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Original article

AMYLOIDOSIS OF BLADDER AND URETER A CASE REPORT

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ABSTRACT

Abstract:

Introduction :Theamylodosis is a disorder of protein confirmation and metabolism in which insoulable fibrils are deposited extracellularly in body organs causing organ dysfunction and death. It is associated with inherited and inflammatory disorders. Primary amyloidosis of bladder and ureter is a rare disease and easily confused with neoplasm. Hematuria, irritative or obstructive lower urinary tract symptoms and cystitis-like manifestations are the common clinical presentation. **History :**Presenting a case of 61 year old male patient having gross heamturia and irritative urinary tract symptoms. **Conclusion** On radiology there is a wall thickening of bladder with calcification and wall thickening of right lower ureter. Biopsy was sent to histopathology department and histopathological examination demonstrated amyloidosis of bladder and ureter.

Key words : AMYLOIDOSIS, BLADDER ,URETER

INTRODUCTION

Amyloidosis is a heterogenous group of disorder in which misfolded proteins resist to body's catabolic processes and deposit extracellularly as insoluble fibrils in either 1(localized amyloidosis) or in multiple organs (systemic amyloidosis).[1] [2] It was first described by Virchow in 1853.[3] The fibrillar deposits bind a variety of proteoglycans and glycosaminoglycans and the presence of this abundant charged sugar groups in these adsorbed proteins give the deposit staining characteristics. [1] Localised amyloidosis affects only one organ and is associated with aging.[4] Systemic amyloidosis is a progressive, fatal disorder that predominantly affects the heart, liver, kidney, peripheral nerves, respiratory and GI tract.[5] To date 34 human amyloid proteins have been identified.[6]

Amyloid consists of 95% of fibrillar proteins and 5 % of P component and other glycoproteins. There are various forms of amyloid: amyloid light chain(AL) protein, amyloid associated protein (AA), amyloid transthyretin , and b-amyloid protein. Amyloid light chain is the most common type and is associated with both systemic and localized forms.[7] Systemic AL amyloidosis is characterized by monoclonal gammopathy while localized AL amyloidosis manifest as solitary tumor like lesion.[8] In localized disease most common site involved are urinary bladder, respiratory tract, skin and eyes. Localised AL amyloidosis have excellent prognosis with 1% cases progressing to systemic disease.[9]

Amyloid transthyretin is the second most common type and is associated with systemic disease. Due to genetic mutation or aging, transthyretin tetramers dissociate into monomers, aggregate into amyloid fibrils and typically affect the heart and peripheral nerves. Amyloid associated protein amyloidosis is the third most common type and it is also associated with systemic forms.[7] It predominantly affect the kidneys and are secondary to chronic inflammatory conditions.[10]

In patient with amyloidosis the most common affected organ of urinary tract is kidney followed by bladder, lower ureter and upper ureter in the course of both systemic and localized amyloidosis. [11] Endoscopic appearance and symptoms of amyloidosis are very similar to those of bladder cancer.[12] Painless hematuria and cystitis like symptoms are common clinical presentation. Amyloidosis have benign course and is often cured by endoscopic complete resection.

CASE PRESENTATION

A 61 year old male patient presented with a complaint of painless gross hematuria and irritative voiding symptoms for few days. He had no history of urologic or chronic medical disorders. Hemogram was normal.

S.creatinine 1.25 mg/dl (normal range 0.6-1.2 mg/dl)

B2 microglobulin-2568 ng/ml (normal upto 2157.0 ng/ml)

No evidence of m band or monoclonal gammopathy.

CT IVP STUDY findings: Long segmental circumferential wall thickening with luminal narrowing with at places wall calcification involving ureter from distal to iliac crossing till VUJ on right side with mild proximal hydroureteronephrosis.

Histopathology of biopsied material showed amorphous hyalinised eosinophilic material and no malignant cells. Immunostaining of biopsied material with congo red stain confirmed the presence of amyloid fibrils.

