CASE REPORT

SJOGREN'S SYNDROME PRESENTING AS PYREXIA OF UNKNOWN ORIGIN-A CASE REPORT

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HOW TO CITE THIS ARTICLE:

Imtiaz Pasha, Srinivas Prabhu, Preethika Ravi, Amira. "Sjogren's Syndrome Presenting as Pyrexia of Unknown Origin - A Case Report". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 09, March 3; Page: 2135-2139, DOI: 10.14260/jemds/2014/2116

ABSTRACT: Pyrexia of unknown origin (PUO) is classified according to the underlying disorder. The 4 main clinical categories of PUOs are infectious, malignant, rheumatic/inflammatory, and miscellaneous disorders. Sjogren's syndrome presenting as PUO, have become uncommon in recent years because of better serologic diagnostic tests. Sjogren's syndrome may be difficult PUO diagnosis and should be considered for diagnosis if patient presents with fever, salivary glands enlargement, dry eyes and mouth.

KEYWORDS: Autoimmune disorders, salivary glands, Keratoconjunctivitis sicca.

INTRODUCTION: Sjogren's syndrome is a systemic auto-immune disorder characterized by symptoms of oral and ocular dryness, exocrine dysfunction and lymphocytic infiltration of exocrine glands.¹ It is the most common autoimmune disease next to Rheumatoid arthritis primarily affecting the peri and post-menopausal females in the ratio of 9:1.²

Sjogren's syndrome consists of triad of xerostomia, keratoconjunctivitis sicca and rheumatoid arthritis in half to two-third of patients, hence further classified as Primary and Secondary.

Primary is characterised by dryness of eyes (keratoconjunctivitis sicca) and xerostomia (salivary gland dysfunction) and secondary includes involvement of one or both exocrine tissues associated with other connective tissue disorders like systemic lupus erythematosus, rheumatoid arthritis, scleroderma, primary biliary cirrhosis, systemic sclerosis, polyarteritis nodosa, polymyositis, Raynaud's syndrome and fibromyalgia contributing to 50-60% of cases.³

The antibodies are directed against salivary duct antigen, increase in β -2 microglobulin in saliva and synovial fluid, general immune abnormalities including hypergammaglobulinemia, rheumatoid factor, antinuclear antibody, anti-DNA (Deoxyribonucleic acid) antibody and increased Erythrocyte Sedimentation Rate levels have been observed⁴. Literature reveals that Epstein-Barr virus and Human T lymphotropic virus do play a role in pathogenesis of Sjogren's syndrome.⁵ Other viruses which may be associated in the pathogenesis of Sjogren's sicca syndrome⁶ are cytomegalovirus, Hepatitis C virus, Human T cell leukemia or lymphoma virus-1 & Human Immunodeficiency Virus.²

The diagnosis of Sjogren's syndrome is based on several clinical and laboratory findings. The most accepted criteria are the American-European Consensus group in 2002⁷. The sensitivity and specificity for the diagnosis of primary Sjogren's syndrome using these criteria is 96% and 94%. To be diagnosed as a case of Sjogren's syndrome, the patient must be positive for at least 4 out of 6 criteria. Exclusion criteria include pre-existing Lymphoma, Acquired Immunodeficiency Syndrome, Sarcoidosis, Graft versus Host disease.

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The important diagnostic features are:

I) Ocular Symptoms (1:3)

- Dry eyes daily > 3 months
- Sand or gravel sensitivity in the eyes
- Use of tear substitutes (> three times a day)

II) Oral Symptoms (1:3)

- Dry mouth daily > 3 months
- Recurrent or persistent swollen salivary glands
- Frequent sipping of water to aid in swallowing dry foods

III) Ocular Signs (1:2)

- Positive Schirmer's test (<5mm/5min)
- Rose Bengal score (>4 von Bijesterfeld score)

IV) Salivary Function

- Whole unstimulated saliva <1.5ml/15min (0.1ml/min)
- Positive scintigraphy
- Positive sialography

V) Labial Salivary Gland Biopsy

- Presence of focal lymphocytic sialadenitis in minor salivary glands, 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 mm².

VI) Serum Autoantibodies

- Anti-SS (Soluble Substance)-Ro
- Anti-SS (Soluble Substance)-La
- Rhesus Factor
- Antinuclear Antibodies

CASE REPORT: We describe a 18 year old girl with history of fever since 6 months, high grade, on and off along with repeated swelling and pain in both cheeks since 6 months. Patient also gives history of pain and swelling of hands and feet since 3 months. History of dry mouth and irritation of both eyes was also present.

Patient gives past history of repeated admissions to hospital for fever and swellings in both cheeks and was diagnosed with viral parotitis and treated with intravenous antibiotics and discharged.

