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Primary Sjögren's Syndromewith Granulomatous Interstitial Nephritis

Authors
Walaa H. Mohamad[1], Ahmad B. Elden[2], Wessam Ismail[3], Mahmoud Abd El-Radi[4]
[1]Nephrology Unit, Assiut University, [2]Critical Care Unit, Assiut University,
[3]Pathology Department, Beni Suef University,[4]Ophthalmology Department, Assiut University
Corresponding author
Walaa H. Mohamad
+201005220944
Email: *Walaa.hosny@aun.edu.eg*

Abstract
Sjögren's syndrome (SS) is a systemic autoimmune disease affecting mainly the exocrine glands. Tubulo-interstitial nephritis (TIN) is the most predominant renal involvement with lymphocyte and plasma cells infiltration of the interstitium. We report a case of young female with SSpresented withrenal tubular acidosis (RTA), polyradiculoneuropathy &proteinuria. Renal biopsy revealed granulomatous interstitial nephritis. Granuloma formation is rarely seen in cases of SS.
Key Words:*Sjögren's syndrome, Granulomatous tubulo-interstitial nephritis*

Introduction

SS is a systemic autoimmune disease that mainly affects the exocrine glands and usually presents as persistent dryness of the mouth and eyes due to functional impairment of the salivary and lachrymal glands [(1)]. A widely accepted criterion for histopathological confirmation of SS is focal lymphocytic sialadenitis of the labial salivary glands[(2)].TIN is the most predominant clinical manifestation of renal involvement in SS characterized by RTAtype (I) and less frequently RTA type (II) [(3)]. Sensory neuropathyandsensorimotor neuropathyare among the features[(4).]

Case Report

AFemale patient 29 years old, presented to ER withsevere upper and lower limbs weakness.The conditionbegan one week agowithseveral attacks of watery diarrhea and vomiting per day, followed bya rapid progressive courseof four limbs weakness that the patient became bed ridden within 2 days. Examination at presentation; BP: 90/70 mmHg, P:110 b/min, RR: 15 c/min, Temp: 37.5C^{o}, mild conjunctival pallor, four limbs proximal musclepowerwere2/5, distal muscle power were 3/5 with hypotonia and absent deep reflexes, intact cranial nerves and sensory system. Investigations at admission areshown in table (1).

Table(1): Investigations at time of first admission

Serum Na	140 mmol/L
Serum K:	2mmol/L
Serum Mg:	2.12 mg/dl
Serum Cl	117 mmol/L
Serum Ca^+	8.7 mg/dl
Blood pH	7.3
Po_2	98 mmHg
PCO_2	28 mmHg
HCO_3	12 mmol/L
Base deficit	-10
CBC	HGB= 9g/dl, Plt= 224x10^3/ mm^3, WBCs= 6.6 x10^3/ mm^3
BUN	3.9 mmol/L
Serum creatinine	93.33µmol/L
Total protein	6.3 g/dl
Serum Albumin	2.7 g/dl

CBC: complete blood picture, HBG: hemoglobin, Plt: platelets, WBCs: white blood cells, Po_2: partial pressure of o_2, Pco_2: partial pressure of co_2, BUN: blood urea nitrogen.

4 Liters of IV normal saline were used to correct hypovolemia with slow potassium infusionto correct hypokalemia.Diarrhea and vomiting spontaneously stopped and3 days laterthe patient regained movement gradually with improvement of all laboratory abnormalities.The patient was discharged on oral iron andK^+supplementation,and follow up scheduled at weekly intervals.Patient showed normal muscle power in follow up visits.

Three months later,the patient presented to ERby severe four limbs weakness.Examination was unremarkable except for muscle power 2/5with hypotonia and absent deep reflexesin all four limbs both proximal as distal muscles, stock and glove hypoesthesia with intact cranial nerves. Investigations at second admission are shown in table (2).

Table (2): Investigations at second admission

Serum Na	138mmol/L
Serum K:	1.7mmol/L
Serum Mg:	2.12 mg/dl
Serum Cl	114mmol/L
Serum Ca^+	8.7 mg/dl
Blood PH	7.3
Po_2	98 mmHg
PCO_2	28 mmHg
HCO_3	12 mmol/L
Base deficit	-10
CBC	HGB = 10 g/dl, Plt = 344 x10^3/ mm^3, WBCs = 7.6 x10^3/ mm^3
BUN	8mmol/L
Serum creatinine	90µmol/L
Total protein	6.3 g/dl
Serum Albumin	3.5 g/dl

CBC: complete blood picture, HBG: hemoglobin, Plt: platelets, WBCs: white blood cells, Po_2: partial pressure of o_2, Pco_2: partial pressure of co_2, BUN: blood urea nitrogen.

