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An Unusual Presentation of Sjogren's Syndrome

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A 44-year-old woman presented with a long history of nausea and vomiting and was found to have hypokalemic metabolic acidosis with elevation of the urine bicarbonate level consistent with the new onset of renal tubular acidosis, type I. Her laboratory findings and histologic picture of a buccal biopsy sample of two minor salivary glands were consistent with Sjogren's syndrome. Treatment with steroids markedly improved her symptoms.

Sjogren's syndrome (SS) is a chronic inflammatory autoimmune disease which primarily affects the salivary and lacrimal glands, leads to progressive destruction of these organs, and results in decreased production of saliva and tears. The disease can be primary in nature (the sicca complex) or secondary to rheumatoid arthritis or another connective-tissue disease. In some cases, it is characterized by lymphoproliferation of either a benign or malignant nature.

Extraglandular involvement occurs more often in the primary form of the disease. Raynaud's phenomenon is present in 20% of patients. Diffuse interstitial pneumonitis may result from lymphocyte infiltration of small airways. The most common renal involvement affects the tubules and results in latent renal tubular acidosis. The following case illustrates a very unusual presentation of SS.

A 44-year-old white female presented with a 6-month history of nausea and vomiting. She had been generally well until she visited a local horse show and since that time had thrice-daily episodes of nausea and vomiting accompanied by vague, crampy, and dull epigastric and suprapubic abdominal pain not associated with meals.

She was initially started on omeprazole (Prilosec) for the vague epigastric pain, without resolution of her symptoms. One month after the onset of her illness, she was admitted to a community hospital, where the workup included upper endoscopy, showing only mild gastritis and minimal esophagitis, thyroid evaluation, and no evidence of porphyria. An ultrasound of the right upper quadrant showed no abnormality.

Her problems had not improved, and she was referred for psychiatric evaluation of pyschogenic pain and anxiety. She was treated sequentially with paroxetine (Paxil), fluoxetine (Prozac), and nortriptyline (Pamelor), without any significant change in her symptoms. Her symptoms worsened, with almost constant nausea and vomiting two to three times every day. The abdominal pain diminished but persisted as a dull ache.

Because of the progressive symptoms and failure to improve on the aforementioned drugs, cerebral vasculitis was considered by the patient's local physicians. At this point she transferred her care to a tertiary-care center.

When admitted to the Hospital of the University of Pennsylvania, she was found to be severely hypokalemic and to have profound metabolic acidosis with a bicarbonate level of 14 mmol/liter and an anion gap of 15. The serum creatinine concentration was slightly elevated at 1.5 mg/dl. Urinalysis showed moderate protein but no leukocytes, erythrocytes, or casts. Electrocardiographic analysis showed no ischemic changes but did show U waves. Her antinuclear antibody titer was found to be elevated at 1:5,120, and the rheumatoid factor titer was elevated at 1:2,080. The sedimentation rate was 52 mm/h.

With a history of possible depression, positivity for antinuclear antibody, abdominal symptoms consistent with serositis, and the finding of mild proteinuria, a diagnosis of lupus was considered. Because of the history of behavioral changes, a computerized tomography (CAT) scan of the brain was performed to rule out a structural lesion, and the results were entirely normal.

Review of the patient's history for evidence suggestive of lupus revealed only a history of mild hair loss. Given the overwhelming nausea and vomiting that she continued to experience, a gastric-emptying study was performed, and the results were normal. A trial of cisapride did not affect the symptoms.

Serum protein electrophoresis and urine electrophoresis were performed to rule out myeloma. Because of a history of well water contamination at her home, a heavy-metal screen was performed, with normal results.

The renal service was consulted, and it was found that the urinary pH was 6.5, the serum pH was 7.27, and the serum bicarbonate level had dropped to 9 mm/liter. These values were thought to be consistent with type I renal tubular acidosis (RTA). The presence of RTA and considerably elevated titers of antinuclear antibody and rheumatoid factor led to the consideration of SS. A Schirmer test was performed, and the results were consistent with SS. A buccal mucosal biopsy sample of two minor salivary glands was obtained, and the findings were also consistent with SS. The patient noted a marked improvement in the dryness of her eyes following treatment with Lacri-Lube.

Further serological studies were performed. Antibodies against SSA and SSB were present, but no antibodies against SCL-70 or double-stranded DNA were found. C3 and C4 levels were normal. The prolactin level was within normal limits.

The patient was initially treated with pulse-dose (1.0 g) steroids and intravenous fluids. Her symptoms decreased within several days. Therefore, she was switched to oral medications and was discharged markedly improved on the following regimen: potassium chloride (K-Tab) at 40 meq every day, potassium citrate (Urocit-K) at four tablets four times a day, Lacri-Lube at bedtime, calcium carbonate (Os-Cal) at 500 mg four

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times a day, phosphorus, sodium, and potassium (Neutrophos) at two tablets every day, and prednisone at 40 mg every day.

SS classically presents as a sicca syndrome. This case shows an unusual but reported presentation with metabolic acidosis and weakness, nausea, and vomiting. A review of the literature found 46 reports. Nagayama et al. (4) reported a case of a woman with a 16-year history of polyuria and polydipsia who was found to have hyposthenuria and a hyperchloremic metabolic acidosis secondary to RTA. Siamopoulos et al. (6) reported a case of hypokalemic paralysis as the presenting manifestation of primary SS.

The mechanisms involved in SS and RTA are postulated by Cohen et al. (2), among others, to involve the absence of H(+)-ATPase in the cortical collecting tubules. However, other authors, such as Siamopoulos et al. (7), feel that the pathogenesis of RTA is multifactorial and involves the effects of excreted monoclonal proteins and immunologically induced interstitial inflammation.

Pokorny et al. (5) reported a group of 65 patients with primary SS with extraglandular symptoms either at the onset of or during the disease. The mean age of the patients at onset was 41.8 years and at the time of definite diagnosis was 45.8 years. There was a 10:1 female predominance. Articular (32 cases), lacrimal (30 cases), and salivary (30 cases) manifestations were the most frequent initial symptoms. Other symptoms were found to be related to chronic atrophic gastritis (35 patients). Renal involvement was detected in 15 of the 65 patients.

Graninger et al. (3) found that patients with systemic lupus erythematosis and overt RTA appeared to have concomitant SS. For cases in which renal involvement in SS is diagnosed by biopsy or suspected from clinical evidence, Bailey and Swainson (1) have reported an impressive response to corticosteroid therapy, as we found in this case. Six months after the diagnosis, the patient was doing well on prednisone at 5 mg every other day and potassium replacement.

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