Sjogren syndrome and kidney involvement

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خانم۳۰ ساله با سابقه سندرم شوگرن از ۱۰ سال قبل بدلیل راش پوستی و افزایش کراتینین بستری شده و مشاوره نفرولوزی برای وی تقاضا شده

در ازمایشات: اوره =۴۵ میلی گرم در دسی لیترو کراتینین ۱/۶ میلی گرم در دسی لیتر

هموگلوبین =گرم در دسی لیتر۹ و در ازمایش ادرار:

Pr++

Blood++

در ادرار ۲۴ ساعته :کراتینین ۹۱۲ و پروتیین ۲۰۸۶ و حجم ۲۰۰۰ است

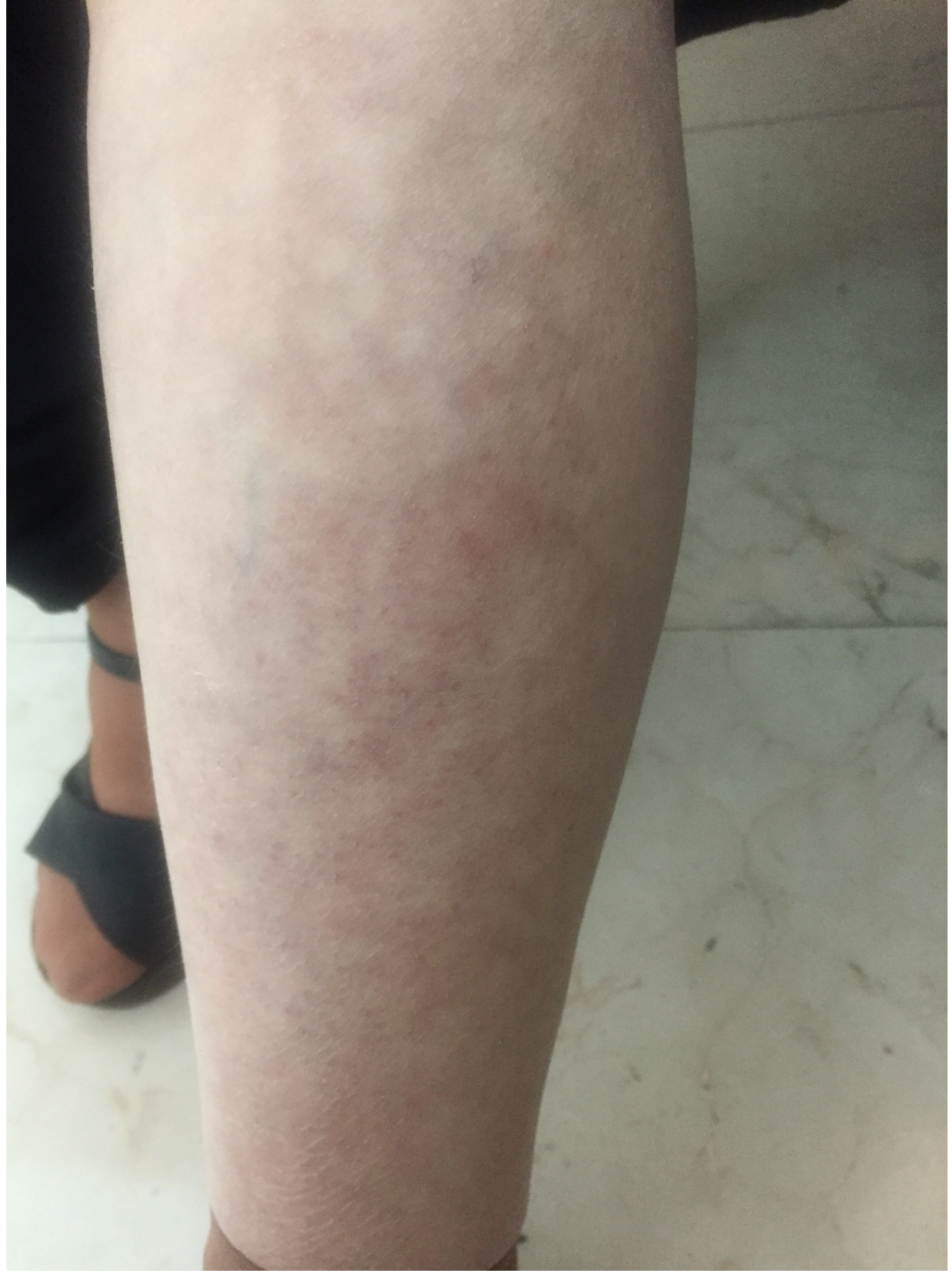
کرایوگلوبولین++

شرح حال دارویی قبل از بستری :

قرص آزاتیوپرین -پردنیزولون و هیدروکسی کلروکین است

در تاریخچه در سال ۱۳۹۱سیکلوفسفامایدبمدت ۶ ماه دریافت کرده بود و متذکر است چند نوبت IV IG دریافت کرده که مقدار ان را نمیداند.

- در معاینه نکات مثبت : فشار خون ۱۵۰/۱۰۰میلی متر جیوه میباشد. وزن وی ۵۹ کیلوگرم است
- مخاط رنگ پریده و ادم ۲+اندام تحتانی دارد و در اندام تحتانی تصویر زیر دیده میشود



Introduction

- Primary Sjögren's syndrome (pSS), described by Henrik Sjo¨gren in 1933, is a chronic inflammatory disorder characterized by a wide spectrum of clinical manifestations varying from limited exocrine dysfunction to extraglandular, multi-systemic organ involvement.

- The histological hallmark is a focal lymphocytic infiltration of the exocrine glands, presumably resulting into sicca symptoms, such as xerostomia and keratoconjunctivitis sicca seen in the majority of patients.

- Most notably, 30–50% of the pSS patients develop systemic manifestations during the course of their disease and about 5% develop non-Hodgkin lymphoma largely of B cell lineage.

Introduction

- It may occur alone (primary SSpSS) or in association with other autoimmune diseases (e.g. SLE).
- It classically occurs in middle-aged women, but can occur in other groups.
- It has been estimated to affect 0.05-0.23% of the adult population.
- It may be asymptomatic with the incidental discovery of autoantibodies or it may present with the sicca complex, constitutional symptoms or other organ involvement.

Sjögren's Syndrome Symptoms

- **Dry eyes.** .
- **Dry mouth.**

- Because Sjögren’s syndrome primarily involves the eyes and mouth, you may have cavities and infections of the mouth such as oral thrush (a yeast infection) and vision problems including corneal ulcers.

- Sjögren’s syndrome can often be difficult to diagnose, as these symptoms are very general and can indicate a range of conditions.

More Sjogren's Syndrome Symptoms

- The disease can affect parts of the body other than the eyes and mouth. You may experience dryness in your nose or throat or on your skin. Sjögren's syndrome can also affect the joints, lungs, kidneys, blood vessels, digestive organs and nerves, causing symptoms such as:
- Swollen glands, specifically behind the jaw and in front of the ears
- Joint pain, swelling or stiffness
- Prolonged dry skin
- Skin rashes
- Chronic dry cough
- Vaginal dryness
- Problems urinating, including pain, urinating more than usual, getting up at night often to urinate and needing to urinate suddenly
- Numbness or tingling in your fingers and toes
- Prolonged fatigue and/or a feeling of tiredness that keeps you from daily activities

The main immunological markers of pSS

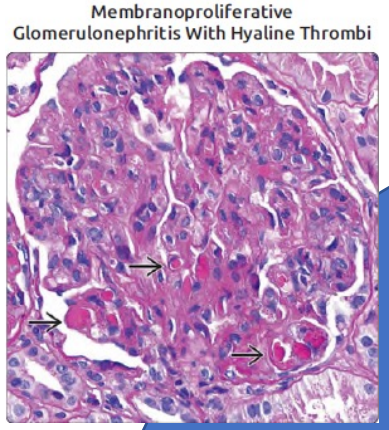
- Anti-SSA,
- Antinuclear antibodies,
- Rheumatoid factor,
- Low complement,
- Hypergammaglobulinemia.

