ORIGINAL ARTICLE

Clinical Profile of Primary Sjogren's Syndrome with Hypokalemic Periodic Paralysis

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Abstract

Introduction: Primary Sjogren's Syndrome (pSS) with Hypokalemic Periodic Paralysis(HPP) whether an association or a different clinical subset needs review.

Methods: Cross-sectional retrospective study of subjects of Primary Sjogren's Syndrome with Hypokalemic Periodic Paralysis(HPP) identified from database maintained at Centre For Rheumatic Diseases, Pune since 1996 with records of over 50000 patients. The diagnosis was clinical. Clinical and investigations data was extracted pertaining to initial examination and follow up. Standard investigations & ELISA, immunoblot and nephelometry to assay autoantibodies (AAb) were done

Results: 16 patients of Primary Sjogren's Syndrome (pSS) with Hypokalemic Periodic Paralysis (HPP) were identified in the period 2000-2014. Presenting feature was HPP in 86% with Dry eye (4%) and Arthralgias (10%) in remaining. Distal Renal Tubular Acidosis was identified in all. All were females with average age of 26 years. Symptomatic ocular sicca noted in 60% & Oral sicca in 50% patients. Other features – Arthralgias (91%), arthritis (42%), mucositis (38%), Neuropathy (30%), skin rash (20%) cytopenias (19%), Erosive arthritis (10%), interstitial lung disease (10%) and Raynaud Phenomenon (10%). 100% were positive for ANA. SSA was positive in 100%, SSB in 50% of patients & Rheumatoid Factor in 70 %. Hypothyroidism was associated in 70% patients.

Conclusion: We present a large series of Primary Sjogren's Syndrome with Hypokalemic Periodic Paralysis(HPP) from India. Prominent features of female dominance, younger age of onset and SSA positivity noted in this cohort of patients on Routine clinical and serology phenotype suggests existence of a distinct subset. HPP was presenting feature in majority

Introduction

Sjogren's Syndrome(SS) is reported as most common connective tissue disorder.[1] SS can be primary or secondary associated with various connective tissue disorders(eg Rheumatoid Arthritis, Systemic lupus erythematosus, etc).[2] Primary SS comprise about half of the cohort.[1] SS is characterized by autoimmune exocrinopathy of salivary and lacrimal glands.[1] Patients present with symptoms of dryness of eyes and mouth. SS is associated with multiple extraglandular features.[2] Association of pSS and Hypokalemic Periodic Paralysis (HPP) first described in 1981[3] has been infrequently reported. First description from India dates back to 1996. Whether pSS and HPP occurrence is an association or different clinical subset needs review. Current study describes clinical phenotype of this co-expression.

Material and Methods

Aim: To study clinical phenotype of co-occurence of Primary Sjogrens Syndrome and Hypokalemic Periodic Paralysis.

Design: The study was a retrospective cross sectional analysis design using a rheumatology database.

Site: Single center study. Data of patients attending a popular community based rheumatology clinic [Centre For Rheumatic Diseases (CRD] based in Pune metropolis in West India (www.rheumatologyindia.org) was assessed. A comprehensive patient data base is maintained in CRD since 1998.

Selection: The principle criteria for inclusion in the study was a clinical diagnosis of Primary SS made by a senior rheumatologist (AC). Ocular sicca was confirmed by Schirmer's test and tear film breakage time by Ophthalmologist. Oral sicca was a clinical assessment on patient symptom confirmation. Salivary functional tests could not be conducted All patients were required to have been followed for at least one year after the initial diagnosis. The current study cohort was identified from the database during period of 2002 to 2014

Examination, Follow up: All patients were examined by senior rheumatologists (AC). A standard rheumatology case record form recorded detail history and clinical evaluation. A comprehensive laboratory and plain Skiagram evaluation results were available. Blood was tested for Rheumatoid Factor (RF, nephelometry with cut off at 40 IU/ml) and Anti Cyclic Citrullinated Polypeptide (ACCP, second generation, ELISA with cut off at 5 RU/ml) and anti-nuclear antibody (ANA, ELISA) and ANA profile analysis (ANA Blot, ELISA) were conducted along with all routine hemogram, biochemistry and urine analysis. Hypokalemic periodic paralysis (HPP) was identified by Neurologist. Distal renal tubular acidosis was identified in each patient.

All other rheumatic diagnosis were clinical though standard classification criteria were referred to.

