Case Report

An unusually dry story

Srinivas Rajagopala, Gurukiran Danigeti, Dharanipragada Subrahmanyan

Abstract

We present a middle-aged woman with a prior history of central nervous system (CNS) demyelinating disorder who presented with an acute onset quadriparesis and respiratory failure. The evaluation revealed distal renal tubular acidosis with hypokalemia and medullary nephrocalcinosis.Weakness persisted despite potassium correction, and ongoing evaluation confirmed recurrent CNS and long-segment spinal cord demyelination with anti-aquaporin-4 antibodies.There was no history of dry eyes or dry mouth.Anti-Sjogren's syndrome A antigen antibodies were elevated, and there was reduced salivary flow on scintigraphy. Coexistent antiphospholipid antibody syndrome with inferior vena cava thrombosis was also found on evaluation. The index patient highlights several rare manifestations of primary Sjogren's syndrome (pSS) as the presenting features and highlights the differential diagnosis of the clinical syndromes in which pSS should be considered in the Intensive Care Unit.

Keywords: Acute demyelinating encephalomyelitis, distal renal tubular acidosis, hypokalemic paralysis, nephrocalcinosis, neuromyelitis optica, Sjogren's syndrome

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.164808

Quick Response Code:

Introduction

Primary Sjogren's syndrome (pSS) is a relatively common autoimmune disease affecting 2–3% of the adult population. It is characterized by lymphocyte infiltration and destruction of exocrine glands. Extraglandular manifestations, including renal disease, can occur in a third of patients. Undiagnosed pSS presenting with severe hypokalemia and demyelination in the absence of dryness is rare but can occur in 2–7%.

Case Report

A 36-year-old lady presented with weakness of upper and lower limbs progressing to complete inability to move her limbs over a 12-h period. She did not report diplopia or urinary retention and denied any fever, neck pain, or trauma. She was a homemaker, did not smoke and denied any alcohol or substance abuse. Her medications included 100-μg levothyroxine daily. She was diagnosed with postviral encephalomyelitis 3 years ago and treated with steroids with complete resolution of symptoms and signs. She had normal menstrual cycles and had one spontaneous second trimester abortion 8 years ago. She had one living child and had undergone tubal ligation after medical termination of pregnancy 4 months prior to this presentation.

On evaluation, she was afebrile, normotensive with a respiratory rate of 25-breaths/min and resting pulse oximetry of 98%. There was flaring of alae nasi during quiet respiration. Mini-mental state examination was normal, and there was no evidence of cranial nerve deficits. Ocular fundus examination was normal. Power was 2/5 on the medical research council scale in the proximal muscles of the upper limbs and 1/5 in the lower limbs throughout. There was evidence of neck

From:
Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Dhanvantri Nagar, Puducherry, India

Correspondence:
Dr. Srinivas Rajagopala, Department of Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Dhanvantri Nagar, Puducherry - 605 006, India.
E-mail: visitsrinivasan@gmail.com

How to cite this article: Rajagopala S, Danigeti G, Subrahmanyan D. An unusually dry story. Indian J Crit Care Med 2015;19:550-3.

flop and paradoxical movement of the abdomen. Sensory examination was normal. Deep tendon reflexes were not elicited, and plantar reflexes were mute. Abdomen was distended with absent bowel sounds. The rest of the physical examination was unremarkable. Arterial blood gas showed combined respiratory and normal anion gap acidosis (pH 7.23, $PaCO_2$ 46 mmHg, PaO_2 88 mmHg, HCO_3 18 mEq/L, chloride 105 mEq/L, and corrected anion gap 10 mEq/L). She was electively intubated and ventilated for impending respiratory failure with deep venous thrombosis prophylaxis, enteral feeding, and evaluation for acute onset quadriparesis. Chest radiographs were normal, and electrocardiography showed prolonged PR interval, prominent "U" waves and "T" inversions. Serum biochemistries confirmed severe hypokalemia (2.1 mEq/L, normal 3.5–5 mEq/L) and deranged renal function (serum creatinine 2.1 mg/dL, normal 0.8–1.2 mg/dL and blood urea 60 mg/dL, normal 20–40 mg/dL). Serum sodium, calcium, phosphate, magnesium levels, and plasma glucose were normal. Liver function tests revealed hypoalbuminemia (2.8 g/dL, normal 4–6 g/dL); enzymes were normal. Urine microscopy was normal. Urinary electrolytes showed potassium level of 45 mEq/L and positive urine anion gap. 24-h urinary calcium excretion levels were elevated (550 mg/24-h, normal 20–275 mg). Random serum cortisol and thyroid hormone levels were normal. Parenteral potassium and Ringer's lactate were administered. The absent tendon reflexes, prior neurological illness, and lack of complete improvement with potassium replacement prompted re-evaluation. Cerebrospinal fluid examination was acellular with raised proteins (65 mg/dL, normal 15–45 mg/dL); oligoclonal bands were negative. Computed tomography (CT) head was normal, and nerve conduction tests showed normal sensory and motor conduction. CT -abdomen showed medullary nephrocalcinosis [Figure 1, left] with an incidental suprarenal inferior vena cava thrombus (IVC). There was no evidence of deep venous thrombosis by Doppler and echocardiography was normal. 1 mg/kg enoxaparin twice a day was initiated. Magnetic resonance imaging of the head and spine with contrast showed extensive demyelination of the brain and spinal cord [Figure 2]. Anti-aquaporin-4 antibodies were strongly detected by enzyme-linked immunosorbent assay (ELISA). Pulse methylprednisolone 1 g was administered for 3 days followed by 1 mg/kg/day enteral prednisolone.

