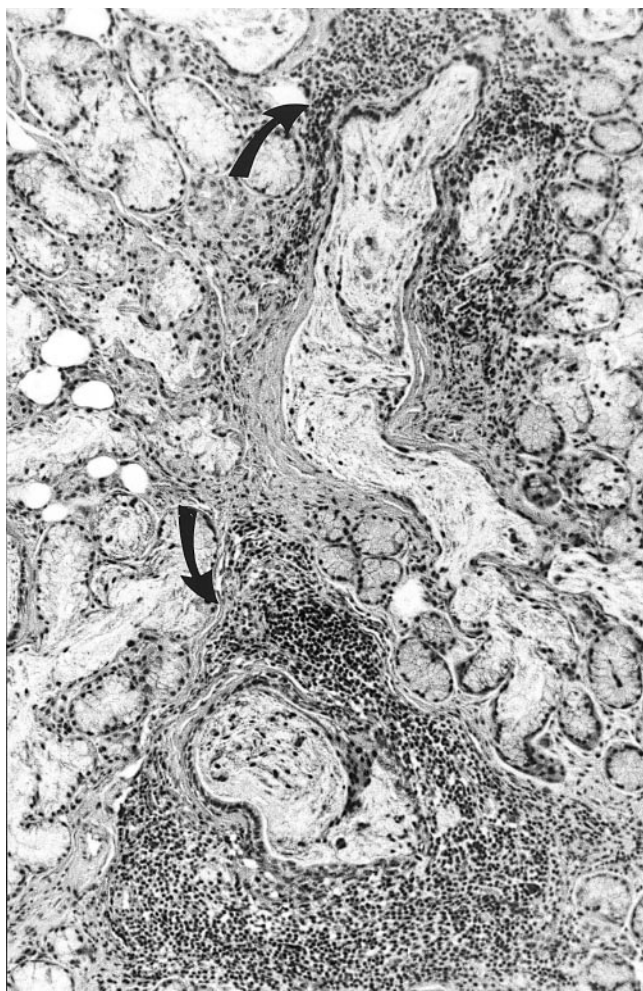


Figure 2. Minor salivary gland biopsy from age 7 years. Two discrete lymphocytic foci (arrows) are seen within an area of well-preserved glandular tissue, consistent with multifocal sialadenitis. Staining for specific lymphocytic markers did not reveal a monoclonal population or other evidence for neoplastic transformation. Hematoxylin-eosin stain, original magnification $\times 20$, 1 mm² field of view.

Additional studies confirmed a diagnosis of Sjögren's syndrome. A Schirmer's I test was 8 mm and 5 mm in the right and left eyes, respectively (positive ≤ 5 mm). Rose-Bengal staining was negative. The original lip biopsies (ages 4–7 years) were re-reviewed and demonstrated multifocal sialadenitis (>1 focus/4 mm², >50 lymphocytes/focus) (Figure 2). As the patient fulfilled the criteria for primary Sjögren's syndrome,⁶ and in the face of ongoing neurologic complications, she was treated with pulse intravenous methylprednisolone, up to 30 mg/kg/day, for a total of 5 days. Her diplopia, disequilibrium, and ataxia rapidly improved, and the ptosis was less prominent, with the facial diplegia unchanged. She was discharged on oral prednisolone, 2 mg/kg/day, which was slowly tapered over the next 3 months. Six months after admission, a follow-up brain MRI revealed full resolution of the midbrain lesion. She has continued to improve off corticosteroids, with full conjugate extraocular movements, minimal ptosis, and stable facial diplegia.

Discussion

Sjögren's syndrome is predominantly a disease of women in the fifth and sixth decades of life,^{1,2} with a prevalence estimated between 0.3 and 3% of the adult population.^{7,8} In contrast, its appearance in

the pediatric population is much lower. In one study of 200 consecutive patients with Sjögren's syndrome, only 10 (5%) were under 12 years of age.⁹ Although keratoconjunctivitis sicca and xerostomia are cardinal features of adult Sjögren's syndrome, the presentation may differ in children. A survey of 39 pediatric patients showed that recurrent parotid swelling was the most common initial finding, whereas sicca symptoms were less frequent.³ Such was the case in our patient, when at age 4 years she presented with chronic, episodic parotid and submandibular enlargement. Dry eyes and mouth appeared only months later, when dry eyes, conjunctivitis, dental caries, and vaginal dryness signaled an incipient sicca complex.