Data and Statistics: Data was extracted from the database and entered into an Excel (MS) worksheet

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Table 1: Extra-glandular features

Extra glandular features	Frequency (%)
Arthralgias	90
Arthritis	20
Mucositis	40
Neuropathy*	30
Skin Rash**	20
Cytopenias	20
Interstitial Lung Disease	10
Raynaud's Phenomenon	10

*Identified on Nerve Conduction Velocity. **Rash characteristic of Connective Tissue Disorders

for demographics and other variables Frequency percentage of these parameters were calculated.

Results

A total of 19 patients with Primary SS and HPP were identified during the study period. Complete data of 16 patients was available for analysis. All patients were females. The mean age of occurrence was 26 years. There was no family history of connective tissue disorders or neuro-muscular diseases in any patient. About 70% of patients were from rural background. Hindu ethnicity was noted in 88% while rest 12% were Muslims. Distal Renal Tubular Acidosis was identified in all patients.

HPP was the onset feature in majority (70%). Inflammatory Arthritis and ocular sicca were onset features in remaining 20% and 10% patients respectively. The average time interval between disease onset and presentation to Rheumatologist was 6 months.

The average serum potassium level was 2.6 meq/dl during the attacks. The paralysis resolved in all patients after potassium supplementation. All patients were advised life long potassium supplementation. Relapse of paralysis was noted in 3 patients who stopped potassium supplementation.

Clinical Features

Sicca symptoms in eye were reported by 60% patients. Objective evidence was established in all 16 patients. Oral sicca was reported by 50% patients. Many extra-glandular features apart from HPP were noted in patients of this cohort. The details of the same are mentioned in (Table 1). One patient developed arthritis mutilans while one patient with Raynaud's Phenomenon also had digital gangrene. Hypothyroidism as a co-morbidity was present in 60% patients.

Serological Tests

Antibody to SSA antigen was noted in all patients. Antibody to SSB was identified in 50% of them. Rheumatoid Factor was positive in 60% patients. Patients also demonstrated presence of Anti Cyclic Citrullinated Polypeptide (ACCP) (40%), Antibody to double stranded DNA (Anti dsDNA) (60%) and other ANA antigens (20%). Among ACCP positive patients, 50% were positive for Anti dsDNA. 1 patient was positive for SSA, SSB, RF, ACCP, Anti dsDNA, Histone. Absence of Sm, n-RNP, SCL-70, CENP, PM-SCl, JO-1, PCNA, Nucleosome, ribosomal P-protein was noted in ANA profile in this cohort.

Discussion

We present a case series of patients with Primary SS with HPP. This retrospective analysis highlighted some unique features of this cohort. This association was noted only in females. Young age of onset was common. HPP was presenting feature in majority. This cohort displayed had multiple extra-glandular features. All patients had Anti SSA antibody.

Primary SS has high female dominance as reported in western[5] and Indian literature.[6] This cohort though is characterised by only female presence. Case reports of Primary HSS with HPP highlight this phenomenon (international).[7-9]. Similar case series from India has also reported only a female dominant pattern.[10] Only one record of such occurrence in male was found in literature.[11]

The age of onset of Primary SS has been reported to be in forth-fifth decade of life.[5,6] Contrary to this finding the age of onset is younger in third decade in this cohort. Similar observations noted in other case series of Primary SS with HPP.[10]

Renal involvement in Primary SS has been well described. Interstitial nephritis and Glomerulonephritis are two main forms. Interstitial Nephritis which can be seen in about one third patients can produce latent or complete distal renal tubular acidosis and rarely proximal.[12] Hypokalemic Periodic Paralysis is associated with distal renal tubular acidosis. HPP was a presenting feature in majority in current cohort. Similar findings were noted in other case reports.[7-10]

Multiple extraglandular features are associated with Primary SS.[2] The frequency reported in India was 76.9% from one of the studies.[6] Apart from HPP the frequency of extraglandular features was very high in current cohort (100%). No studies were available to our knowledge to compare these findings. Current study is the largest series of Primary Sjogren's Syndrome with Hypokalemic Periodic Paralysis (HPP). Prominent features of female dominance, younger age of onset and SSA positivity noted in this cohort of patients on Routine clinical and serology phenotype suggests existence of a distinct subset. HPP was presenting feature in majority. Further studies and genotypic analysis would strengthen this finding. Young women with Primary SS may benefit by screening for distal renal tubular acidosis. A clinical suspicion for Primary SS must be maintained in all young female patients presenting with HPP. A thorough clinical search recommended for extraglandular features in patients with this co-occurrence.

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