

Etiological surprises in a series of sterile central corneal melts as a rare ocular presenting feature of systemic autoimmune disease

Dr.M.Hemanandini¹, Dr. C.Jeevakala², Dr.K.Nithya³,
Dr.P .A .Kochami⁴

Abstract:

Aim: To evaluate the etiology of sterile central corneal melt in four consecutive cases.

Settings and Design: Tertiary Care Referral Centre in Tamilnadu. Prospective, single institution, interventional case-series.

Materials and Methods: Four patients of sterile central corneal melts with suspected systemic association were included. Investigations done and systemic associations were confirmed. All the four cases were started with systemic immunosuppressants by Rheumatologist. Three of the sterile central corneal melts were managed with Tectonic penetrating keratoplasty (PKP). One case was managed with bandage soft contact lens (BCL).

Results: All the four sterile central corneal melts were associated with systemic autoimmune diseases: Secondary Sjogrens with Systemic lupus erythematosus (SLE), Rheumatoid arthritis, Takayasu Arteritis, Not yet diagnosed autoimmune disease.

Conclusion: This report highlights the sterile central corneal melt as a rare ocular presenting feature and the association of systemic autoimmune disease.

Keywords: Sterile central corneal melt, systemic autoimmune disease, Takayasu Arteritis.

Sterile central corneal melt is a rare condition and it being an initial presenting feature of systemic autoimmune disease is still more rare. Any case presenting with extensive corneal infiltration or thinning not explainable by the ocular disease should prompt an investigation for any associated systemic autoimmune etiology⁽¹⁾.

We describe four consecutive cases of sterile central corneal melts as initial ocular presentation of SLE with secondary Sjogren's syndrome, Rheumatoid arthritis, Takayasu arteritis, Not yet diagnosed autoimmune disease. We report the rare presentation of sterile central corneal melt associated with systemic autoimmune diseases.

I. Materials and Methods

This study is a prospective review of four consecutive cases presented with sterile central corneal melt in a tertiary care centre in Tamilnadu. Our centre serves as a tertiary eye-care referral hospital.

Case 1- SLE with secondary Sjogren's syndrome

A 20- year- old female who is a proven case of SLE presented with history of (H/O)foreign body sensation and redness on and off for 4 months in both eyes (BE). She had low grade fever on and off with joint pain at knees, shoulders and wrist since one year. She had loss of appetite and loss of weight. She also gave H/O parotid swelling for 6 months, which resolved spontaneously and H/O difficulty in swallowing for 6 months. Examination showed dry oral cavity and oral ulcers. On ocular examination, best corrected visual acuity (BCVA) in right eye (RE) was 6/24, and 5/60 in left eye (LE). Slit lamp examination revealed lustreless cornea in RE and severe corneal thinning of LE [Fig.1]. Corneal sensation was normal in the periphery. Schirmer's test revealed 4 mm wetting in BE indicating severe dry eye. BE fundus was normal.

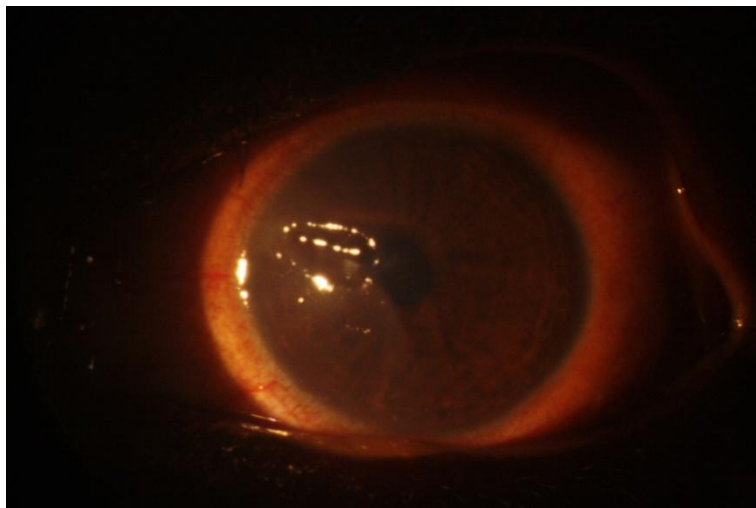


Figure 1 :Central sterile corneal melt in LE

Blood investigations were done, which again confirmed SLE with secondary Sjogren's syndrome. She was started on topical tear substitutes and BCL was applied to the LE in addition to her immunosuppressants.