Renal involvement in pSS-1

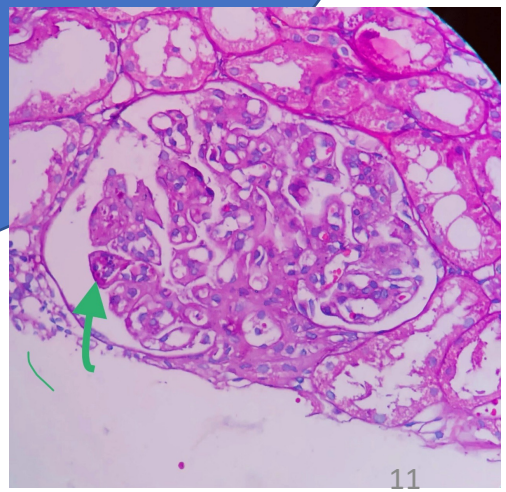
- Renal involvement in pSS was first described in the 1960s with reports of the typical tubular defects.
- These included biopsy series that highlighted tubulointerstitial inflammation as the most common renal lesion.
- Renal involvement in pSS is the result of two distinct pathophysiological processes:

➢epithelial disease with a predominantly mononuclear lymphocytic infiltration resulting in tubulointerstitial nephritis (TIN) and

➢non-epithelial disease with a secondary immune complex-mediated process resulting in glomerulopathy.



Pathology of kidney biopsy in Sjogren,s syndrome



MICROSCOPIC

- Chronic tubulointerstitial nephritis
  - Plasma cell-rich infiltrate
  - Tubular atrophy and interstitial fibrosis

- Acute tubulointerstitial nephritis
  - Active tubulitis and edema

- Glomerulonephritis
  - Many forms described,most commonly MPGN and membranous GN

- ~ 85% have diffuse membranoproliferative pattern (MPGN)
  - Duplication or "tram tracking" of GBM appreciated most readily on PAS or Jones stain
  - Mesangial hypercellularity and increased matrix
  - Diffuse intracapillary hypercellularity with glomerular capillary loop occlusion
    - Leukocytes, particularly monocytes, compose the hypercellularity
    - May be exudative (neutrophils prominent)

– > 50% have pseudothrombi

□ Eosinophilic, rounded refractile PAS(+) deposits in capillary lumina

Known as pseudothrombi since they are not actually composed of fibrin

– ~ 15% have crescents

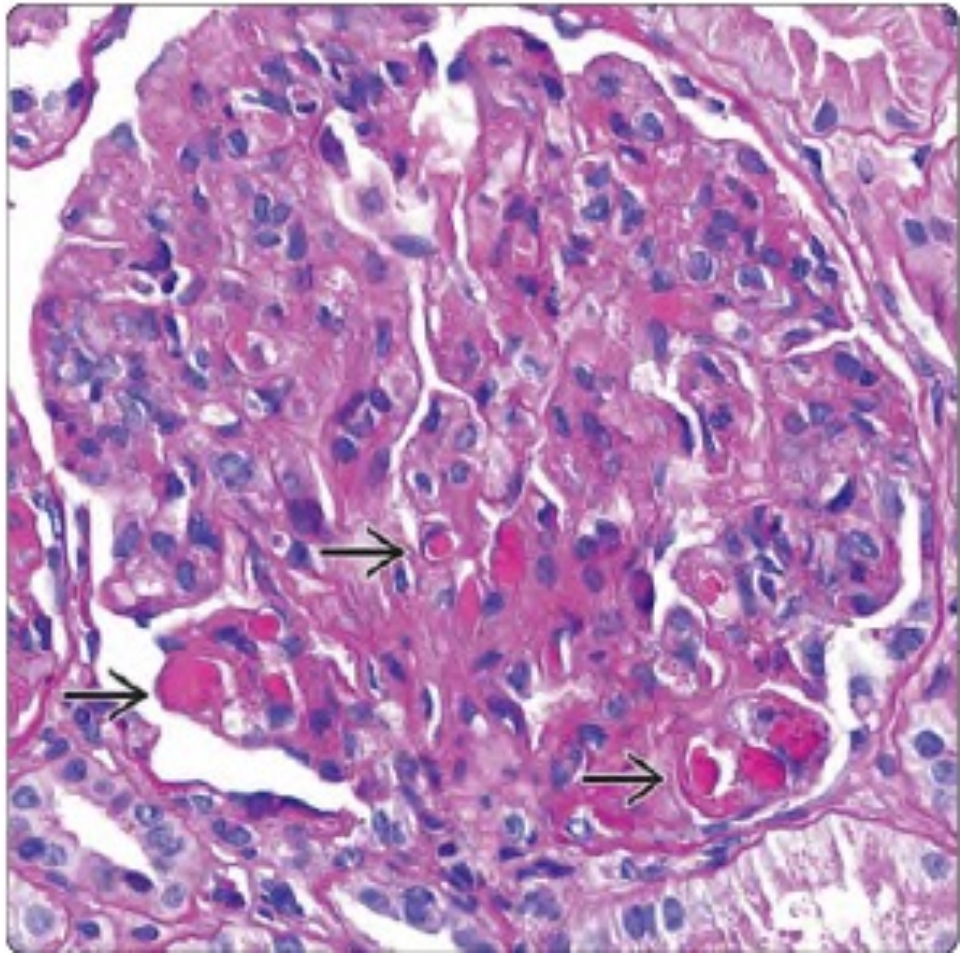
○ ~ 8% have mesangial proliferative pattern

– Global and diffuse slight mesangial matrix expansion;

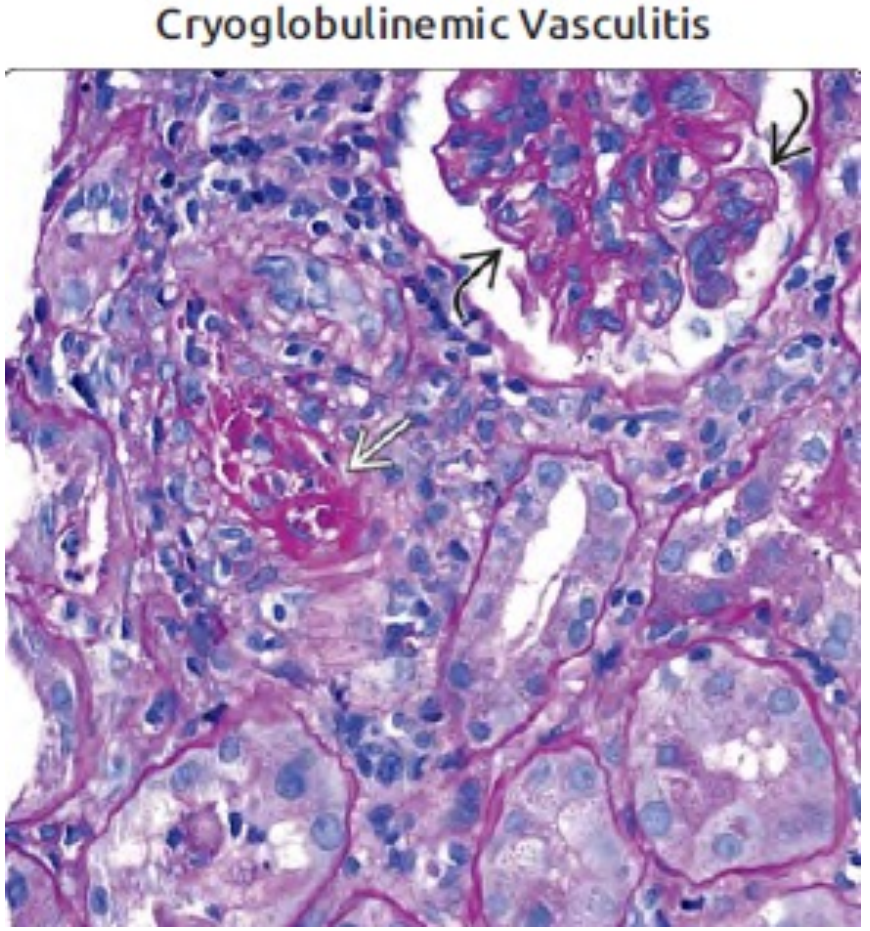
○ ~ 8% have focal membranoproliferative pattern

– Mild and irregular proliferation, exudation, and thickening of capillary wall;

