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Case Report

Recurrent Pregnancy Loss in Women with Asymptomatic Sjogren's Syndrome - A Rare Case Reported from Pakistan

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ABSTRACT

Sjogren's syndrome is systemic autoimmune disorder affecting multiple systems. It predominantly affects females and is characterized by dryness of eyes and mouth. It is association with pregnancy may result in Neonatal Lupus presenting prenatally, postnatally or both. Complications may include congenital heart block (CHB), cutaneous lesions and hematological abnormalities. Usually, titre of anti Ro/SS-A and anti La/SS-B antibodies in maternal serum are proportional to fetal outcomes. However, these antibodies can affect fetus even in asymptomatic mothers. We hereby report the first case of an adult female with asymptomatic Primary Sjogren's syndrome, presenting with recurrent miscarriages due to trans-placental passage of auto-antibodies resulting in CHB. Knowledge of this disorder can help in early diagnosis and prevention of pregnancy associated morbidity and mortality.

Keywords: Autoantibodies, Recurrent Miscarriages, Sjogren's Syndrome.

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INTRODUCTION

Neonatal Lupus (NL) is an autoimmune disorder resulting from the trans-placental passage of maternal anti SS-A/Ro, anti SS-B/La to the fetus. Mostly at time of diagnosis 50% of mothers are asymptomatic. This multisystem disease can present prenatally, post-natally or both and may include congenital heart block (CHB), cutaneous lesions and hematological abnormalities. CHB is reported in 0.5% of live births and is a severe condition resulting in intrauterine death.[1-3]

Sjogren's syndrome is multisystem autoimmune disease, mainly affecting females and can occur alone (primary) or in association with systemic autoimmune rheumatic diseases (secondary).[4] It is characterized by dry eyes and mouth secondary to lymphocytic infiltration of the lacrimal and salivary glands. It's association with pregnancy has been seen and titre of anti Ro/SS-A and anti La/SS-B antibodies in maternal serum are proportional to fetal outcomes.[2]

Incidence of recurrent miscarriages in women of reproductive age group is 0.5%–3.[5] Recurrent pregnancy related morbidity associated with an underlying autoimmune milieu especially asymptomatic primary SJOGREN'S SYNDROME is an evolving area of clinical research. In addition to psychological effects on women and families, such scenario can become a diagnostic enigma leading to critical delay in institution of effective therapeutic measures endangering life of both mother and fetus.

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CASE REPORT

A 35-year old female consanguineously married for last 12 years presented with history of recurrent miscarriages. Past history revealed first miscarriage occurred after 3 years of marriage at 6th week of gestation, it was tubal pregnancy after which right salpingectomy was performed. At 5 and 6 years of marriage in-vitro fertilization (IVF) and then implantation was also tried, which resulted in miscarriage at 15th and 8th weeks respectively. At 9 years of marriage, spontaneous conception was achieved, subsequently leading to miscarriage at 6 weeks. It is pertinent to mention that all her periodic ultrasound scans were unremarkable, there were no anatomical abnormalities and semen analysis of husband was within normal limits. Her laboratory work up revealed strong Anti Nuclear Antibodies positivity (Figure-A), strong Anti SS-A Antibody and very strong Anti Ro-52 and Anti SS-B Antibody positivity (Figure-B) (Table). Rest of the laboratory and radiological investigations were unremarkable. It is pertinent to mention that presently she do not have symptoms of dry eyes or mouth, joint pains and rash. Past medical history revealed that she has been using thyroxin 25mg 1 tablet daily, Glucophage 1000mg 1

tablet daily and folic acid 1 tablet daily for past 9 years as advised by gynecologist since first miscarriage.