Case 2 - Rheumatoid arthritis

A 65 year old female, presented with history of defective vision in BE for the past 2 months. On ocular examination, BCVA of RE was HM+, and 6/18 in LE. RE cornea showed 4mm central sterile corneal melt [Fig.2]. Corneal sensation was normal in periphery. LE showed thinning of cornea. Schirmer's test revealed 3mm wetting in BE indicating severe dry eye. BE were pseudophakic with normal fundus.

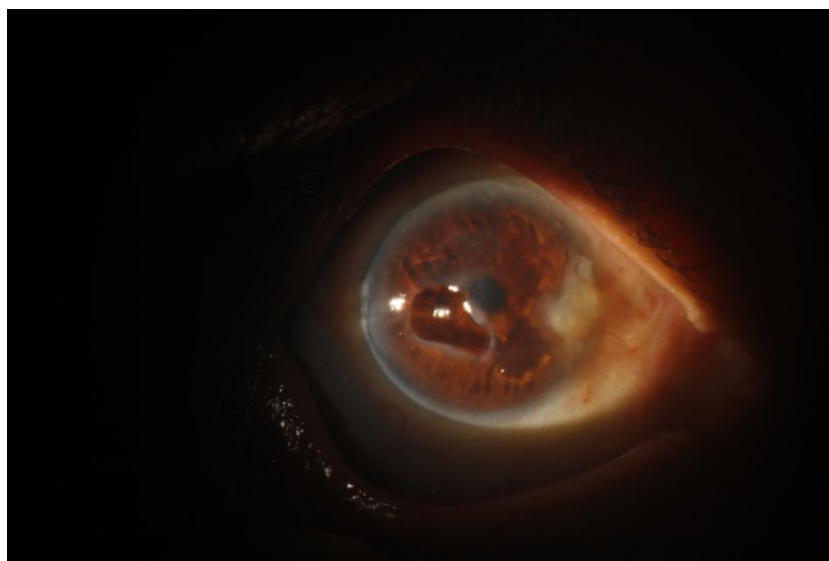


Figure 2: Corneal melt in RE

General examination revealed swan neck deformity of both hands & swelling of knee joints suggestive of Rheumatoid arthritis [Fig.3].



Figure 3 : Knee joint swelling and hand deformities

Blood investigations confirmed Rheumatoid arthritis. Patient was started on a single weekly dose of T. Methotrexate 7.5 mg with T. Folic acid 5mg by Rheumatologist. Patient was started on oral ocular hypotensive drugs, topical artificial eye drops and gels. Tectonic PKP for RE was done on the next day. Post operative period was uneventful [Fig.4]. Her visual acuity in RE improved to 6/36. Patient was advised to continue artificial eye drops & gels for both eyes along with systemic drugs, as advised by the Rheumatologist.



Figure 4 : Tectonic PKP in RE

Case 3 -Takayasu arteritis

A 38-year-old female presented with the history of pain and redness in RE since 1 month followed by diminished vision. Examination showed BCVA of 1/60 in RE and 6/18 in LE. RE showed sterile corneal melt with iris prolapse [Fig.5]. Corneal sensation was normal in periphery. LE showed severe corneal dryness. Schirmer's test showed 4 mm wetting in BE indicating severe dry eye.



Figure 5: Corneal melt with iris prolapse in RE

Interestingly she also had feeble pulse, very low blood pressure (BP) for which physician opinion was sought immediately. She was diagnosed to be a case of Takayasu arteritis, based on the clinical findings of absent brachial, radial, ulnar pulsations and presence of wide and fixed split second heart sound, systolic murmur in pulmonary area and carotid thrill with bruit on the right side. Upper limb BP was 80/50mmHg, and lower limb BP was 140/70mmHg.

Systemic evaluation confirmed Takayasu arteritis. Tectonic PKP was done for RE with an uneventful post operative period [Fig.6].