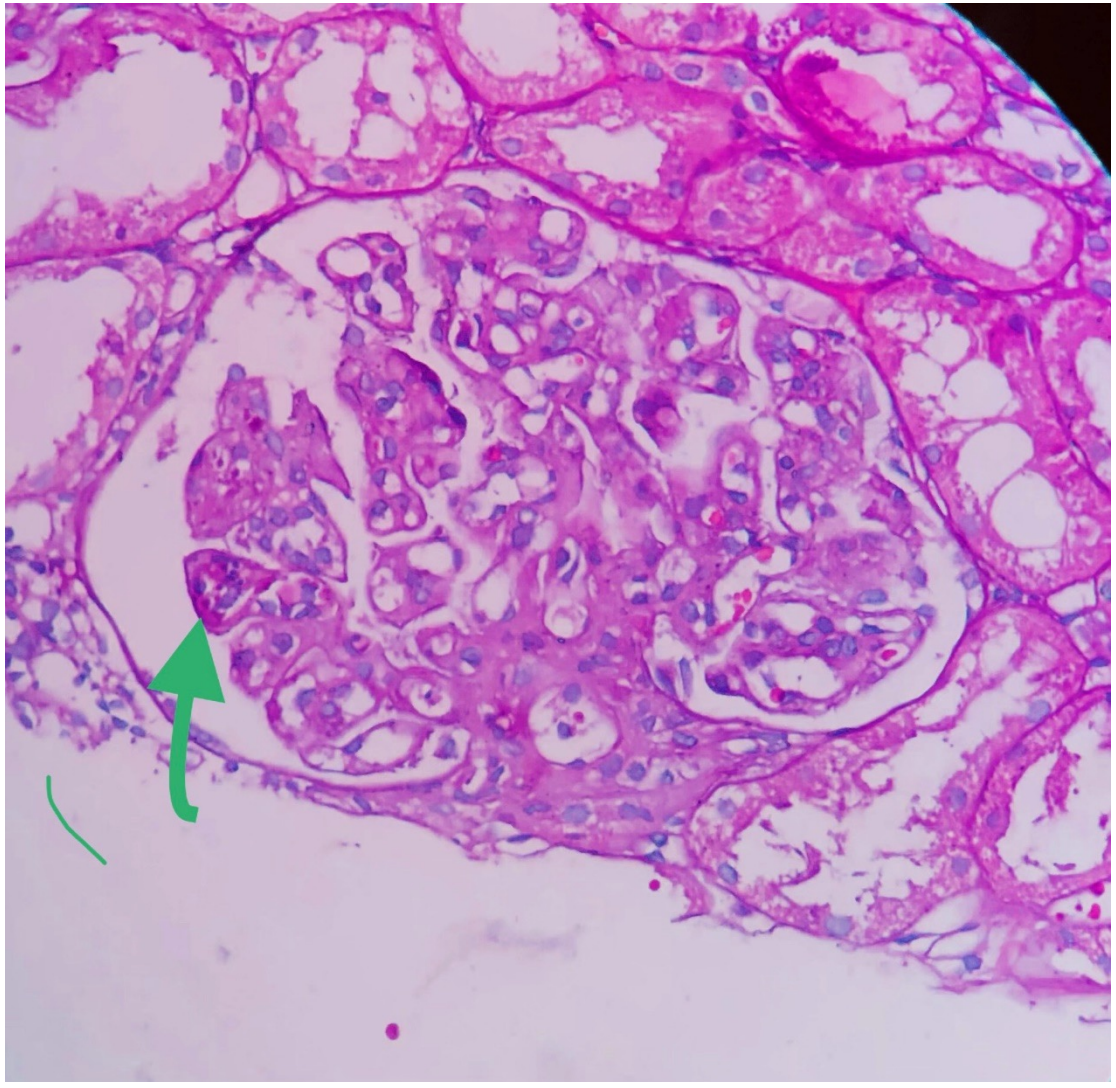
Membranoproliferative Glomerulonephritis With Hyaline Thrombi