On examination, a young female patient moderately built and nourished with heart rate of 110/min, blood pressure 130/80mmhg and temperature of 103° F. General physical and systemic examination was normal. Local examination revealed swelling of around 10X5 cms, irregular in shape, situated in front, below and back of ears, tender and with well-defined margins.

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Laboratory findings included white blood cell count of 5800/mm³, haemoglobin 10.9mg%, platelet count 254000/mm³, ESR 99mm/1st hour, Thyroid and renal function tests were normal, liver function tests were normal, random blood sugar level was 99mg%. Peripheral blood picture showed normocytic, normochromic anemia. Serological tests for HIV, HBsAg, HCV, Syphilis, Typhoid, Malaria, Dengue, and Mumps were negative. Rheumatoid factor is strongly positive and CRP is positive. Chest x-ray and ultrasonography of abdomen and pelvis were normal. Ultrasound of parotid glands revealed both parotids enlarged with multiple focal hyperechoic areas. Biopsy of minor salivary glands of lips showed dense infiltrates of lymphocytes and a few plasma cells. Immunological study revealed the presence of anti-SS (Soluble Substance)-A-165RU/ml, anti-SS (Soluble Substance)-B autoantibodies 175RU/ml and Anti-Ro52 and Antinuclear Antibody (HeP2-Fine Speckled & Homogenous) positive. Schirmer's test of both eyes showed 8 mm at the end of 5 minutes (positive).

MRI of parotid glands showed bulky both parotid glands with multiple tiny focal cystic areas and punctate calcifications. No ductal dilatations/intraductal calculi suggestive of inflammatory/lymphoproliferative disease such as Sjogren's syndrome.

Patient was treated with tapering dose of prednisolone along with hydroxychloroquine. Patient showed improvement in fever, parotid swelling and joint pains after starting the treatment.

DISCUSSION: Sjogren's syndrome, a well-known autoimmune disease, often affects women in fourth or fifth decades of life⁸. Prevalence of primary Sjogren's syndrome in the general population has been estimated to be around 1 to 3%⁹. It is reported that the enlargement of the major salivary glands occurs in 25-66% of primary Sjogren's syndrome patients but is uncommon in patients with secondary Sjogren's syndrome⁹. Our patient exhibited fever of unknown origin, persistent swelling of the parotid glands, dryness of mouth and eyes since 6 months. The incidence of symptoms/ signs of eye involvement among the reported cases were 86.1%¹⁰. Complete physical examination of our patient at presentation and during a follow-up period of three months failed to reveal evidence of any associated connective tissue disease.

Serologic studies in our patient revealed the presence of anti-SS (Soluble Substance)-A, anti-SS (Soluble Substance)-B autoantibodies and Anti-Ro52 and Antinuclear Antibody (HeP2-Fine Speckled & Homogenous) which is in accordance to the previous reports in the literature wherein positivity for anti-SS-B and Rheumatoid factor were found in 54.7% and 61.4% cases respectively¹¹. Histopathologically, minor labial salivary gland biopsy revealed a lymphocytic score of ≥ 1 in a periductal location, which according to criteria of American-European Consensus group in 2002⁷ supports the diagnosis of Sjogren's syndrome¹². Our patient revealed fever, arthralgia which according to Robert Fox et al is present in 25% of patients with Sjogren's syndrome.

Treatment of Sjogren's syndrome depends on the extent and severity of the clinical manifestations and is better instituted through a multidisciplinary approach. Symptomatic treatment includes artificial tears, salivary substitutes to relieve the symptoms and prevent local infectious complications like conjunctivitis and corneal inflammation. Finally corticosteroid and hydroxychloroquine should be reserved for all the cases showing evidence of organ damage, significant leucopenia or severe clinical symptoms. We are reporting a case wherein the patient presented with pyrexia of unknown origin and we reinvestigated her to diagnose Primary Sjogren's syndrome and advised appropriate treatment. Henceforth, the patient is under regular follow-up.

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CONCLUSION: Sjogren's syndrome is a chronic autoimmune disease affecting the exocrine glands, with a prevalence rate of 1 to 3%. Although malignancy remains the most common cause of PUOs, rheumatic/inflammatory disorders remain important diagnostically and therapeutically. Sjogren's syndrome remains a rare but important cause of PUO in adults and should be considered for diagnosis if patient presents with fever, salivary glands enlargement, dry eyes and mouth.

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Fig. 1: showing bilateral parotid gland enlargement with dry eyes

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Fig. 2: MRI parotid gland showing bulky parotid glands with multiple tiny focal cystic areas and punctate calcifications suggestive of Sjogren's syndrome

Fig. 3: Showing normal parotid glands with improvement in general condition

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Date of Submission: 10/02/2014.

Date of Peer Review: 11/02/2014.

Date of Acceptance: 17/02/2014.

Date of Publishing: 25/02/2014.