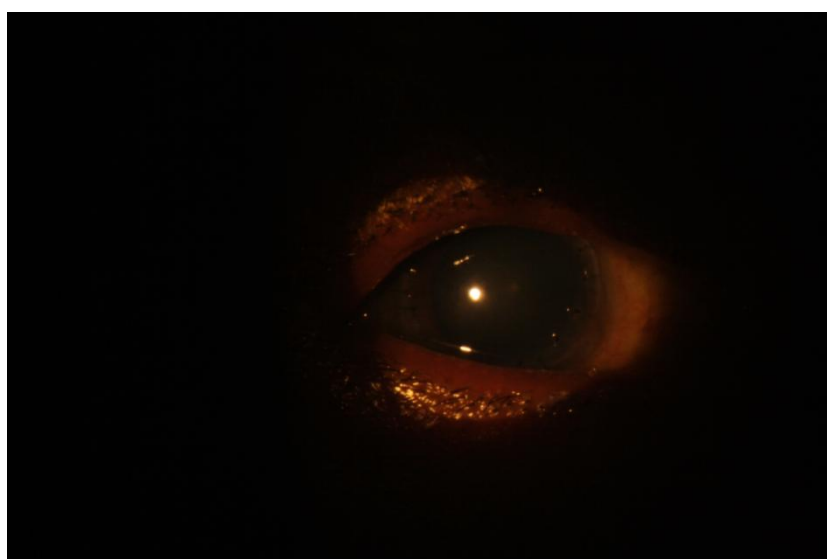


Figure 6 : Tectonic PKP in RE

Case 4 -Not yet diagnosed autoimmune disease

A 65 year old female, presented with history of pain RE for the past 1 month. She gave H/O defective vision RE for past 6 years following cataract surgery, details of which was not known. On examination, BCVA in RE was ?PL and 6/9 in LE. RE cornea showed subtotal melting with rest of cornea showing leucomatous opacity. She also had 360 posterior synechiae, iris atrophic patches, and an insitu PCIOL [Fig.7]. Corneal sensation was normal in periphery. Schirmer's test revealed 4 mm wetting in BE. BE were pseudophakic.

Tectonic PKP for RE was done with an uneventful post operative period [Fig. 8].



Figure 7 : Subtotal corneal melt with iris prolapse in RE



Figure 8 : Tectonic PKP in RE

II. Results

Demography, clinical features and investigations

The study included four consecutive patients with central corneal melts with 3 of whom were investigated for systemic associations and one patient was already diagnosed as a case of SLE. All the patients were females. Age group varied widely. Youngest patient was 20 years old and oldest patient 65 years old. All the patients were non diabetic. The demographic details of the patients are summarized in table 1.

Table 1 : Demographic details of patients with corneal melts		
Age/Sex	Laterality	Duration of ocular symptoms(months)
20 / F	OS	4
65 / F	OD	2
38 / F	OD	1
65 / F	OD	1

Clinical features of all the patients showed severe dry eye. Among the four patients one patient had severe thinning of cornea alone and other three patients had corneal melt with iris prolapse. Schirmer's test showed less than 5mm of wetting in all the patients. BCVA was less than 5/60 in all patients. These clinical features are summarized in table 2.

Cornea Thinning/melt	Hypopyon	Scleral Involvement	Schirmer's (mm)	Vision	Diagnosis
Severe thinning	-	-	4	5 / 60	SLE with Secondary Sjogren's syndrome
Central melt	-	-	3	HM +	Rheumatoid arthritis
Melt with iris prolapse	-	-	4	1 / 60	Takayasu arteritis
Melt with Iris prolapse	-	-	4	? PL	Not yet diagnosed autoimmune disease

Blood investigations were done. Erythrocyte sedimentation rate (ESR) was highly raised in all four patients. c-reactive protein (CRP) was positive in all the patients. Rheumatoid factor (RF) was positive in two patients. Anti nuclear antibody (ANA) profile was positive in two patients. ANA profile of the patient with secondary Sjogren's syndrome showed a strongly positive result for SS-A, Scl-70, SS-B, RP-52, positive PM-Scl, Rib, P-Protein, dsDNA, Nucleosome. This patient was also positive for RF. ANA profile of the Not yet diagnosed autoimmune disease was Anti Centromere protein B (ACA) strong positive. The details of the blood investigations summarized in table 3.

Case	ESR (mm/hour)	CRP	RF	ANA
1.SLE with Secondary Sjogren's Syndrome	135	+	+	Strongly positive Ss-A, Scl-70,SS-B, RP-52 with positive PM-Scl, Rib,P- Protein, dsDNA,Nucleosome
2.Rheumatoid arthritis	94	+	+	-
3.Takayasu Arteritis	100	+	-	-
4.Not yet Diagnosed Autoimmune disease	68	+	-	Anti Centromere protein B strong positive (ACA)

Clinical examination and relevant imaging studies were done to confirm these systemic autoimmune diseases.