DISCUSSION

Amyloidosis may found as unsuscpected anatomical change with no clinical manifestation or may cause serious clinical problems and death. Amyloidois has incidence of 8 million people each year. [13] Urinary bladder is most commonly affected by localized amyloidosis compared to systemic amyloidosis. This disease mostly occurs in older patients but can manifest at any age. Its symptoms and endoscopic appearance display great variety and hence require increased clinical awareness.

Amyloid may or may not be apparent on macroscopic examination but when accumulates in larger amounts, the tissue appears grey with waxy firm consistency. Diagnosis is based on histologic demonstration of amyloid in tissue and its staining characteristics under light microscopy. Histologically, the amyloid deposition is extracellular closely adjacent to basement membrane. H&E stain shows amorphous eosinophilic hyaline extracellular substance. Congo red stain imparts pine or red color to amyloid deposit. Congo red stained amyloid shows apple green birefringence under polarized light. This reaction is caused by beta pleated sheet configuration of amyloid fibirils. On electron microscopy it appears as randomly arranged 8-10 nm non branching fibrils.

Amyloidosis can also be misdiagnosed as malignancy, since it commonly manifests with hematuria and hydronephrosis and sometimes exhibit overlapping histopathological features, which can pose challenges in their differential diagnosis.

Tissue architecture disruption: Both carcinoma and amyloidosis can disrupt the normal architecture of tissues. Cancer cells can invade and disrupt the surrounding tissue structures, while amyloid deposits can accumulate extracellularly, leading to distortion of tissue architecture.

Mass effect: Both carcinoma and amyloidosis can form masses or tumors within tissues.

Similar clinical presentations: Depending on the site and extent of involvement, cancer and amyloidosis can present with similar clinical symptoms such as organ dysfunction, mass effect, or systemic manifestations.

While carcinoma and amyloidosis can share some clinical and histopathological features, careful evaluation of additional histological, immunohistochemical, and clinical parameters is essential for accurate diagnosis and differentiation.

In some cases, the histological appearance of amyloidosis and tuberculosis can overlap or mimic each other, leading to potential challenges in their differentiation on histology. Here are some scenarios where they may appear similar:

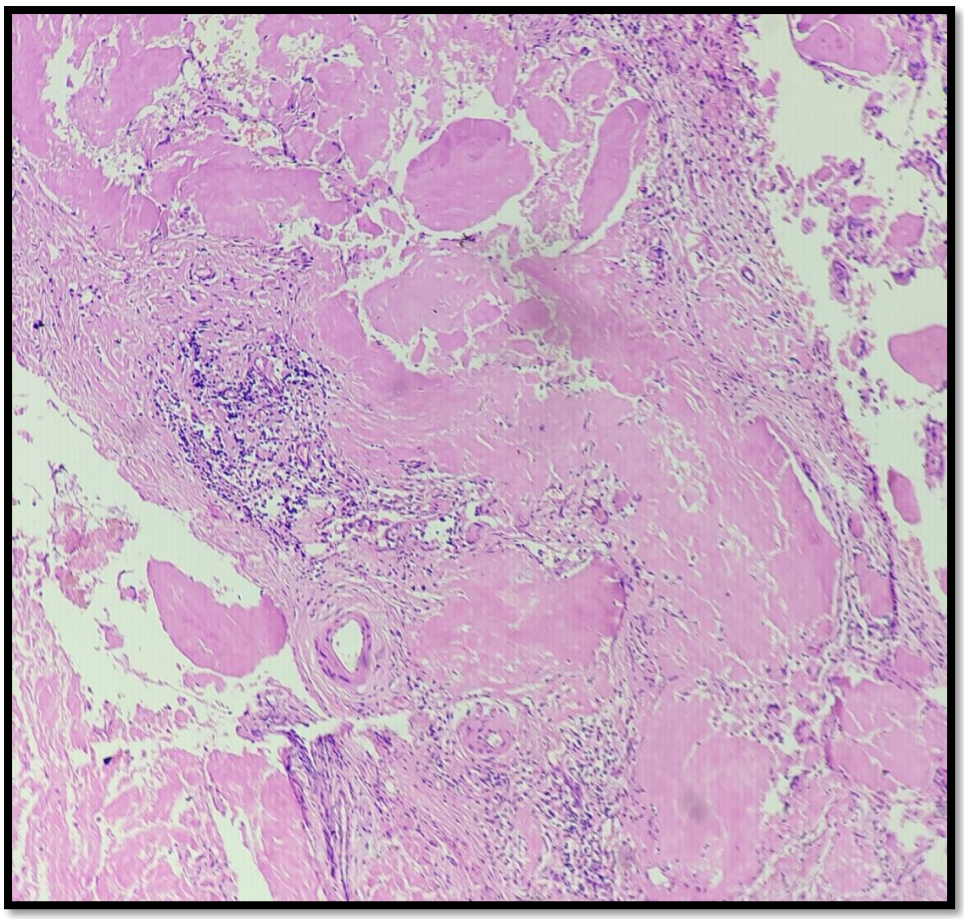
1. Granulomatous amyloidosis: In rare cases, amyloid deposits can be associated with a granulomatous reaction, resembling tuberculosis histologically.