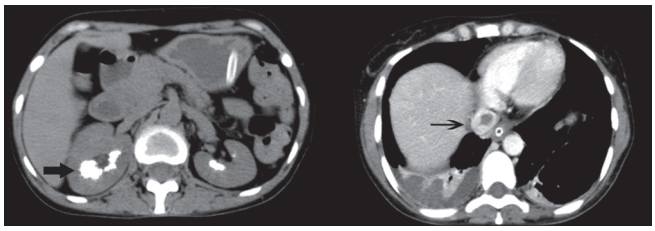

Figure 1: Composite images of the computed tomography of the abdomen (computed tomography, left) at the level of the kidneys showing large chunky calcification due to medullary nephrocalcinosis related to untreated distal renal tubular acidosis and (right, arrow) contrast-enhanced computed tomography-abdomen showing a suprarenal inferior vena cava thrombosis

She did not report ocular or oral dryness, oral ulcers, malar rash, and photosensitivity or joint pains. In view of distal renal tubular acidosis (RTA) with nephrocalcinosis, recurrent central nervous system (CNS) demyelination and unprovoked unusual site thrombosis, and antinuclear antibodies (ANA) were obtained. ANA was 3+ by immunofluorescence with a speckled pattern; anti-SS-A (Ro) antibodies were positive by ELISA (1:1280). Serum rheumatoid factor antibodies were also markedly elevated (1:640). Schirmer's I test showed normal tear flow (>15 mm at 5 min). Salivary scintigraphy showed markedly diminished salivary gland flow [Figure 3]. Serum immunoglobulin levels were normal, and the results of HIV and hepatitis C antibodies by ELISA were negative. Antiphospholipid antibodies (APLAs, IgM anticardiolipin antibody by ELISA) were elevated. Lip biopsy was planned but was refused by the patient. A diagnosis of pSS with distal RTA and medullary nephrocalcinosis, recurrent CNS demyelination with quadriparesis (neuromyelitis optica) and respiratory failure and secondary APLA syndrome with IVC thrombosis was made. Current classification criteria[1,2] [Table 1] are specific but insensitive and may not be fulfilled in up to 13–17% of the cohort with pSS.[3]

Discussion

pSS is a relatively common autoimmune disease, affecting 2–3% of the adult population. It is characterized by lymphocyte infiltration and destruction of exocrine

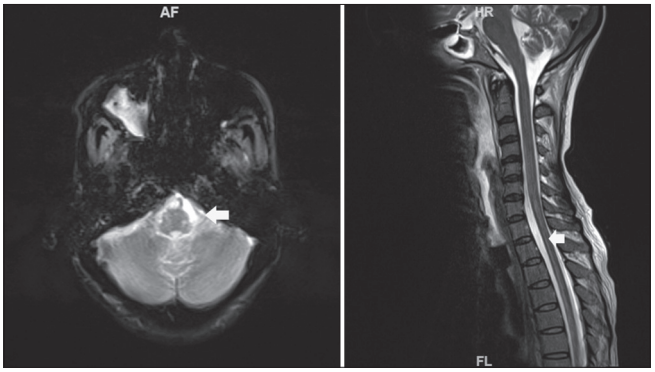

Figure 2: Magnetic resonance imaging (left) of the head and spine (right) with contrast revealed T2 hyperintensities in the left middle cerebral peduncle (white arrow), superior medulla and a long segment spinal cord (C7–T3, block arrow) T2 hyperintensity with mild cord swelling suggestive of demyelination