Case 1-SLE with secondary Sjogren's syndrome

Investigations revealed an ESR of 135 mm/hour, positive CRP and RF with strongly positive ANA. ANA profile showed strongly positive for SS-A, Scl-70. SS-B and RP-5, positive PM-Scl, Rib, P-Protein, dsDNA, nucleosome and negative RNP/Sm, AMA-M2, PCNA, Histone, Jo-1, ASO titre. USG showed hepatosplenomegaly.

Case 2 - Rheumatoid arthritis

Investigation revealed an ESR of 94mm/hour, elevated ASO titre 400IU/ml. with positive CRP and RF.

Case 3-Takayasu arteritis

Investigations revealed an ESR of 100mm/hour with positive CRP. ANA was negative. Echo showed dilated right atrium, right ventricle, mild tricuspid regurgitation, atrial septal defect with ostium secundum, left to right shunt with moderate pulmonary hypertension. Arterial Doppler of upper limbs revealed diffuse thickening of both subclavian arteries with high velocity biphasic flow. Both axillary and brachial arteries

showed low velocity monophasic flow. Both radial and ulnar arteries showed venous like flow with no pulsatility and no evidence of thrombosis.

Carotid artery Doppler showed intimal and medial thickening of right and left common carotid artery (CCA), internal carotid artery with no evidence of plaque. Bilateral vertebral artery Doppler showed normal study.

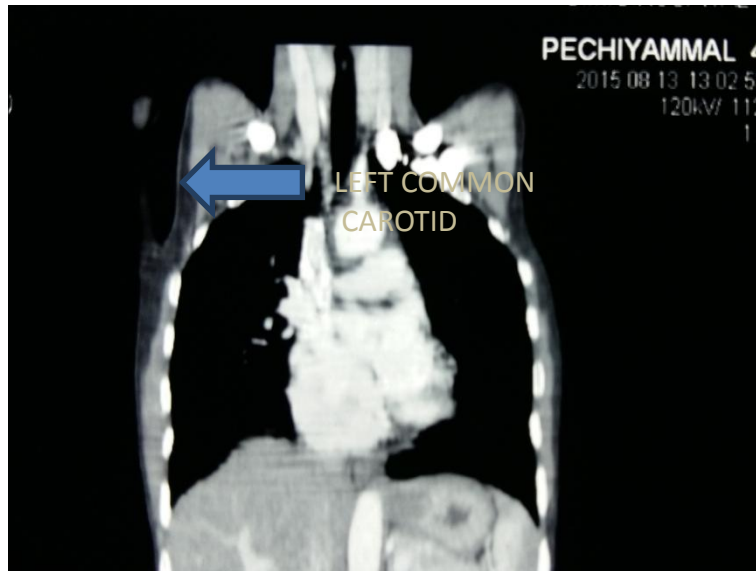


Figure 9 : CTA showing narrowing of left common carotid artery

Computed tomography angiogram (CTA) showed normal ascending, arch and descending aorta with severe ostial stenosis of branches (brachiocephalic, left common carotid artery, left subclavian artery)[Fig.9] and severe narrowing of right subclavian, right common carotid artery[Fig.10]. Such a picture of large vessel vasculitis was suggestive of Takayasu arteritis and started on oral immunosuppression by the Rheumatologist.