2. Amyloidosis with secondary infection: Amyloid deposits can sometimes become secondarily infected, leading to inflammation and granuloma formation. This can make the histological appearance resemble tuberculosis granulomas. During chronic infections underlying tuberculosis, serum amyloid A (SAA) levels often increase to 1000 folds. [14] This induces cleavage of the SAA protein by cathepsins and MMPs to form N-terminal fragment. [15,16] This truncated form of SAA gets deposited as amyloid fibrils in the extracellular spaces of various organs especially in the liver, spleen and kidney. Moreover, the presence of proteases having an affinity for SAA like MMPs and cathepsins in AA amyloid deposits strengthens the fact that these cleaved SAA fragments form fibrils, leading to the onset of secondary amyloidosis in tuberculosis. Besides, SAA cleaving proteases like MMPs are known to play a role in tuberculous granuloma formation and disease progression post-Mtb infection. [17] Enhanced expression of MMP 1 and MMP 9 is often seen associated with tuberculous granuloma of TB patients. [18] Cathepsins, another class of proteases specific for SAA cleavage also contribute to tuberculous granuloma formation.

3. Coexistence of amyloidosis and tuberculosis: In patients with concurrent amyloidosis and tuberculosis, both histological patterns may be present in the same tissue sample, further complicating the interpretation.

4. Atypical presentations: In some cases, tuberculosis may present atypically without classical granulomas or with sparse inflammation, making it difficult to distinguish from other diseases including amyloidosis solely based on histology.

To overcome these challenges and ensure accurate diagnosis, additional tests such as special staining for amyloid (e.g., Congo red stain) and acid-fast staining for tuberculosis should be performed. Additionally, clinical correlation and consideration of the patient's history, symptoms, and other laboratory findings are essential for reaching the correct diagnosis.