Table: Results of Laboratory Investigations

Parameters	Results
Result of Immunological Tests	
Anti Nuclear Antibodies	Positive Intensity: ++ Pattern: Speckled Titre: 80
Anti SS-A Antibodies	Positive (++)
Anti Ro-52 Antibodies	Strong Positive (+++)
Anti SS-B Antibodies	Strong Positive(+++)
Anti ENA Antibodies	Positive
RA Factor	Negative
Anti dsDNA Antibodies	Negative
Anti Neutrophil Cytoplasmic Antibodies	Negative
Anti Cardiolipin Antibodies (IgG and IgM)	Negative
Anti Beta-2 Microglobulin Antibodies	Negative
Anti Thyroid Microsomal Antibodies	Negative
Anti Thyroglobulin Antibodies	Negative
Anti Endomyseal Antibodies (IgG and IgM)	Negative
Serum Immunoglobulin IgG Level	19 (5.3-16.5 g/L)
Serum Immunoglobulin IgA Level	2 (0.8-4.0 g/L)
Serum Immunoglobulin IgM Level	1.4 (0.5-2.0 g/L)
Serum Complement C3 Level	1.2 (0.7-1.7 g/L)
Serum Complement C4 Level	0.32 (0.2-0.5 g/L)
Result of Haematological Tests	
Complete Blood Counts	
WBC	5.39 (4-11 x 109 /L)
RBC	4.16 (3.5-5.5 x 1012/L)
Platelets	236 (150-400 x 109 /L)
Hemoglobin	11.8 (12-16 g/dl)
Hematocrit	36.1 (40-52 %)
Lupus Anticoagulant	Negative
APTT	32 (25-35 Seconds)

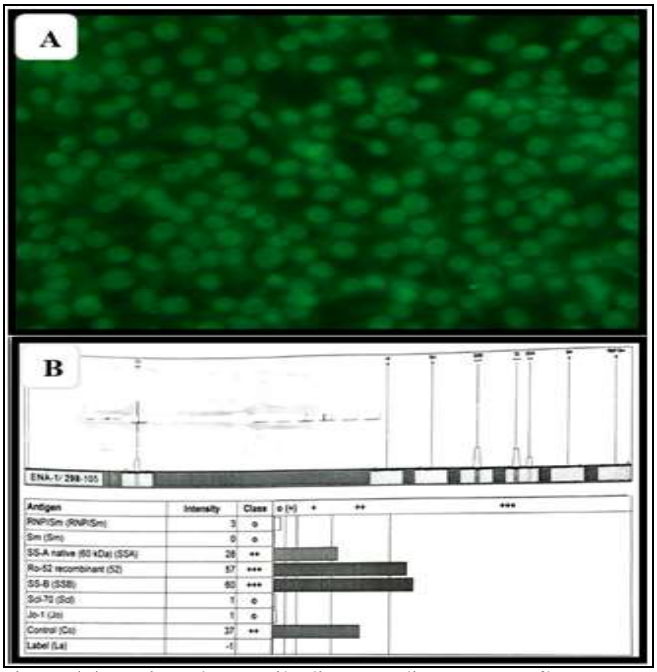

Figure: (A): Anti Nuclear Antibodies on Indirect Immunofluorescence at 400X Magnification, (B): Anti SSA(Ro-60), Ro-52 and SSB Antibodies on Immunoblot

DISCUSSION

Neonatal Lupus caused by trans-placental transfer of maternal antibodies to the fetus is most common cause of CHB. Mostly mothers show no clinical symptoms. Bin *et al.*, reported a case of full-term female neonate with severe bradycardia and ECG showed a third-degree atrioventricular block however echocardiography(ECHO) was unremarkable and after close monitoring the infant was discharged on 6th day of life without pacemaker.[6,7] CHB occurs in 2% of anti Ro/SS-A exposed pregnancies and recurrence is higher in subsequent pregnancies (approximately 9 times). High titer maternal antibodies can identify women at higher risk. Additionally, prolongation of the PR interval by ECHO is useful for "monitoring" and "diagnosis" of CHB.[8] Maternal prophylaxis with HCQ is recommended in women at risk in few studies.[9,10]

Extremely rare occurrence and scarcity of knowledge about CHB in fetus secondary to asymptomatic SJOGREN'S SYNDROME in mothers can present diagnostic and therapeutic challenge endangering two precious lives. Therefore, further multi-centre studies are required to aware clinicians and to have better insights regarding pathogenesis, clinical course and prognosis of this rare phenotype.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MZA & MS: Data acquisition, data analysis, critical review, approval of the final version to be published.

DA & AT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

YR & HSM: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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