The patient received potassium infusion and partially regained her muscle power within 3 days.Nerve conduction study showed polyradiculoneuropathy affecting lower limbs more than upper limbs. With reviewing the patient history, shereported dry mouth 3 months agowithout polyuria, followed by a drynessof both eyes with foreign body sensationone month later.Further investigations areshown in table (3):

Table (3): Further investigations

Fasting blood glucose	4mmol
2-hours PP blood glucose	6.2 mmol
Urinary pH	Alkaline (8)
Urinary proteins	+1
24 hour urinary protein	1.6gm/ay
24 hour urinary chloride	304mmol
24 hour urinary potassium	80mmol
24 hour urinary sodium	307 mmol
ESR	70/125
CRP	17.5 mg/dl
ANA (titer by ELISA)	1.7(positive)
C3	133.8 mg/dl
C4	29.3 mg/dl

PP: Post Prandial, ESR Erythrocyte Sedimentation Rate, CRP: C Reactive Protein, ANA: Anti Nodular Antibodies, C3 and C4: complement 3 and complement 4 respectively.

Renal biopsy was done for the proteinuria and revealed unremarkable tufts appearance(Figure: 1),patchy moderate tubular atrophy with frequent hyaline and proteinaceous casts entangling few inflammatory cells, patchy dense inflammatory interstitial infiltrate mainly formed of lymphocytes and plasma cells with granulomatousformation on a background of moderate interstitial fibrosis. (30% of submitted tissue)(Figure: 2 &3).Arteries showed mild intimal sclerosis. Arterioles were unremarkable.

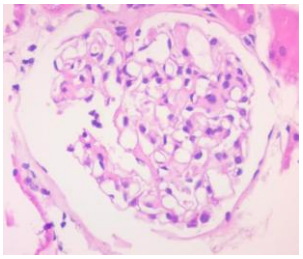

Figure (1): H&E stain of a normal tuft.

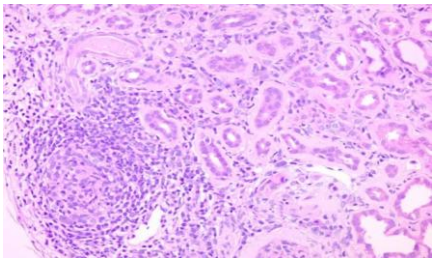

Figure (2): H&E stain section shows; tubules with patchy moderate atrophy, frequent hyaline and proteinaceous casts entangling few inflammatory cells and interstitium with patchy dense inflammatory infiltrate mainly formed of lymphocytes and plasma cells with granulomatous formation.

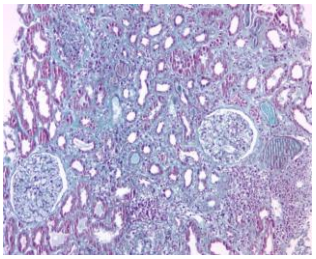

Figure (3): Trichrome stainsection shows moderate interstitial fibrosis.

Ophthalmological workup showed; Tear film breakup time < 6 seconds (abnormal <10 sec.), *Schirmer's* test 1 (without anesthesia) <8mm wetting of *Schirmer's* paper strip (abnormal < 15mm). Schirmer's test 2 (with anesthesia) < 7mm wetting of Schirmer paper strip (borderline). No signs of uveitis. Chest X-ray was unremarkable. Anti Ro and Anti La titers werehighly positive (> 100 U/ml) with polyclonal gammopathy 2.5 g/dl.

The patient refused to undergo biopsy from buccal mucosal. She was prescribed prednisolone 60mg/day with Mycophenolate Mofetil (MMF) 1500 mg/day and potassium supplement with general improvement of her condition. Follow up scheduled at weekly intervalswith adequate stabilization of the patient for 3 months till writing.

Discussion

The first presentation of our patient was acute gastroenteritis with hypovolemia followed by four limb weakness. The associated hyperchloremic metabolic acidosis and hypokalemia were considered to be of diarrheal origin, and muscle weakness wasconsidered to be hypokalemic paralysis.

At the second presentation, four limbsweakness was associated with hypokalemia and hyperchloremic acidosis without diarrhea. Furthermore, the weakness was proximal as distal and not completely corrected with eukalemia and was accompanied with sensory affection.
Urinary anion gap revealed a decreased renal ammonium production. The presence of proteinuria mandated renal biopsy, which revealed a granulomatous tubulo-interstitial nephritis.Granuloma formation is rarely seen in SS [(5)].Absence of uveitis excludes Tubulo-interstitial Uveitis syndrome. Diagnosis of sarcoidosis is unlikely in the absence of pulmonary involvement. Positive ANA and highly positive Anti Ro and Anti La titer, polyclonal gammopathy 2.5 g/dl, polyradiculoneuropathy, tubule-interstitial nephritis and renal tubular acidosis were highly suggestive of SS and immunosuppression therapy was initiated.

Zandbelt et al described patients with SS treated with high doses of corticosteroids, who demonstrated an improvement in the main clinical, histological, and immunohistological features after treatment[(6)].*Sonia et al*reported agood response with MMF in SS patients[(7)]In addition to*Dean et al* who reported agood response with this agent in TIN[(8)].

Conflict of interest statement: None

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