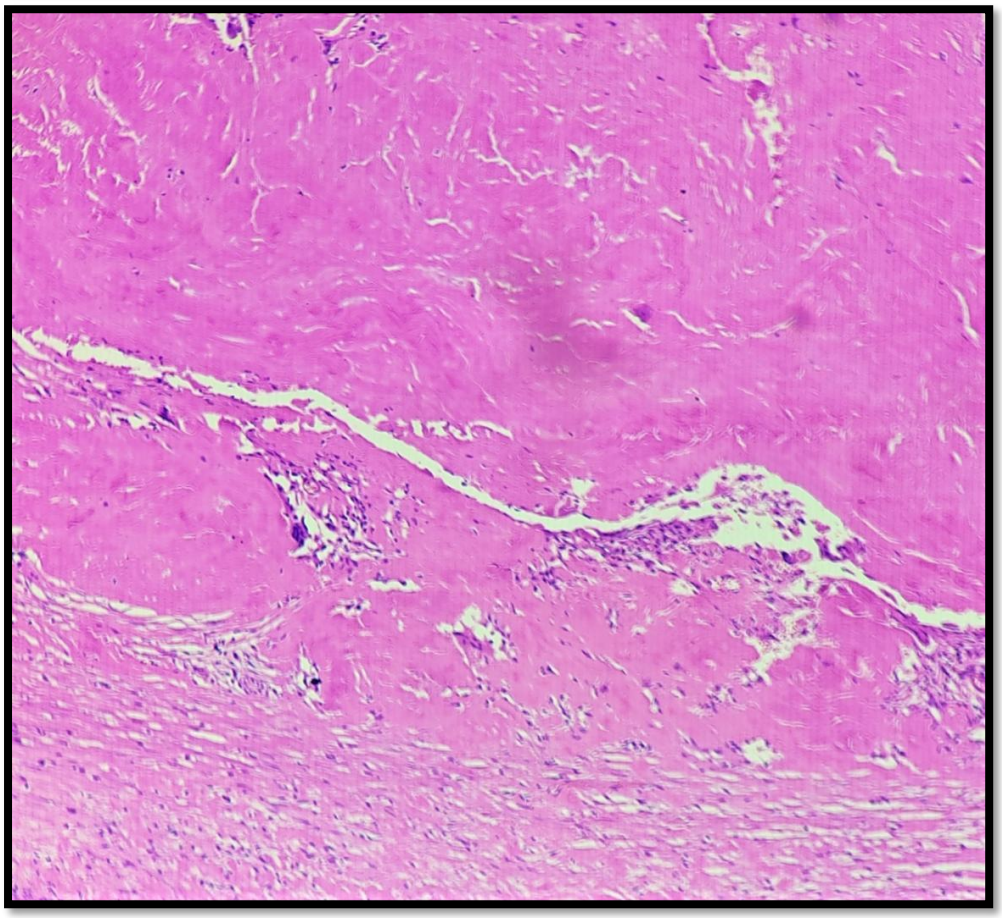


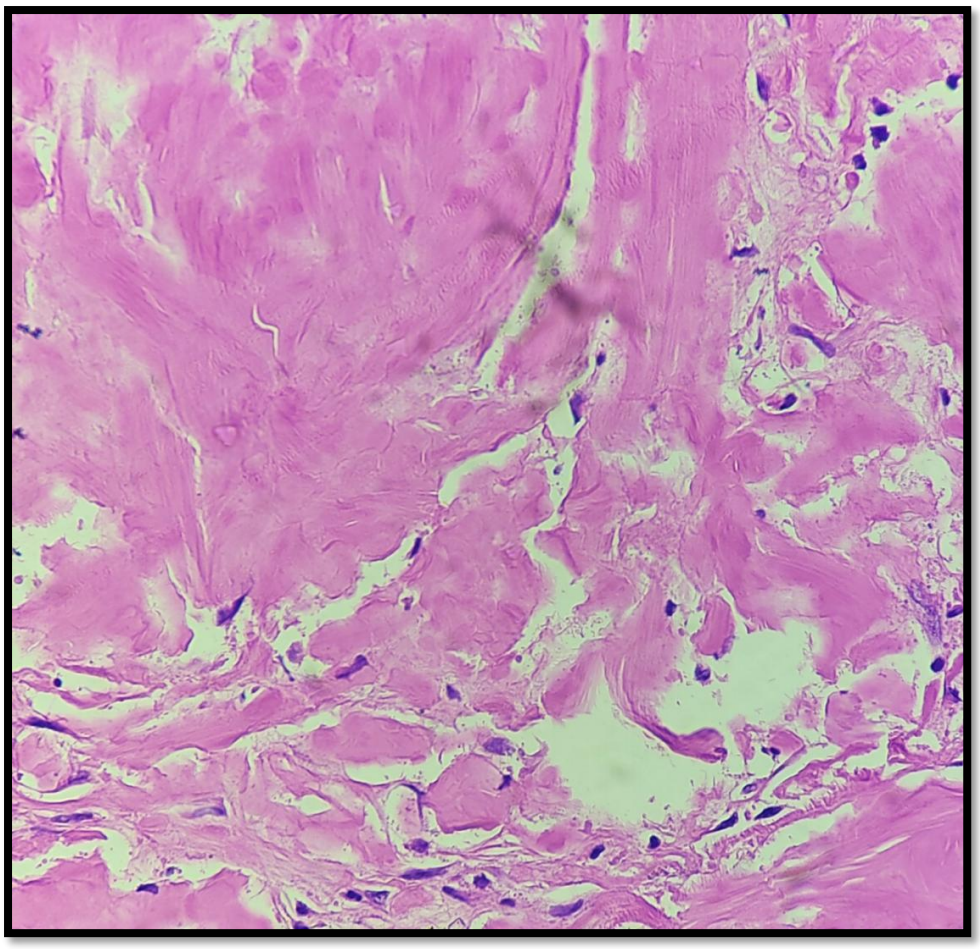
Figure 1 : Abundant eosinophilic acellular material in