- Vasculitis: *cryoglobulinemia associated*
- Thrombotic microangiopathy

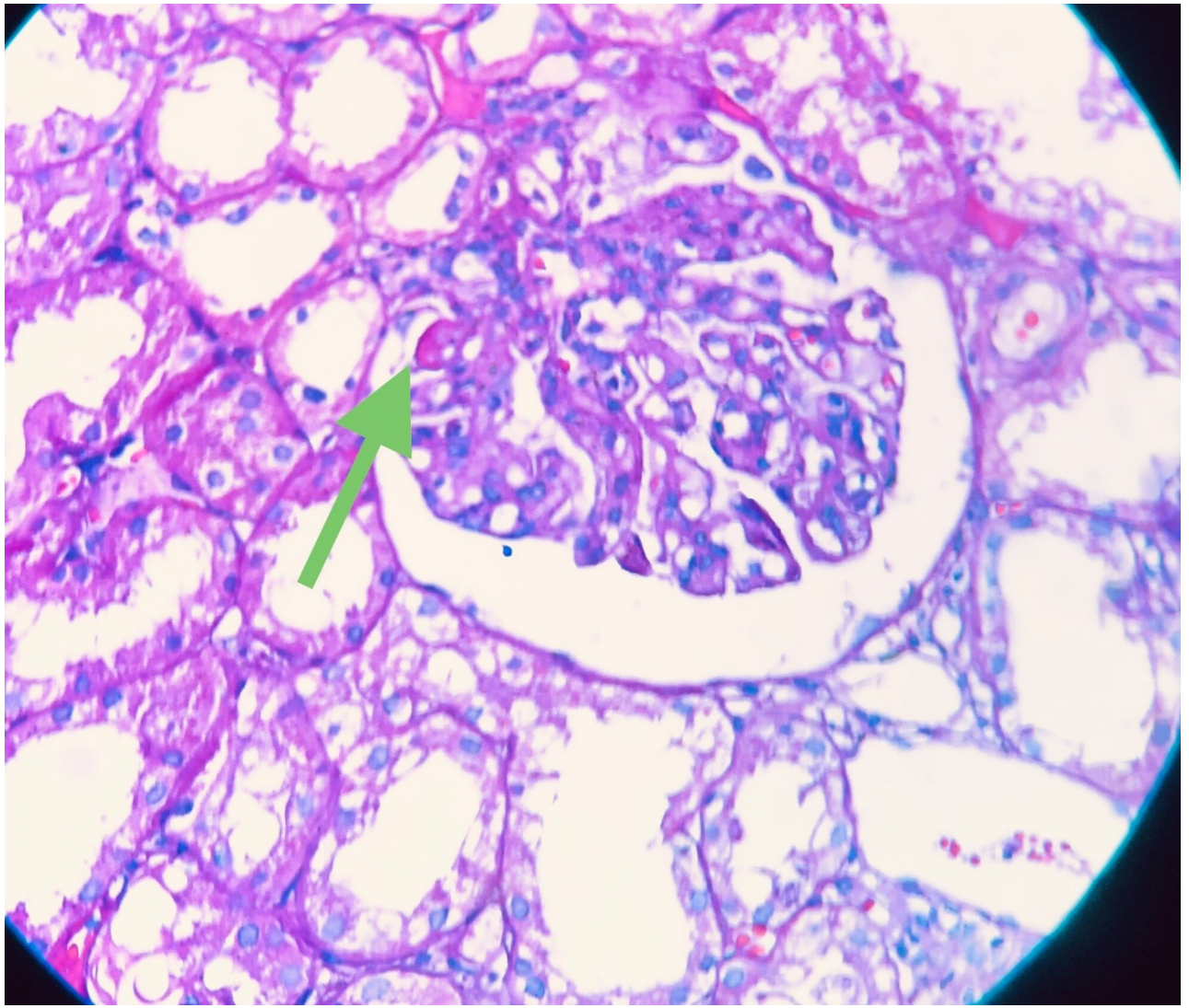


PMN infiltration in the capillaries of biopsy



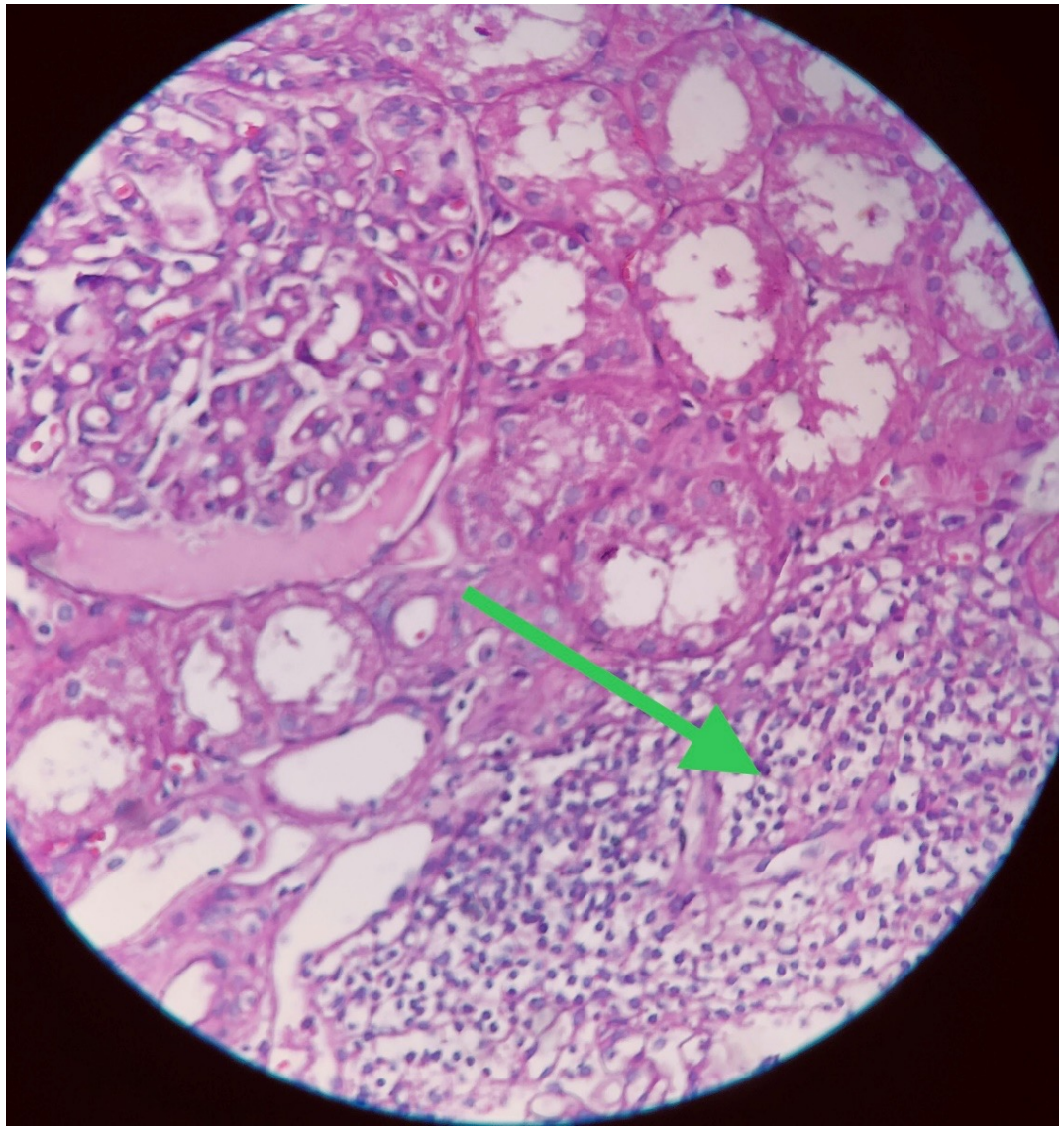
Pseudothrombus and endocapillary proliferation

but not MPGN



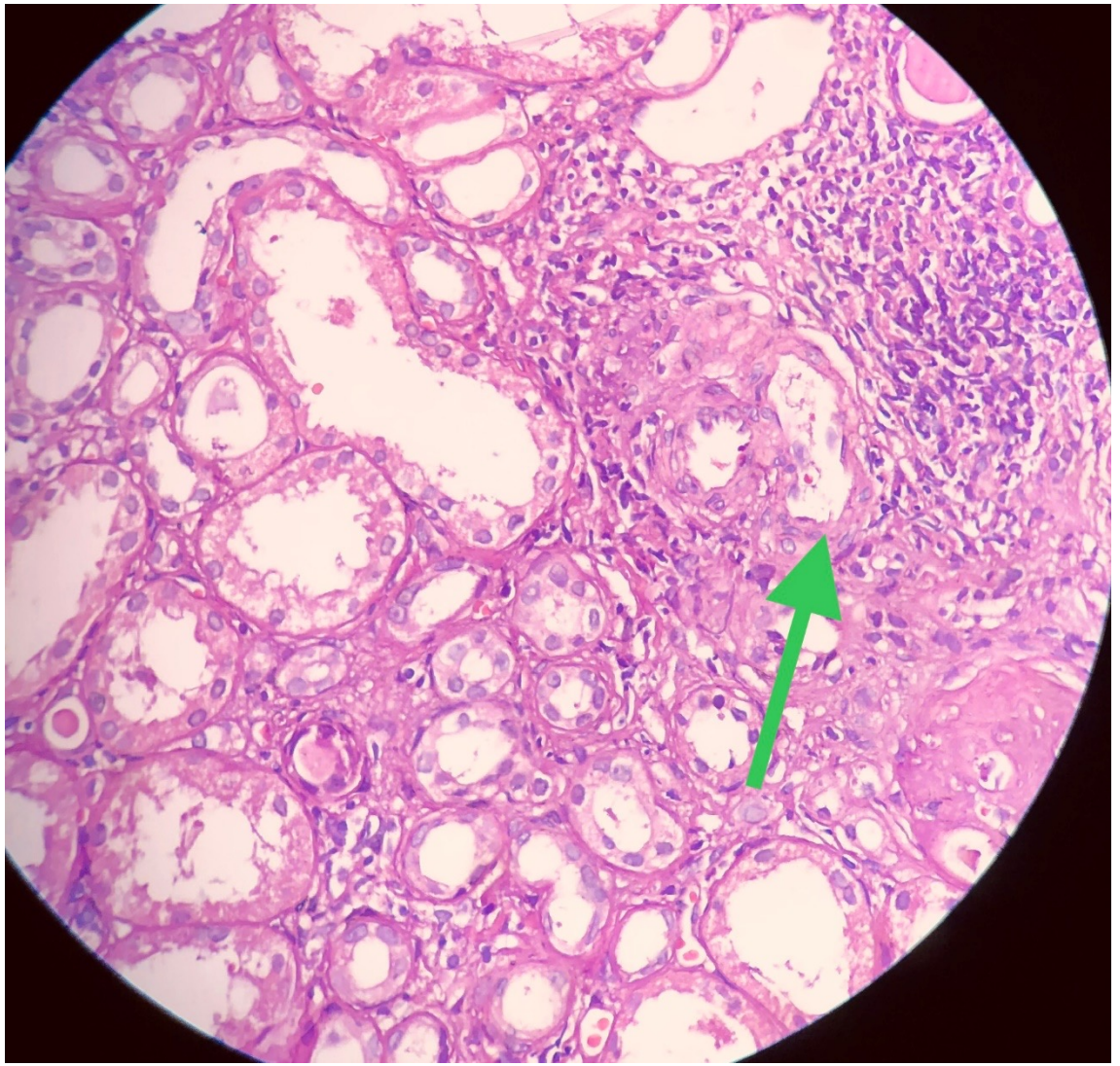
Lymphocytic infiltration in scarred area

but not plasma cell infiltration



Small interlobular artery in the biopsy

but not vasculitis



Epithelial renal disease in pSS

Histopathology of epithelial pSS

- CD8+ T cells were the predominant cell that was responsible for tubular invasion.
- In salivary glands, the type of infiltrate varies and it has been suggested that specific therapies could be employed dependent on the predominant cell subtype found at the presenting biopsy
- Whether the histological severity or the predominant cell subtype correlate with patient outcome is unclear.
-

T cells

- CD4+ cells make up the bulk of the T cells present in labial salivary glands and there is evidence for a role of both Th1 and Th2 subtype.
- IL-22, a cytokine produced by Th17 cells, has increased expression in salivary gland biopsies of pSS.
- After treatment with rituximab (RTX), tissue expression of IL-17 decreased,
- RTX appears to have more than just an anti B cell effect

B cells

- Evidence for an important role of B cells in pSS includes a high prevalence of autoantibodies, hypergammaglobulinaemia, increased risk of lymphoma, germinal centre formation on histology and response of the disease to anti B cell therapy.

- A range of different autoantibodies are seen in pSS patients.

Tubular defects :

TIN may cause different defects in tubular function

Distal renal tubular acidosis:

- dRTA is due to inadequate H+ secretion in the cortical collecting duct by the acid-secreting by intercalated cells.
- dRTA may be complete, with systemic metabolic acidosis and inappropriately alkaline urine, or incomplete, where the acidification defect is insufficient to cause overt acidosis
- dRTA causes urinary K+ wasting.
- Patients may present with hypokalaemic symptoms, including paralysis .
- dRTA may also manifest as nephrolithiasis or nephrocalcinosis , causing renal colic or urosepsis.
- Supportive management of dRTA includes supplementation of bicarbonate and potassium (e.g. oral potassium citrate) and close nephro-urological follow-up to prevent complications from nephrolithiasis.