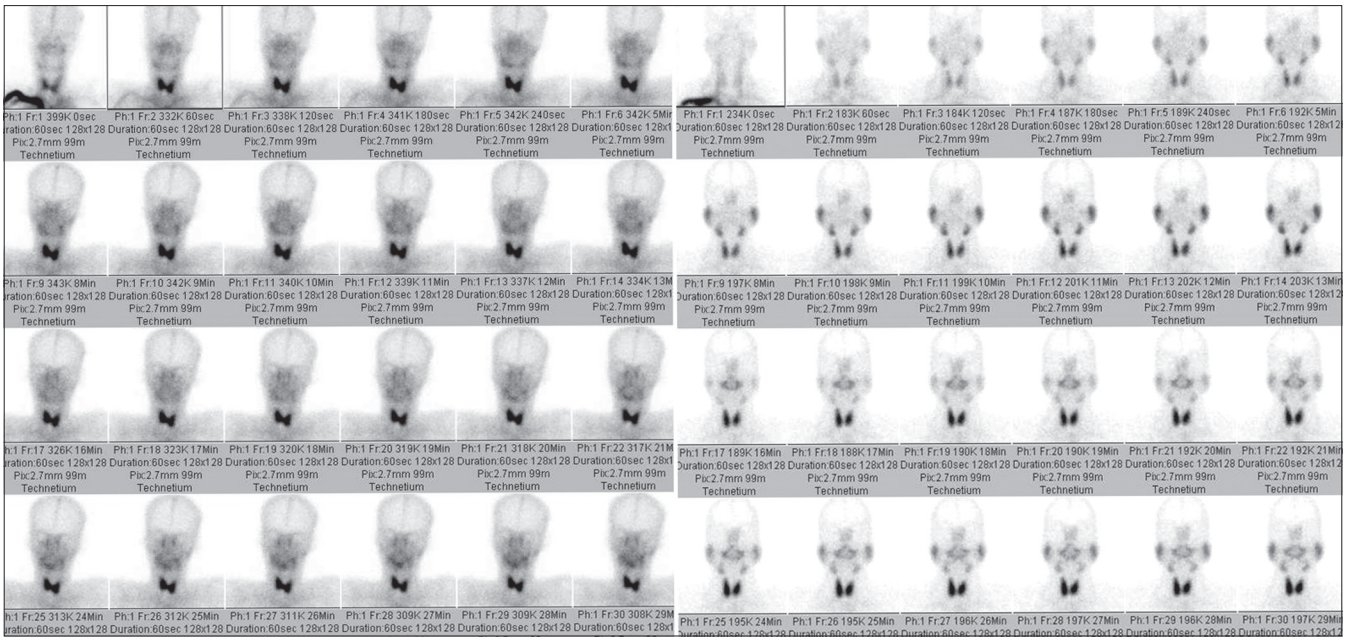

Figure 3: Salivary scintigraphy showing markedly diminished salivary gland flow, including delayed uptake, reduced concentration, or delayed secretion of the tracer (left) when compared to normal (right)

Table 1: Comparison of the revised AECG classification criteria and the ACR criteria for Sjogren's syndrome

Serial number	AECG classification	ACR classification
1	Ocular symptoms: A positive response to ≥1 of below 3 Have you had daily, persistent, troublesome dry eyes for more than 3 months? Do you have a recurrent sensation of sand or gravel in the eyes? Do you use tear substitutes more than 3 times a day?	None
2	Oral symptoms: A positive response to ≥1 of below 3 Have you had a daily feeling of dry mouth for more than 3 months? Have you had recurrently or persistently swollen salivary glands as an adult? Do you frequently drink liquids to aid in swallowing dry food?	None
3	Ocular signs: Objective evidence of ocular involvement to ≥1 of below 2 Schirmer's I test, performed without anesthesia (≤5 mm in 5 min) Rose Bengal score or other ocular dye score ^	Keratoconjunctivitis sicca with ocular staining score ≥3#
4	Histopathology: Focal sialadenitis in minor salivary glands*	Focal sialadenitis in minor salivary glands*
5	Salivary gland involvement: Objective evidence of salivary gland involvement ≥1 of below 3 Unstimulated whole salivary flow (≤1.5 mL in 15 min) Parotid sialography-diffuse sialectasis (punctate, cavitary ,or destructive pattern), without evidence of obstruction in major ducts Salivary scintigraphy showing delayed uptake, reduced concentration and/or delayed excretion of tracer	
6	Autoantibodies: Antibodies to Ro (SSA) or La (SSB) antigens, or both	Positive serum anti-SSA/Ro and/or anti-SSB/La or (positive rheumatoid factor and ANA titer ≥1:320)
Rules	Primary SS: Presence of 4 out of 6 as long as either 4 or 6 positive Secondary SS: 1 or 2 plus any 2 from 3 to 5 in a potentially associated disease	2 out of 3; eliminated the distinction between primary SS and secondary SS
Exclusion	AIDS, hepatitis C, past history of head and neck radiation treatment, sarcoidosis, preexisting lymphoma, graft-versus-host disease, IgG4 disease and use of anticholinergic drugs (for a time shorter than 4 half-lives of the drug)	