Material in subepithelium of bladder tissue.

(H&E x 200)

Figure 2 : Abundant eosinophilic acellular material in

Ureteric tissue. (H&E x 400)



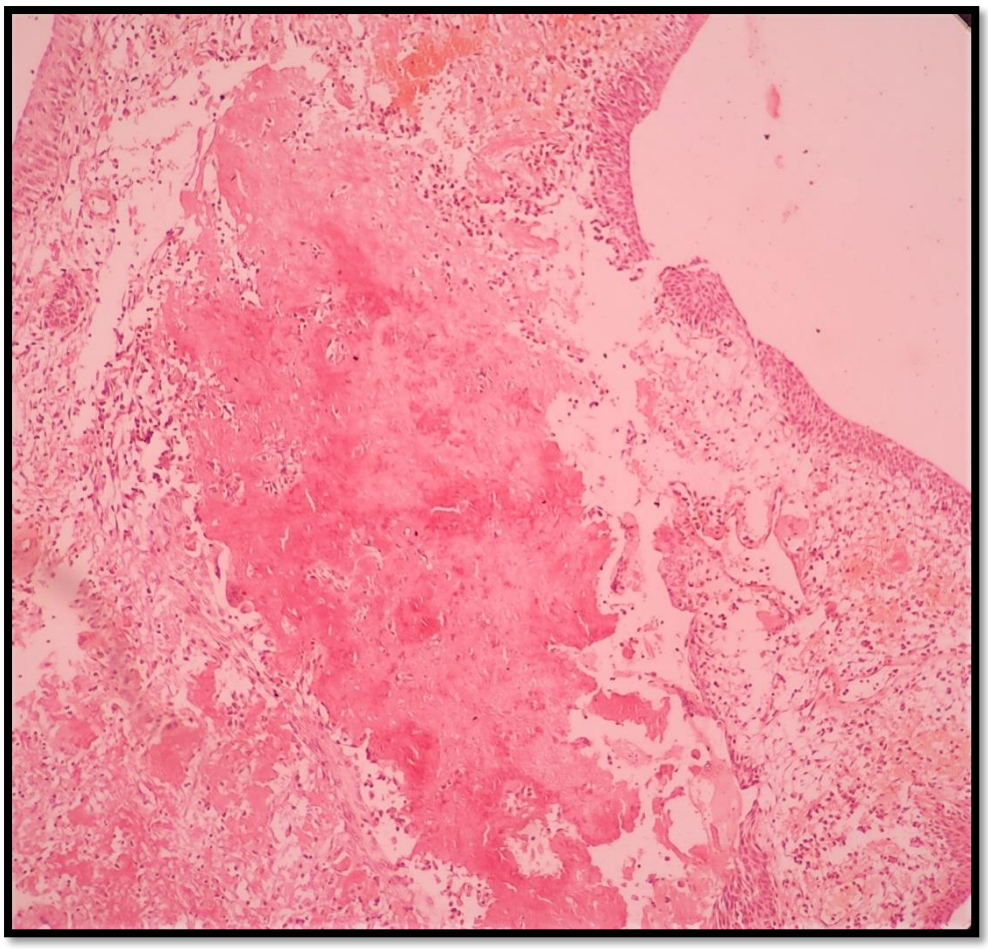


Figure 3 : Abundant eosinophilic acellular acellular material