Given the infrequent occurrence and atypical presentation of pediatric Sjögren's syndrome, it is not surprising that the correct diagnosis was delayed. The initial scenario was interpreted as Melkersson-Rosenthal syndrome, even though she did not have the full triad of facial swelling, facial paralysis, and lingua plicata. Indeed, this triad is rarely found in children since lingua plicata is seen in only 0.37% of patients under 10 years of age.⁵ Other entities, such as multiple sclerosis, systemic lupus erythematosus, lymphoma, and sarcoidosis, can be difficult to distinguish from Sjögren's syndrome⁷ but were not supported on the basis of clinical history, laboratory and imaging studies, and histopathology.

Extraglandular manifestations of Sjögren's syndrome are common and may include involvement of the lung, gastrointestinal tract, kidney, muscle, thyroid, and skin, as well as hematologic derangements and lymphoma.² Peripheral neuropathy has also been well described.¹⁰ The impact on the central nervous system, however, is disputed. Some reports suggest that the incidence of neurologic manifestations approaches 20 to 25%,^{7,11} but these estimates may reflect sample bias and are probably much lower.¹² Typical complications include subcortical strokes, partial seizures, dementia, meningoencephalitis, brainstem and cerebellar deficits, and myelopathy.^{7,11,13} The appearance of central nervous system disease in pediatric Sjögren's syndrome is highly irregular, and only a handful of cases have been published.^{14–17} Curiously, our patient was not diagnosed with primary Sjögren's syndrome until age 9 years, when she developed ptosis, diplopia, and ataxia in the absence of other rheumatologic or systemic disease. Although the majority of MRI abnormalities in Sjögren's syndrome involve subcortical and periventricular white matter,¹³ the dorsolateral midbrain was principally affected in our patient. Similarly, brainstem lesions were clearly demonstrated on MRI in two of the pediatric case reports,^{14,15} suggesting that central nervous system Sjögren's syndrome may have a brainstem predilection in this age group. Cerebral histopathology has shown a small-vessel mononuclear inflammatory vasculopathy that disrupts the blood–brain barrier,⁷ a finding consistent with the MRI characteristics described in our patient.

How might the patient's facial diplegia be understood pathophysiologically? To our knowledge, the association of bilateral VII cranial nerve palsy with Sjögren's syndrome is extremely rare^{18,19} but was described by Sjögren.²⁰ We suspect that the facial nerves were traumatized within the inflamed parotid glands, prior to their division, although such a complication is seldom described in the setting of parotitis of any cause. Alternatively, a small-vessel vasculitis of the vasa nervorum could have resulted in ischemic dam-

age to both facial nerves, except that most of the documented cranial neuropathy in Sjögren's syndrome involves the trigeminal nerve.¹⁰ The peripheral pattern of facial weakness in the absence of other brainstem symptoms likely excludes significant pontine involvement at the time of initial presentation at age 4 years. An explanation for the patient's neurologic decline at age 9 years is less ambiguous and almost certainly a product of brainstem inflammation and vasculopathy. Prompt treatment with pulse corticosteroids led to the rapid clinical and radiographic reversal of her central nervous system disease, illustrating the importance of an accurate diagnosis. As discussed, age-based differences in the mode of onset present a diagnostic challenge, and in a child who presents with orofacial swelling, facial nerve palsy, or stroke-like symptoms, Sjögren's syndrome should be considered.

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Cavernous Hemangioma in a Child Presenting With Hemichorea: Response to Pimozide

ABSTRACT

The case of a 9-year-old boy with hemichorea due to cavernous hemangioma in the left caudate nucleus is presented. To our knowledge, only two children have been reported with hemichorea associated with cavernous hemangioma. Hemichorea in our patient responded to pimozide, a neuroleptic that blocks central nervous system dopaminergic receptors. (*J Child Neurol* 2001;16:685-688).

Cavernous hemangioma, also known as angioma or cavernoma, is a congenital vascular malformation. Although rare in the brain, it can be found in the cerebral subcortical region, pons, and cerebellum. The typical age of presentation is 20 to 40 years; the incidence in children has not been determined.^{1,2} The common clinical symptoms are seizures, focal neurologic deficits, bleeding episodes, headache, or involuntary movements like hemidystonia or hemiballismus. Presentation with hemichorea is very rare: to our knowledge, only two children have been reported with hemichorea associated with cavernous hemangioma.^{3,4} We present the third case with this symptom.