^ ≥4 according to van Bijsterveld's scoring system; *In a biopsy obtained through normal-appearing mucosa and evaluated by an expert histopathologist evidence of focal lymphocytic sialoadenitis, with a focus score ≥1, defined as number of lymphocytic foci (which are adjacent to normal-appearing mucous acini and contain more than 50 lymphocytes) per 4 mm^2 of glandular tissue; #Not currently using daily eye drops for glaucoma and has not had corneal surgery or cosmetic eyelid surgery in the last 5 years. AECG: American-European Consensus Group; ACR: American College of Rheumatology; ANA: Antinuclear antibodies; SSA: Sjögren's syndrome A antigen; SSB: Sjögren's syndrome A antigen

glands. Dry eyes and dry eyes are the hallmark of this disease and 93% and 98% in large prospective series have evidence of dry eyes and dry mouth, respectively.[4]

Extraglandular manifestations are seen in a third of patients with SS, including renal involvement in 4%.[5,6] Renal manifestations include interstitial nephritis and RTA.[5] The reported prevalence of CNS manifestations in SS [Table 2] range from 0% to 60%;[7] a high index of suspicion is needed. Recurrent signs and positive anti-aquaporin-4 antibodies favored SS rather than APLA as the cause of CNS manifestations.[7]

Her further course was complicated by *Pseudomonas*-related ventilator-acquired pneumonia and severe weakness with prolonged ventilation. Tracheostomy was performed and enoxaparin, prednisolone, piperacillin-tazobactam, pantoprazole, good hydration, enteral Shohl's solution (60 mEq/d alkali), and potassium (40 mEq/day) were administered. She was weaned off the ventilator by day 25 and warfarin overlapped. Repeat anticardiolipin antibodies were persistently elevated at 6 weeks. Pulse cyclophosphamide 600 mg/m^2 was initiated a week after resolution of pneumonia and continued monthly for 3 months. She was decannulated and discharged with a proximal power of 4/5 and the international normalized ratio of 2.1 by D48 of admission. She is ambulatory with minimal support for activities of daily living, normal renal functions, and potassium at 3 months of discharge. Oral azathioprine has been initiated along with warfarin with a plan to continue treatment for 2 years and anticoagulation for life.

Table 2: Spectrum of central nervous system disease in pSS

Anatomical location	Manifestation
Brain	Motor deficit
Focal	Sensory deficit
	Cranial nerve deficits
	Aphasia
	Dysarthria
	Brain stem syndrome
	Cerebellar syndrome
	Seizures
	Migraine
Nonfocal	Encephalopathy (acute/subacute)
	Aseptic meningitis
	Cognitive dysfunction/dementia
	Movement disorder
	Psychiatric disorder
	Sleep disorder
Spinal cord	Transverse myelitis
	Neuromyelitis optica-like syndrome
	Chronic progressive myelopathy
	Neurogenic bladder
	Lower motor neuron disease
	Brown-Sequard syndrome
Others	Optic neuritis
	Multiple-sclerosis like syndrome

pSS: Primary Sjogren's syndrome

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, *et al.* Classification criteria for Sjögren's syndrome: A revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002;61:554-8.
2. Shiboski SC, Shiboski CH, Criswell L, Baer A, Challacombe S, Lanfranchi H, *et al.* American college of rheumatology classification criteria for Sjögren's syndrome: A data-driven, expert consensus approach in the Sjögren's International Collaborative Clinical Alliance cohort. Arthritis Care Res (Hoboken) 2012;64:475-87.
3. Rasmussen A, Ice JA, Li H, Grundahl K, Kelly JA, Radfar L, *et al.* Comparison of the American-European Consensus Group Sjogren's syndrome classification criteria to newly proposed American college of rheumatology criteria in a large, carefully characterised sicca cohort. Ann Rheum Dis 2014;73:31-8.
4. Garcéía-Carrasco M, Ramos-Casals M, Rosas J, Pallarés L, Calvo-Alen J, Cervera R, *et al.* Primary Sjögren syndrome: Clinical and immunologic disease patterns in a cohort of 400 patients. Medicine (Baltimore) 2002;81:270-80.
5. Goules A, Masouridi S, Tzioufas AG, Ioannidis JP, Skopouli FN, Moutsopoulos HM. Clinically significant and biopsy-documented renal involvement in primary Sjögren syndrome. Medicine (Baltimore) 2000;79:241-9.
6. Dowd JE, Lipsky PE. Sjögren's syndrome presenting as hypokalemic periodic paralysis. Arthritis Rheum 1993;36:1735-8.
7. Soliotis FC, Mavragani CP, Moutsopoulos HM. Central nervous system involvement in Sjogren's syndrome. Ann Rheum Dis 2004;63:616-20.