material in bladder tissue.

(H&E x 400)

Figure 4 : Abundant congophillic

in bladder tissue. (Congo red x 400)

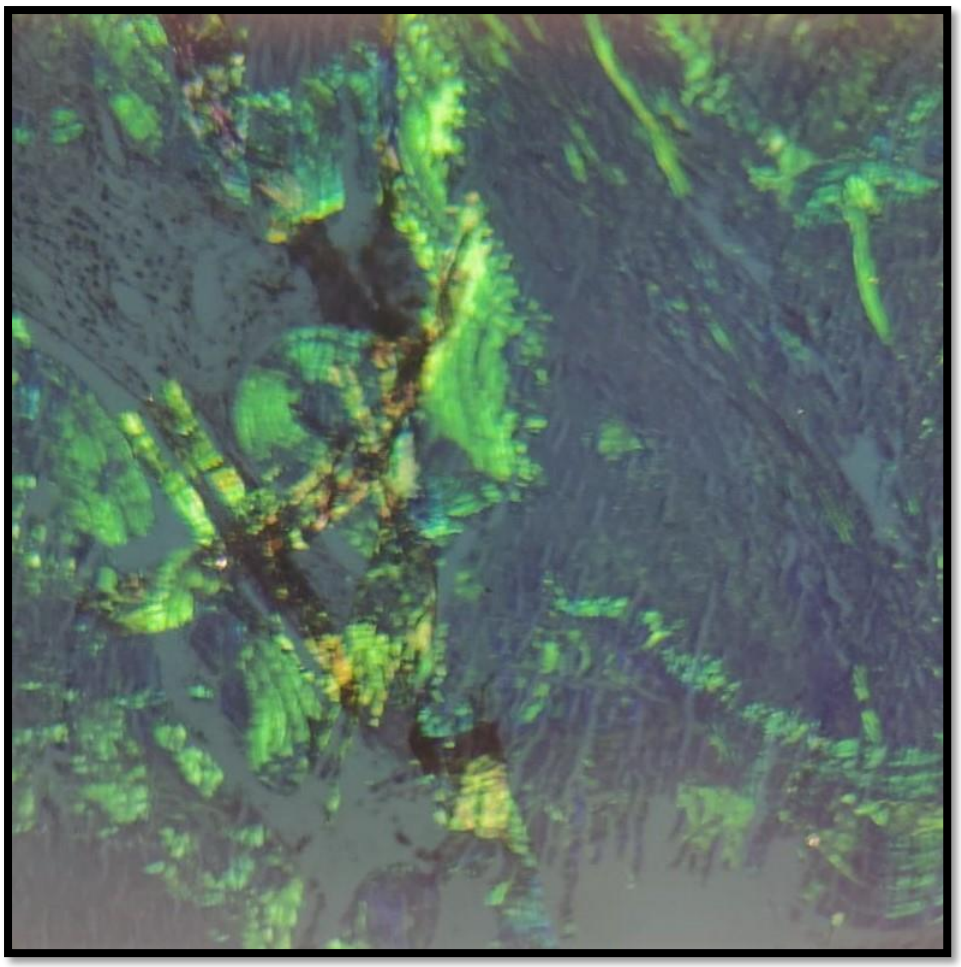


Figure 5 : Amyloid deposition shows Apple Green

birefringence on Polariser. (Congo red x 400)