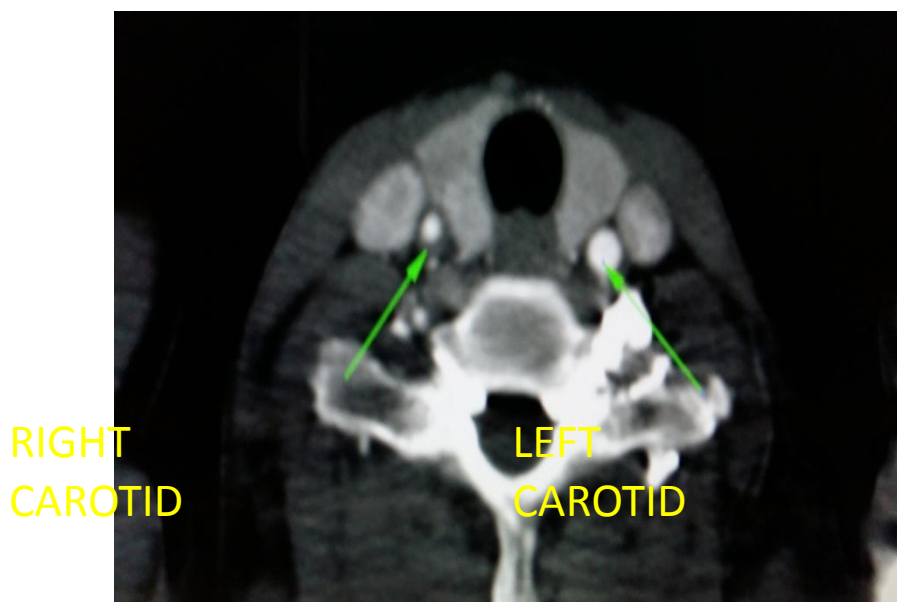


Figure 10 : CTA showing narrowing of both common carotids (Rt> Lt)

Case 4– Not yet diagnosed autoimmune disease

Investigations revealed an ESR of 68mm/hour, with positive CRP and ANA and negative RF. Table-4 showing ANA profile of the patient.

AMA-M2	NEGATIVE
CENP B	STRONG POSITIVE
DsDNA	NEGATIVE
Histone	NEGATIVE
Jo-1	NEGATIVE
nRNP/Sm	NEGATIVE
Nucleosome(NUC)	NEGATIVE
PCNA	NEGATIVE
PM – Scl	NEGATIVE
Rib.P – Protein	NEGATIVE
Ro – 52	NEGATIVE
Scl – 70	NEGATIVE
Sm	NEGATIVE
SS – A	NEGATIVE
SS – B	NEGATIVE

Serum Retinol level was 1.12mg/L .

Liver function test and ultrasound abdomen was normal.

III. Discussion

Unlike peripheral ulcerative keratitis which is the commonest corneal presentation in systemic autoimmune disease, here we report a series of sterile central corneal melts.

Case 1-SLE with secondary Sjogren's syndrome

The criteria to diagnose secondary Sjogren's syndrome in patients with defined major connective tissue disease are as follows:

The presence of one symptom (I or II) plus 2 of the 3 objective criteria (III, IV and V) is indicative of secondary Sjogren's syndrome^[7].

American-European Consensus Sjögren's Classification Criteria

I. Ocular Symptoms (at least one)

Dry eyes >3 months?

Foreign body sensation in the eyes?

Use of artificial tears >3x per day?

II. Oral Symptoms (at least one)

Dry mouth >3 months?

Recurrent or persistently swollen salivary glands?

Need liquids to swallow dry foods?

III. Ocular Signs (at least one)

Schirmer's test, (without anesthesia) ≤ 5 mm/5 minutes

Positive vital dye staining (van Bijsterveld ≥ 4)

IV.Histopathology Lip biopsy showing focal lymphocytic sialoadenitis(focus score ≥ 1 per 4 mm²)

V. Oral Signs (at least one)

Unstimulated whole salivary flow (≤ 1.5 mL in 15 minutes)

Abnormal parotid sialography

Abnormal salivary scintigraphy

VI. Autoantibodies (at least one)

Anti-SSA (Ro) or Anti-SSB (La)

In this case eventhough minor salivary glands biopsy proved to be nonspecific patient was still diagnosed as a case of secondary Sjogren's syndrome based on the clinicalfeatures and the fact that she is a proven case of SLE.

Case 2- Rheumatoid arthritis

Peripheral ulcerative keratitis is the most common presentation of rheumatoid arthritis in eye. It affects the patients during the late and advanced vasculitic phase. Patients with rheumatoid arthritis may also develop

the following non – ulcerative types of keratitis: A) Peripheral Stromal Thinning leaving the epithelium intact. B) Sclerosing keratitis C) Acute central corneal melting –which is very rare. In our patient, central corneal melt was the initial presenting feature, which is rare in Rheumatoid arthritis^[1,3-6].

Case 3- Takayasu arteritis

In this patient Takayasu arteritis was diagnosed based on the criteria in accordance with the 1990 American College of Rheumatology (ACR)

1.Age at onset \leq 40yrs, 2.Limb claudication, 3.diminished brachial pulse, 4. difference of $>$ 10mmHg systolic pressure between arms, 5.bruit over the subclavian artery or aorta, 6.abnormal angiogram if \geq 3 criteria diagnosed as Takayasu arteritis (sensitivity 90.5%,specificity 97.8%). This patient fulfilled 5 criteria.