Nephrogenic diabetes insipidus

- The initial reports of tubular dysfunction in pSS were of nephrogenic diabetes insipidus (NDI) ,it is caused by dysfunction of the principal cells of the collecting duct.
- Presentation is with polydipsia, polyuria and nocturia.

- NDI in pSS is a disease of adulthood, and the thirst mechanism is almost always robust enough to maintain the serum sodium within the normal range ,thus specific therapies for NDI (e.g. NSAIDs, diuretics) are not warranted.

Proximal tubular dysfunction

- Proximal tubular cells (PTCs) are responsible for the reabsorption of most filtered electrolytes as well as low molecular weight (tubular) proteins, amino acids, glucose and urate.
- Together, tubular proteinuria, aminoaciduria, glycosuria, phosphaturia, uricosuria and bicarbonaturia comprise the Fanconi syndrome of generalized PT C dysfunction.
- This may lead to osteomalacia as a consequence of phosphate wasting.
- The full Fanconi syndrome is rare in pSS TIN (3%)but evidence of PTC dysfunction is much more common.
- The most sensitive marker, tubular proteinuria (e.g. retinol binding protein), is present in 10-42% in the general pSS series and up to 87% of those with known renal disease.

Other acquired tubular defects

- There are case reports of pSS affecting other tubular segments, causing acquired Bartter or Gitelman-like syndromes .

Non-epithelial renal disease in pSS

- The majority of glomerular disease reported in pSS is immune complex mediated, usually the characteristic

(MPGN), which is the most common glomerular lesion in pSS.

❖ MPGN is caused by the deposition of immune complexes, which are often cryoglobulins

❖Cryoglobulins are the result of B cell expansion causing the synthesis of IgM, which binds antigen and IgG.

❖ These immune complexes bind to endothelial cells, activate complement and recruit inflammatory cells, causing small vessel vasculitis.

Non-epithelial renal disease in pSS

- ❖GN in pSS occurs later in the disease course than TIN.
- ❖ It is also associated with lymphoma development and thus increased morbidity and mortality
- ❖Glomerulopathy presents with typical glomerular features including haematuria, proteinuria, hypertension, reduced glomerular filtration rate and nephrotic syndrome

TESTING FOR RENAL DYSFUNCTION IN SJOGREN'S SYNDROME

frontiers in Immunology

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Biomarkers and Diagnostic Testing for Renal Disease in Sjogren's Syndrome

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TESTING FOR RENAL DYSFUNCTION IN SJOGREN'S SYNDROME: FROM SCREENING TO CONFIRMATION

- Due to the progressive nature of renal disease in pSS and the overall excellent response to treatment, timely diagnosis is essential.
- It is suggested that screening for all patients should include urinalysis and serum creatinine when manifestations of systemic disease are present.
- Furthermore, serum electrolytes should be measured in all patients in order to detect disturbances due to TIN presenting as RTA.
- These should not be limited to measurements of sodium and potassium but should include chloride and bicarbonate.
- This will allow detection of hyperchloremic metabolic acidosis and potential hypokalemia

TESTING FOR RENAL DYSFUNCTION IN SJOGREN'S SYNDROME: FROM SCREENING TO CONFIRMATION

- Phosphate and uric acid, relevant to diagnosis of pRTA, should be included in the serum panel.
- Furthermore, urinary analysis of pH, osmolality, proteinuria, calciuria, citraturia, urinary sediment, should be performed.
- As it was mentioned before, testing for proteinuria should not be specific for albumin, so that tubular proteinuria can be reliably diagnosed.
- Renal sonography should be similarly performed twice a year if hypercalciuria is present, to rule out nephrolithiasis
- In this case, a nephrologist may be consulted and kidney biopsy taken into consideration.

TESTING FOR RENAL DYSFUNCTION IN SJOGREN'S SYNDROME: FROM SCREENING TO CONFIRMATION

- When hyperchloremic acidosis is detected in the patient's serum, the following diagnostic approach may be helpful in evaluating the etiology .

➢Firstly, the serum anion gap (AG) should be calculated to confirm the presence of an hyperchloremic, or normal AG, metabolic acidosis.

➢A normal AG is usually considered to be 8–12.

➢ Hypoalbuminemia may lead to pseudonormalization of the AG, so that 2.5 mEq/L should be added to the AG measurement for each 1 g/dL decrease in albumin levels from 4.5 g/dL.

TESTING FOR RENAL DYSFUNCTION IN SJOGREN'S SYNDROME: FROM SCREENING TO CONFIRMATION

- Hypophosphatemia can be observed in both dRTA and pRTA.
- Hypophosphatemia may lead to acquired hypophosphatemic osteomalacia, a disease of bone metabolism which presents with bone pain, weakness and increased susceptibility to fractures.


Treatment

Management

- No systemic immunosuppressive treatment is of proven benefit in pSS and treatment is largely based on extrapolations from treatment of other inflammatory conditions (e.g. SLE) and small open-label studies.

- While HCQ or MTX is the mainstay of uncomplicated pSS, steroids, CYC, anti-proliferative agents, calcineurin inhibitors and biologic agents (e.g. RTX) have been used to manage resistant or extraglandular disease.

Current treatment recommendations for systemic manifestations

- The systemic clinical spectrum in pSS is clearly dominated by articular involvement (ca. 50%), followed by lung (15%) as well as cutaneous and peripheral nerve involvement (10%), with renal, and central nervous system (CNS) manifestations affecting less than 5% of pSS patients

EULAR recommendations for treatment

- Given this heterogeneous manifestations, treatment of systemic disease should be tailored according to severity of the involved organs using the European Sjögren's Syndrome Disease Activity Index (ESSDAI) definitions.
- This composite scoring system includes 12 domains (constitutional, lymphadenopathy, glandular, articular, cutaneous, respiratory, renal, muscular, peripheral nervous system, CNS, haematological and biological) with different levels of activity.
- As important prerequisites, a EULAR Task Force on pSS developed two new tools for standardized pSS outcomes measures:
- Assessing disease activity and patient-reported outcomes: EULAR Sjögren's syndrome disease activity index (ESSDAI,) and patient- reported indexes (ESSPRI,).
- Together with the recent publication of updated EULAR recommendations for the management of Sjögren's syndrome, these documents provide a framework for a more standardized and homogeneous approach to align clinical studies and management of pSS.

TIN

- In Maripuri et al.’s cohort ,88% were treated with steroids and 53% had additional immunosuppression.
- The majority had stable renal function; only 18% had progressive renal disease.
- The Greek group gave supportive treatment but not immunosuppression to those with interstitial disease.

GN

- Treatment of glomerular disease is based on the histological lesion.
- Most patients were treated with steroids with or without an additional immunosuppressant or plasma exchange.

cryoglobulinaemic vasculitis in the setting of pSS.

- The CryoVas study included 242 cases of non-infectious vasculitis, 25% of which were due to pSS.
- In this retrospective cohort, treatment with RTX and corticosteroids was superior to either corticosteroids alone or corticosteroids in combination with an alkylating agent.
- We therefore favour a steroid and RTX regimen for cryoglobulinaemic vasculitis in the setting of pSS.
- We reserve plasma exchange for rapidly progressive glomerular or life- threatening disease.

RTX in pSS

- There has been much interest in the use of RTX in pSS in the light of our understanding of the important role B cells play in disease pathogenesis, but also because of the effect RTX has on T cells, in particular modulation of the Th17 response .
- The majority of recent randomized data in pSS concerns RTX use.
- .

Belimumab , secukinumab and Abatacept in Treatment of PSS

- pSS patients may have increased levels of B cell activating factor ,especially those with lymphoma.
- Belimumab, an anti B cell activating factor antibody, has been trialled successfully in phase 2 studies in pSS ,improving symptom scores.
- As Th17 cells appear to have an important role in epithelial inflammation in pSS, secukinumab, an anti- IL17 antibody, may have a role in the treatment of pSS, including renal SS.
- Furthermore, abatacept is another potential therapy for renal pSS; a recent study showed that it improved salivary histology and saliva production in pSS.