CONCLUSION

Amyloidosis of urinary tract is a rare heterogeneous disease that mandates clinical awareness, as it mimics bladder cancer. Localised amyloidosis is a benign disorder, with minimal risk of progression to systemic amyloidosis that requires resection of these lesions and surveillance. Contrary to localized amyloidosis, the systemic disease reduces survival and is associated with high symptom burden, and impairment of quality of life. By clinical manifestation and radiological investigation it is difficult to differentiate this condition from urothelial carcinoma hence biopsies prior to surgery which yielded diagnosis of amyloidosis could help avoid unnecessary surgery.

REFERENCES

1.Vinay K, Abul KA, jon CA. robbins and cotran pathologic basis of disease.10th edition. Elsevier; philadephia; 2021.

2.Gertz MA, Dispenzieri A. Systemic amyloidosis recognition ,prognosis and therapy: a systemic review. JAMA.2020;324:79-89.

3.Lehtonen T,Makinen J, Wikstrom S. localised amyloidosis of urinary bladder.Eururol. 1991;20:113-6

4.Westermark P. Localised amyloidosis: a suicidal neoplasm? Ups J Med Sci.2012; 117:244-250

5.Muchtar E,Gertz MA, Kyle RA, et al. Amorden primer on light chain amyloidosis in 592 patients with mass spectrometry- verified typing. Mayo clin proc. 2019;94: 472-483.

6.Benson MD,buxbaumJN,Eisenberg DS, et al.amyloid nomenclature 2018: recommendation by the international society of amyloidosis nomenclature committee. Amyloid Int J Exp Clin Investing Off J Int Soc Amyloidosis. 2018;25:215-219.

7. Ravichandran S, Lachmann HJ, Wechalekar AD. Epidemiologic and survival trends in amyloidosis, 1987-2019. N Engl J Med. 2020;382:1567-1568.

8.Kourelis TV, Kyle RA, Dingli D, et al. Presentation and outcome of localized immunoglobin light chain amyloidosis: the myoclinic experience. Mayo Clin Proc. 2017;92:908-917.

9. Mahmood S, Bridoux F, Venner CP, et al. Natural history and outcomes in localized immunoglobin light chain amyloidosis: a long term observational study. Lancet Haematol. 2015;2:e241-e250.

10. Lachmann HJ, Goodman HJB, Gilberston JA, et al.Natural history and outcomes in systemic AA amyloidosis. N Engl J Med.2007;356:2361-2371.

11. Javed A, Canales BK, MaclennanGT.Bladder amyloidosis. J Urol.2010;183:2388-2389.

12. Chitale S, Morsey M,Swift L, Sethia K. Limited shock wave therapy vs sham treatment in men with peyronie's disease: results of a prospective randomized controlled double-blind trial. BJU Int. 2010;183: 2388-2389.

13.Kawashima A, Alleman WG, takahashi N. et al.Imaging evaluation of amyloidosis of urinary tract and retroperitoneum.2011;31:1569-82. doi: 10.1148/rg.316115519.

14.Malhotra et al. How long does it take for tuberculosis to cause secondary amyloidosis?

Eur J Intern Med (2005)

15. B.G. Jung et al. Mycobacterium tuberculosis stimulates IL-1β production by macrophages in an ESAT-6 dependent manner with the involvement of serum amyloid A3 . Mol Immunol(2021)

16.S. Seto et al. Proteomic profiling reveals the architecture of granulomatous lesions caused by tuberculosis and Mycobacterium avium complex lung disease

17.J.Prakash et al. The changing pattern of renal amyloidosis in Indian subcontinent: two decades of experience from a single center. Ren Fail (2012)

18.A. Kennedy et al. Tuberculosis as a continuing cause of renal amyloidosis. Br Med J (1974).

Conflict of interest NIl

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