Takayasu arteritis by itself is rare in India and our patient is one among the 2000 cases reported so far in India at present. In this case corneal melt was the initial presenting feature, which is very rare in Takayasu arteritis^[2].

Case 4 –Not yet diagnosed autoimmune disease

In this patient the only positive ANA profile was Anti centromere protein B (ACA). ACA is strongly suggestive of limited systemic scleroderma, the incidence of positivity being 60%, with a specificity $>$ 98%^[8]. ACA also occur in many other auto immune diseases. The second most common being in Primary biliary cirrhosis (PBC). PBC was ruled out as liver function test and ultra sound abdomen were normal with a negative anti mitochondrial antibody. Serum retinol level was also not decreased in this patient.

On reviewing the literature, the presence of Anti centromere protein B without a definite diagnosis of Systemic sclerosis or CREST may indicate the presence of some other severe underlying rheumatic or connective tissue disease^[10]. Hence in spite of the negative profile an element of autoimmunity was thought to be the cause for central sterile corneal melt based on the anti Centromere protein B positivity.

IV. Conclusion

In our study the ocular symptoms were the reason, in three out of four patients seeking medical care. These patients upon further careful systemic and ocular evaluation were diagnosed to have systemic autoimmune disease. Also, the systemic association was different in all the four cases indicating the versatile etiology of central corneal melts. Hence it is important to carefully evaluate any given case of sterile corneal melts to look for systemic associations, as it can be life saving in some cases as in our case of Takayasu arteritis. Further early diagnosis of such associated systemic autoimmune diseases can help to reduce the systemic morbidity in addition to visual rehabilitation.

Author credentials

1. Dr.M.Hemanandini M.S.D.O.,
HOD & Associate Professor of Ophthalmology
2. Dr.C.Jeevakala M.S.D.O.,
Assistant Professor of Ophthalmology
3. Dr.K.Nithya M.S-III Year
Post graduate Resident in Ophthalmology,
Coimbatore Medical College Hospital, Coimbatore.Tamilnadu, India.
4. Dr P.A .Kochami MS- I Year
Post graduate Resident in Ophthalmology,
Coimbatore Medical College Hospital, Coimbatore.Tamilnadu, India

Clinical Investigators

Provided and cared for study patients

1. Dr. Kumar Natarajan, M.D,
Professor of Medicine,
Coimbatore Medical College Hospital, Coimbatore. Tamilnadu. India
2. Dr. P. Vishnuram, M.D,
Assistant Professor of Medicine,
Coimbatore Medical College Hospital, Coimbatore. Tamilnadu. India
3. Dr. A. Mahesh,M.D.D.M,
Rheumatologist,
Coimbatore Medical College Hospital, Coimbatore. Tamilnadu. India.

References

- [1]. Jack J Kanski Brad Bowling. Clinical Ophthalmology A SYSTEMATIC APPROACH. Seventh edition, page 202,203.
- [2]. Rheumatology Marc C. Hochberg ... [et al.].—5th ed.
- [3]. M I Jayson, D L Easty. Ulceration of the cornea in rheumatoid arthritis. *Ann Rheum Dis* 1977;36:428-432.
- [4]. Bernauer W, Ficker LA, Watson PG, Dart JKG. The management of orneal perforations associated with rheumatoid arthritis. *Ophthalmology* 1995;102:1325-37.
- [5]. Messmer E, Foster S. Destructive corneal and scleral disease associated with rheumatoid arthritis: medical and surgical management. *Cornea* 1995;14:408-17.
- [6]. Amira Stylianides, Mark N.A. Jones, Stephen B Kaye. Rheumatoid arthritis – associated corneal ulceration: mortality and graft survival.
- [7]. Hung-Chi Jesse Chen, Ju-Chuan Cheng, Ching-Hsi Hsiao . Systemic Lupus Erythematosus presenting as corneal perforation . Volume 21, Issue 2, June 2009, pp 169-171.
- [8]. JB Imboden, DB Hellmann, JH Stone. *Current Rheumatology Diagnosis & Treatment*, Second Edition. McGraw-Hill, 2007.
- [9]. J A Goldman. Anticentromere antibody in patients without CREST and scleroderma: association with active digital vasculitis, rheumatic and connective tissue disease. *Ann Rheum Dis*. 1989 Sep; 48(9): 771-775.