TABLE 2 A summary of the different clinical features associated with the different lesions of renal pSS

	Mechanism	Presentation
Epithelial disease—secondary to lymphocytic infiltration		
Cortical collecting duct dysfunction (α-intercalated cells)	dRTA: hypokalaemia	Asymptomatic (routine blood tests) Paralysis
	dRTA: nephrolithiasis/nephrocalcinosis, hypercalciuria, hyperphosphaturia, hypocitraturia	Asymptomatic (imaging for other indication) Stones, nephrocalcinosis
Cortical collecting duct dysfunction (principal cells)	Concentrating defect	Polydipsia, polyuria, nocturia
Proximal tubular dysfunction	Phosphaturia	Asymptomatic (routine blood tests)
	Proximal renal tubular acidosis	Osteomalacia Stones, nephrocalcinosis
	Glycosuria Low molecular weight proteinuria	Asymptomatic (routine urinalysis)
Loop of Henle and distal convoluted tubule dysfunction (acquired Gitelman or Bartter syndrome)	Salt loss	Asymptomatic (routine bloods or urinalysis)
	Hypokalaemia alkalosis	Non-specific
	Hypomagnesaemia (more common with Gitelman phenotype)	Hypovolaemia and hypotension
	Hypocalciuria (Gitelman phenotype only)	
Non-epithelial disease—secondary to immune complexes		
Glomerular disease and vasculitis	Glomerular disease	Asymptomatic urinary abnormalities Nephrotic syndrome Hypertension Reduced excretory function
	Systemic vasculitis (cryoglobulinaemia)	Systemic upset Fevers Purpura Neuropathy Glomerular disease (MPGN)
Both epithelial and non-epithelial disease		
Decreased excretory function		Asymptomatic (routine blood tests) Uraemia

dRTA: distal renal tubular acidosis; MPGN: mesangioproliferative glomerulonephritis.

Table 2
Treatment of primary Sjögren syndrome according to the ESSDAI score by domain.

Domain	ESSDAI score		
	Low	Moderate	High
Glandular	Abstention (D)	Abstention (D)	*Acute swelling (rule out infection)* 1st line: short-term NSAIDs (D) 2nd line: short-term oral glucocorticoids (0.3) (D) Rescue: rule out other diseases - RTX, BLM (C)
Articular	*Arthralgia* 1st line: NSAIDs (C) 2nd line: HCQ (C)	*Synovitis ≤ 5* 1st line: NSAIDs and HCQ (C)	*Synovitis > 5 (rule out RA)* 1st line: HCQ and GC (0.5) (C) 2nd line: oral ID – MTX, LFM, AZA (C) Rescue: RTX or ABA (B)
Cutaneous	*Annular erythema* 1st line: topical GC or HCQ/GC (0.3) (C) 2nd line: other antimalarials ± GC (0.5–1) (D)	*Cutaneous vasculitis* 1st line: GC (0.3) (C)	*Cutaneous vasculitis* 1st line: GC (0.5–1) (4, C)
Respiratory	*Bronchial involvement* 1st line: inhaled Tx (C)	*ILD* 1st line: GC (0.5): LIP & OP, less NSIP, UIP (C)	*ILD* 1st line: GC (0.5–1): for LIP & OP, less NSIP, UIP (C) 2nd line: oral ID–AZA, MMF, CyA (C) Rescue: CyC, RTX (cryo-vasculitis) (C)
Renal	1st line: symptomatic correction of ketoacidosis/K levels (C)	1st line: GC (0.5) (C) 2nd line: oral ID – MMF, AZA, CyA (C)	1st line: GC (0.5–1) (C) 2nd line: RTX (cryo-vasculitis), CyC (C) Rescue: Pex (life-theratening cryo-vasculitis) (C)
Hematologic	Abstention (D)	*Hemolytic anemia (Hb 8–10)* 1st line: GC (0.5–1)	*Hemolytic anemia (Hb 8–10)* 1st line: GC – ivIG (C) 2nd line: RTX (C) Rescue: consider Pex or Cyc (D) *Immune thrombocytopenia (Plat < 20,000)* 1st line: GC (0.5–1) (C) *Neutropenia (< 500)* Consider G-CSF (in recurrent/severe infections) (D)
Peripheral neuropathy	Abstention	*Axonal PN – sensory* 1st line: control neurological pain + CVV risk	*Axonal PN – motor/Ganglionopathy/CIPD* 1st line: ivIG (C) 2nd line: consider pulses MP (D) Rescue: consider CyC (D) *Multineuritis (rule out non cryo-vasculitis)* 1st line: GC (0.5–1) 2nd line: oral ID or RTX (cryo-vasculitis) Rescue: CyC ± Pex (life-threatening cryo-vasculitis)
CNS	NA	*Lymphocytic meningitis* 1st line: symptomatic, rule out trigger by drugs	*CNS vasculitis/NMODS/Encephalitis* 1st line: GC (0.5–1) (C) 2nd line: CyC (C) Rescue: RTX ± Pex (life-threatening cryo-vasculitis) or Ecu (AQP-4+ NMODS) (C) *Multiple sclerosis-like* Consider specific MS therapy (D)

Letters in brackets indicate the level of evidence (LoE) and grades of recommendations (GoR) according to the Oxford Centre for Evidence-Based Medicine Levels of Evidence (March 2009) (see Table 1). DMARD: disease-modifying antirheumatic drug; ESSDAI: EULAR Sjögren's syndrome disease activity index; IV: intravenous; IVIg: IV immunoglobulins; NA: not applicable (high activity is not listed in the ESSDAI); NSAID: non-steroidal anti-inflammatory drug; RTX: rituximab; BLM: belimumab; HCQ: hydroxychloroquine; GC: glucocorticoids; oral ID: oral immune drugs; MTX: methotrexate; LFM: leflunomide; AZA: azathioprine; ABA: abatacept; ILD: interstitial lung disease; Tx: inhaled nasal steroid; LIP: lymphoid interstitial pneumonia; OP: organizing pneumonia; NSIP: nonspecific interstitial pneumonia; UIP: usual interstitial pneu-

Renal	1st line: symptomatic correction of ketoacidosis/K levels (C)	1st line: GC (0.5) (C) 2nd line: oral ID – MMF, AZA, CyA (C)	Rescue: CyC, RTX (cryo-vasculitis) (C) 1st line: GC (0.5–1) (C) 2nd line: RTX (cryo-vasculitis), CyC (C) Rescue: Pex (life-theratening cryo-vasculitis) (C)

Blocking proinflammatory cytokines

- Type I interferons(IFN) :
- Several studies recognized the IFN signature as one of the most biologically relevant pathways in the pathogenesis of pSS, with regard on extra-glandular involvement, correlation with systemic disease activity and risk for anti-SSA/Ro-associated congenital heart block
- Blocking IFN signaling can be achieved by inhibiting the cytokines of this family (monoclonal antibody), its receptor (i.e. anifrolumab) or intracellularly through JAK/STAT inhibition.

TNF inhibition

- Based on experiences in related rheumatic diseases (i.e. RA), TNF inhibitors were soon assessed for efficacy in pSS patients.
- One RCT evaluated infliximab (103 patients ,another etanercept (14 patients for efficacy in fatigue, pain and sicca symptoms

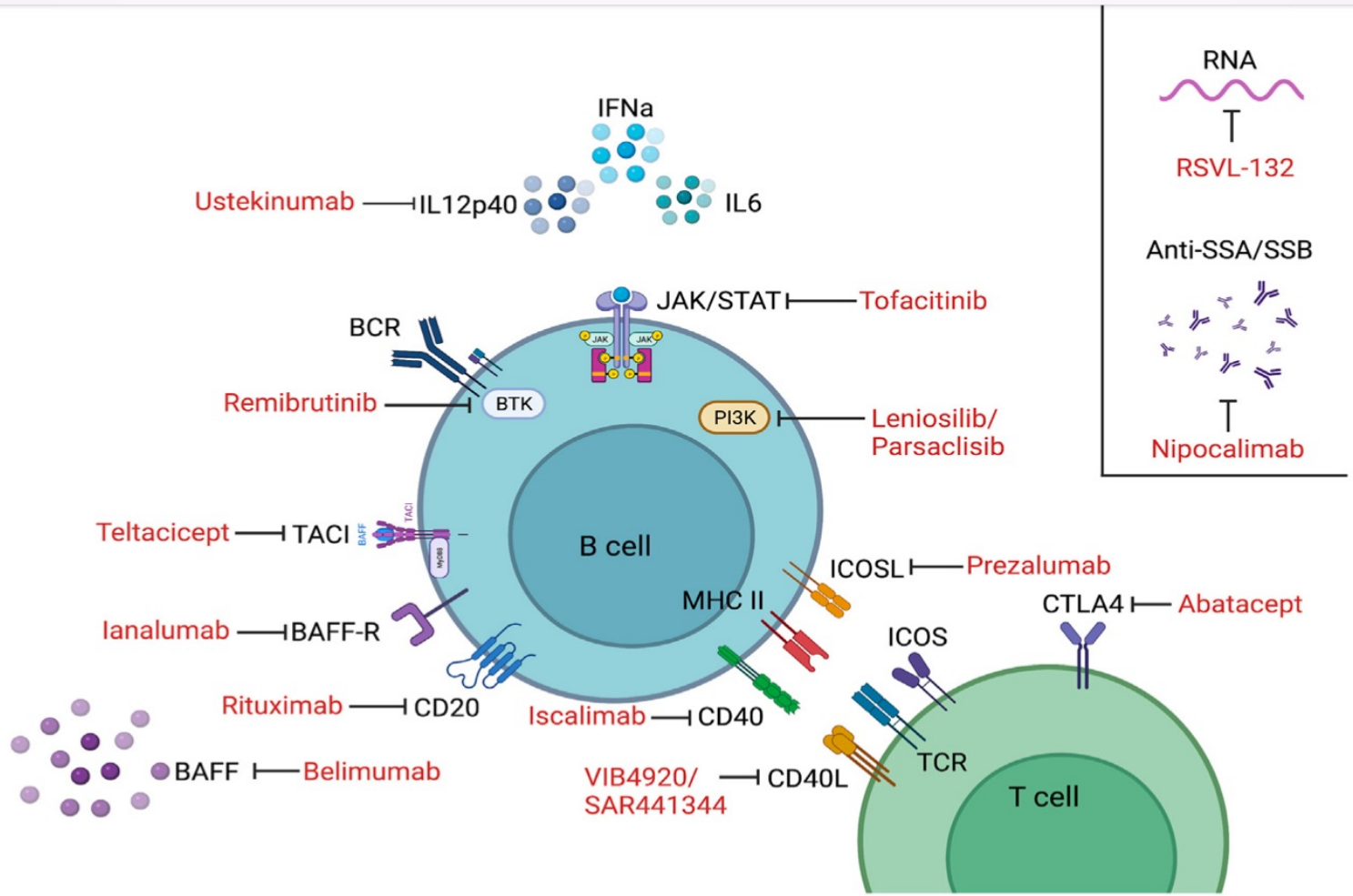


Fig. 1. New therapeutic strategies in primary Sjögren's syndrome. Innovative therapeutic strategies target B cells, T cells, T/B cell interaction, inflammatory cytokines, intracellular signaling and certain selective immune pathways. IFN: interferon; BCR: B cell receptor; BTK: Bruton's tyrosine kinase; TACI: Transmembrane activator and CAML interactor; BAFF: B cell activating factor; MHC II; ICOS: Inducible T-cell Co-stimulator; TCR: T cell receptor; CTLA4: Cytotoxic T-lymphocyte-associated Protein 4; PI3K: Phosphoinositide 3 kinase.

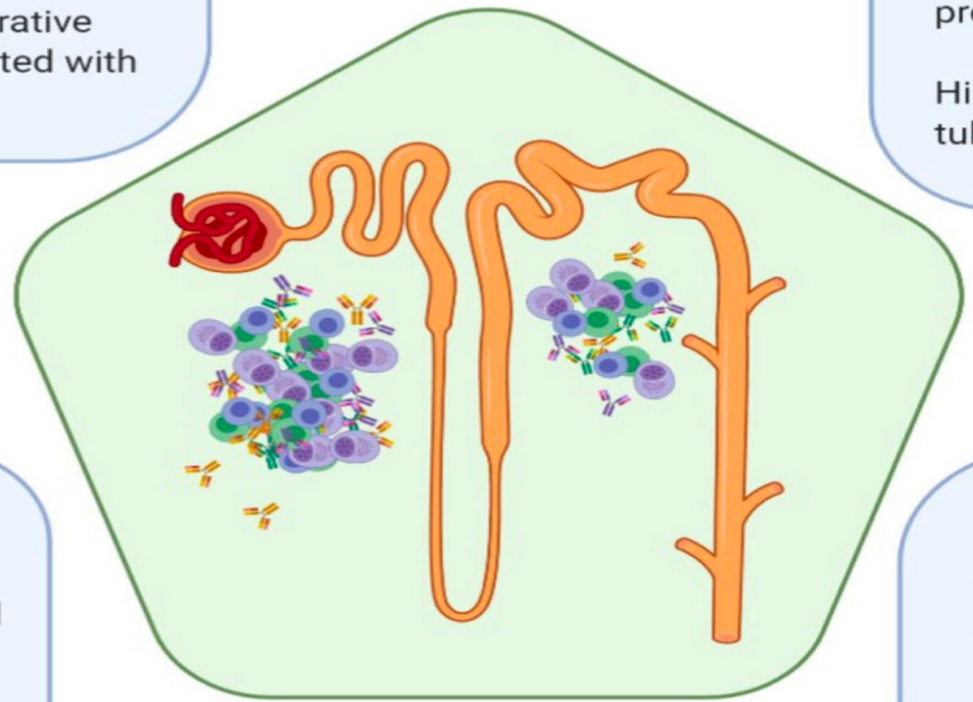

summary

Presentation: Nephritic syndrome (hypertension, haematuria, glomerular proteinuria and renal failure)

Histology: Membranoproliferative glomerulonephritis (associated with cryoglobulinemia)

Presentation: distal RTA (hyperchloremic metabolic acidosis with elevated urinary pH, mild to severe hypokalemia, tubular proteinuria)

Histology: chronic tubulointerstitial nephritis



Presentation: proximal RTA (hyperchloremic metabolic acidosis with low serum phosphate and uric acid, mild hypokalemia and tubular proteinuria)

Histology: chronic tubulointerstitial nephritis

Presentation: nephrogenic diabetes insipidus (polyuria, nicturia, polidipsia, lower urine concentration and lack of response to AVP administration)

Histology: chronic tubulointerstitial nephritis

FIGURE 1 | Most common clinical manifestations of renal disease in pSS and their associated pathologic lesions. RTA, renal tubular acidosis; AVP, arginine vasopressin.

SUMMARY

As an overarching principle, pSS patients should be managed by a multidisciplinary team at centers of expertise.

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REVIEW

Renal Disease in Primary Sjögren's Syndrome

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ABSTRACT

Primary Sjögren's syndrome (pSS) is a chronic autoimmune disorder characterised by lymphocytic infiltration of the exocrine glands, predominantly the salivary and lacrimal glands, leading to sicca symptoms. Patients may have extraglandular disease involving multiple

include renal tubular acidosis with hypokalaemia, Fanconi's syndrome and diabetes insipidus. Glomerular disease is less common and typically involves an immune complex-mediated process. Optimal treatment for kidney diseases in pSS is not established, and treatment is guided by the pattern of disease. For tubulointerstitial nephritis, management involves electrolyte imbalance correction and the use of

EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies

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ABSTRACT

The therapeutic management of Sjögren syndrome (SjS) has not changed substantially in recent decades: treatment decisions remain challenging in clinical practice, without a specific therapeutic target beyond the relief of symptoms as the most important goal. In view of this scenario, the European League Against Rheumatism (EULAR) promoted and supported an international collaborative study (EULAR SS Task Force) aimed at developing the first EULAR evidence and consensus-based recommendations for the management of patients with SjS with topical and systemic medications. The aim

modest) and TF agreement (mostly very high) are provided. The 2019 EULAR recommendations are based on the evidence collected in the last 16 years in the management of primary 2002 SjS patients and on discussions between a large and broadly international TF. The recommendations synthesise current thinking on SjS treatment in a set of overarching principles and recommendations. We hope that the current recommendations will be broadly applied in clinical practice and/or serve as a template for national societies to develop local recommendations.

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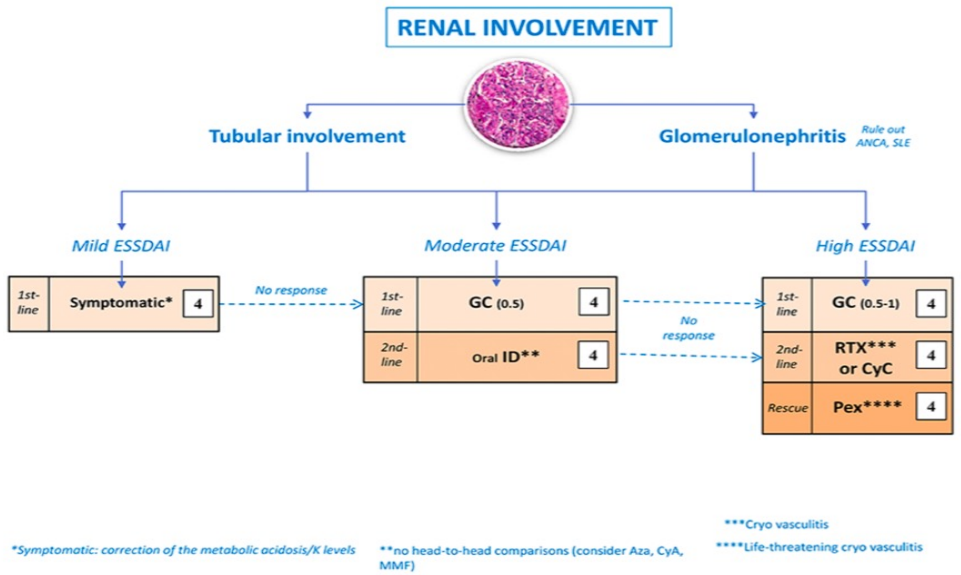

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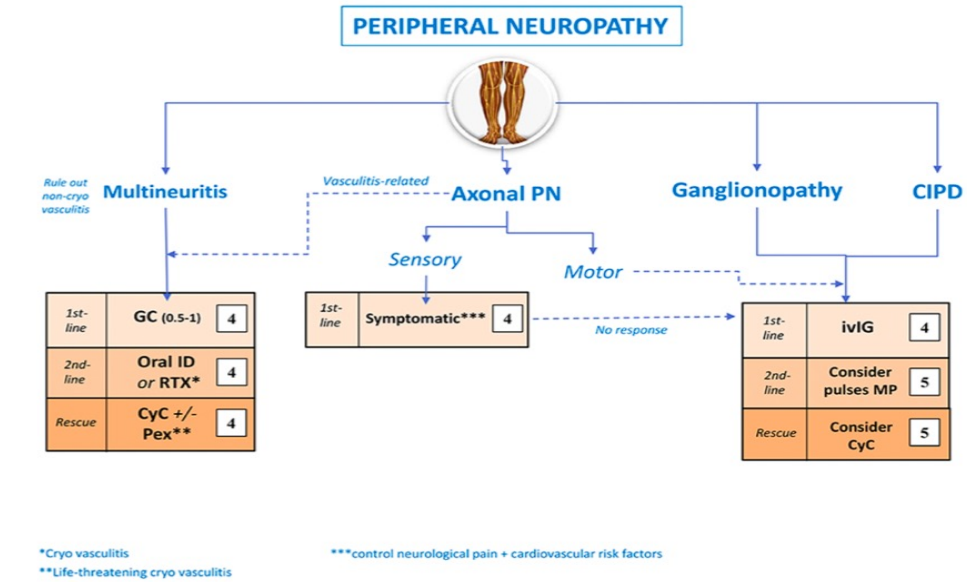

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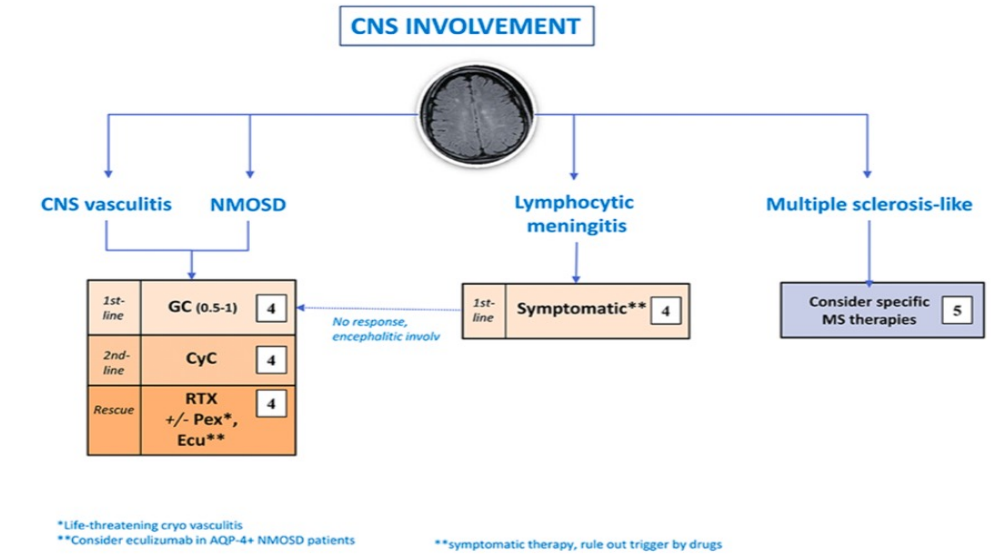

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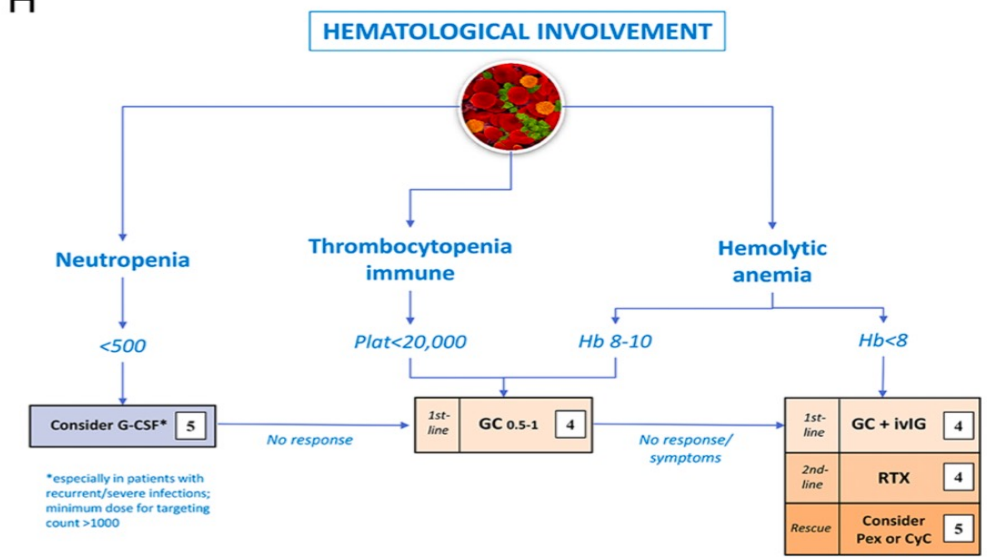

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Review

Current and future treatment in primary Sjögren's syndrome – A still challenging development

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ABSTRACT

Primary Sjögren's syndrome (pSS) is a chronic autoimmune disease characterized by sicca symptoms, systemic manifestations and constitutional symptoms substantially diminishing patient's quality of life. In this review, we summarize recent recommendations for management of pSS patients and current clinical studies in pSS addressing unmet medical needs. Expanding knowledge about disease pathogenesis and the introduction of validated outcome measures, such as capturing disease activity (ESSDAI) and patient-reported outcomes (ESSPRI) have shaped recent developments. In contrast, lack of evidence for current treatment options remarkably limits the management of pSS patients as reflected by the 2019 updated EULAR recommendations for management of Sjögren's syndrome. In this context, symptomatic treatment is usually appropriate for sicca symptoms, whereas systemic treatment is reserved for moderate to severe organ manifestations including care by a multidisciplinary team in centers of expertise. Most promising targets for new treatment modalities are based on immunopathological insights and

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Review

Renal involvement in primary Sjögren's syndrome

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Abstract

SS is a prevalent and underdiagnosed systemic disease that primarily affects epithelial tissue. It may affect renal function either as epithelial disease causing tubulointerstitial nephritis or as an immune complex–mediated glomerulopathy. These lesions may cause a variety of clinical features, both overt and occult. The epithelial disease is mediated by B and T cells, notably the Th17 subtype. We review the prevalence of renal SS, its presentation, likely pathogenesis and treatment.

Key words: Sjögren's syndrome, tubulointerstitial nephritis, autoimmune epithelialitis, Th17 cells, B cells, distal renal tubular acidosis, Fanconi syndrome, autoantibodies, vasculitis, hypocomplementaemia.

Rheumatology key messages

- Renal disease in primary SS is often occult and needs to be specifically looked for.
- Renal disease in primary SS may be associated with serious morbidity and even mortality.
- Renal primary SS is mainly epithelial and is likely to be driven by the same processes as in other tissues.


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