GP Refresher

Discrepant Urine PCR and ACR: i.e. PCR >2 x ACR: An early indicator of Myeloma with potential renal involvement

Original Observation:

SB, 71 years female, presented with free light chain myeloma in June 2014 (Free lambda on electrophoresis was 9.1 g/L, Free lambda on freelite assay was 23,660 mg/L and Serum Creatinine was 400μmol/L)

Please note that her Urine PCR and ACR were discrepant and abnormal in the preceding 2 years as follows:

	09/06/14	**30/09/13**	**21/08/12**
Urine PCR	1312	1317	476
Urine ACR		16.3	10.7
Urine Protein	5.51 g/L	6.32 g/L	3.62 g/L
Urine albumin		78 mg/L	81 mg/L
Hb	89 g/L	Not done	Not done
Serum Creatinine	403 μmol/L	58	77

Urine PCR (Protein Creatinine ratio) is the total urine protein excretion (albumin, light chains and other globulins) divided by urine creatinine, whereas, Urine ACR (albumin creatinine ratio) only accounts for albumin concentration divided by urine creatinine. Therefore the difference between the two relates to the presence of proteins other than albumin in the urine. These are simple, non-invasive and relatively inexpensive tests.

This patient had a highly discrepant PCR value i.e PCR was >10 x ACR value since 2012, indicative of a protein in the urine that was not albumin and hence likely to be Bence Jones Protein (light chains). This demonstrates that the patient could have been diagnosed to have Myeloma at least two years prior and her kidney function could have been preserved.

MD, 59 years female presented to GP with backache due to vertebral collapse and was diagnosed to have light chain myeloma in Nov 2015 with free kappa in urine of 1.52 g/L and serum free kappa of 998 mg/L. She could have been diagnosed in an acute medical clinic six months before this (June 2015) as her urine PCR was already 100 times more than ACR. Her PCR was 141 whereas ACR was only 0.3, Urine protein was 340 mg/L out of which urine albumin was only 0.6 mg/L. The remaining protein was Bence Jones in her case.

IH, 86 female, has been diagnosed to have free lambda myeloma in March 2016 when she presented with Hb 103, Creatinine 272 and Serum Free lambda of 8980 mg/L (normal range 5-26). She also had a discrepant PCR >10 times of ACR, a year prior to be diagnosed with a myeloma kidney.

	22/04/2016	**12/02/2015**	**19/03/2013**
Urine PCR (0 – 30 mg/mmol)		118	20.8
Urine ACR (0 – 3.5 mg/mmol)		0.7	0.4
Urine Protein (g/L)		0.32	
Urine albumin (0 – 15 mg/L)		1.9	
Hb	93		133
Serum Creatinine	**272**	64	85

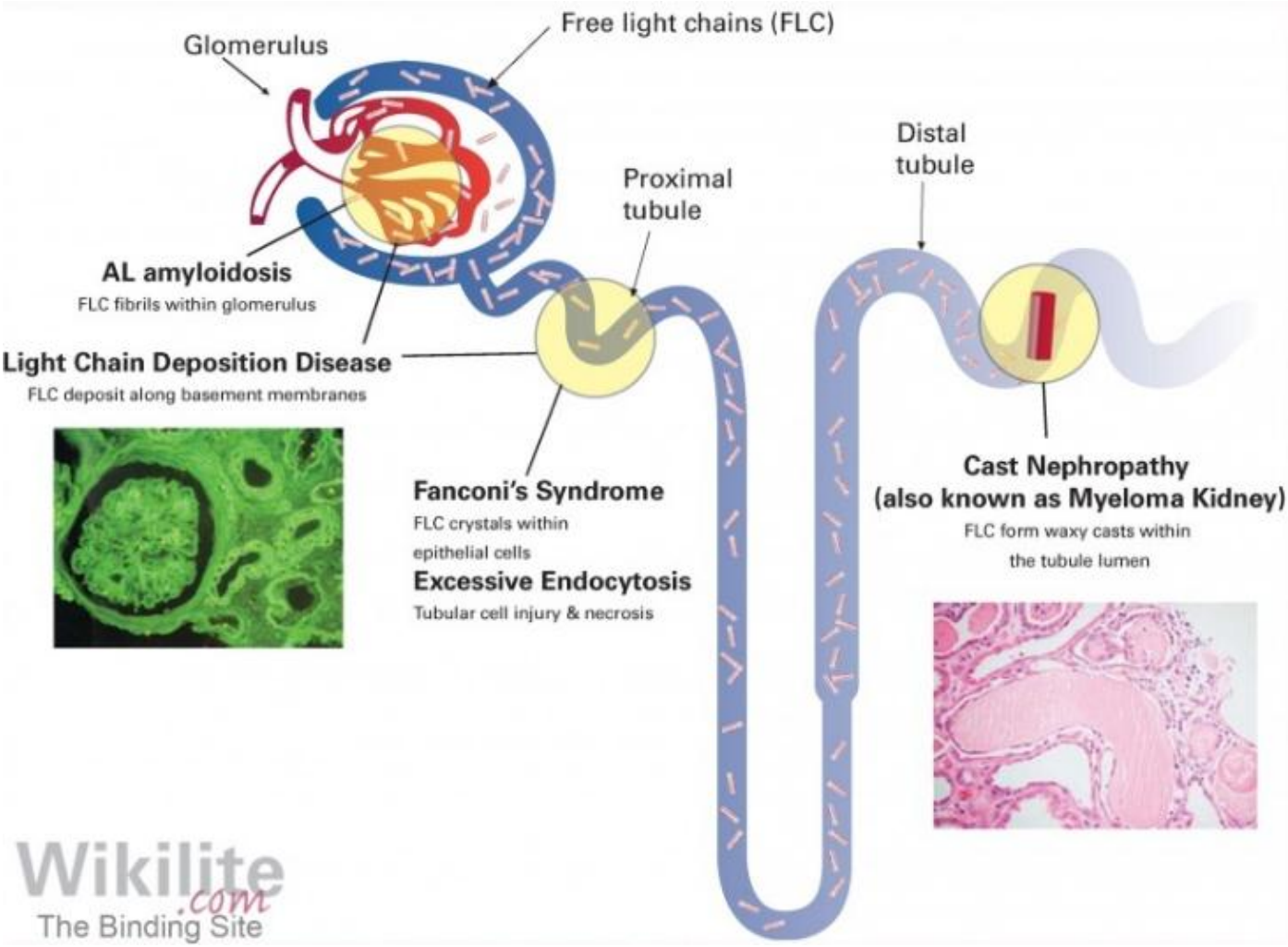
Explanation:

Total urinary protein excretion in the normal adult should be less that 150mg/day and albumin excretion should be less than 30mg/day. Commonly found proteins in the urine are albumin, free light chains (also called urinary bence jones proteins BJP), tubular proteins such as tams-horsfall protein and haemoglobin or myoglobin in specific disease states.

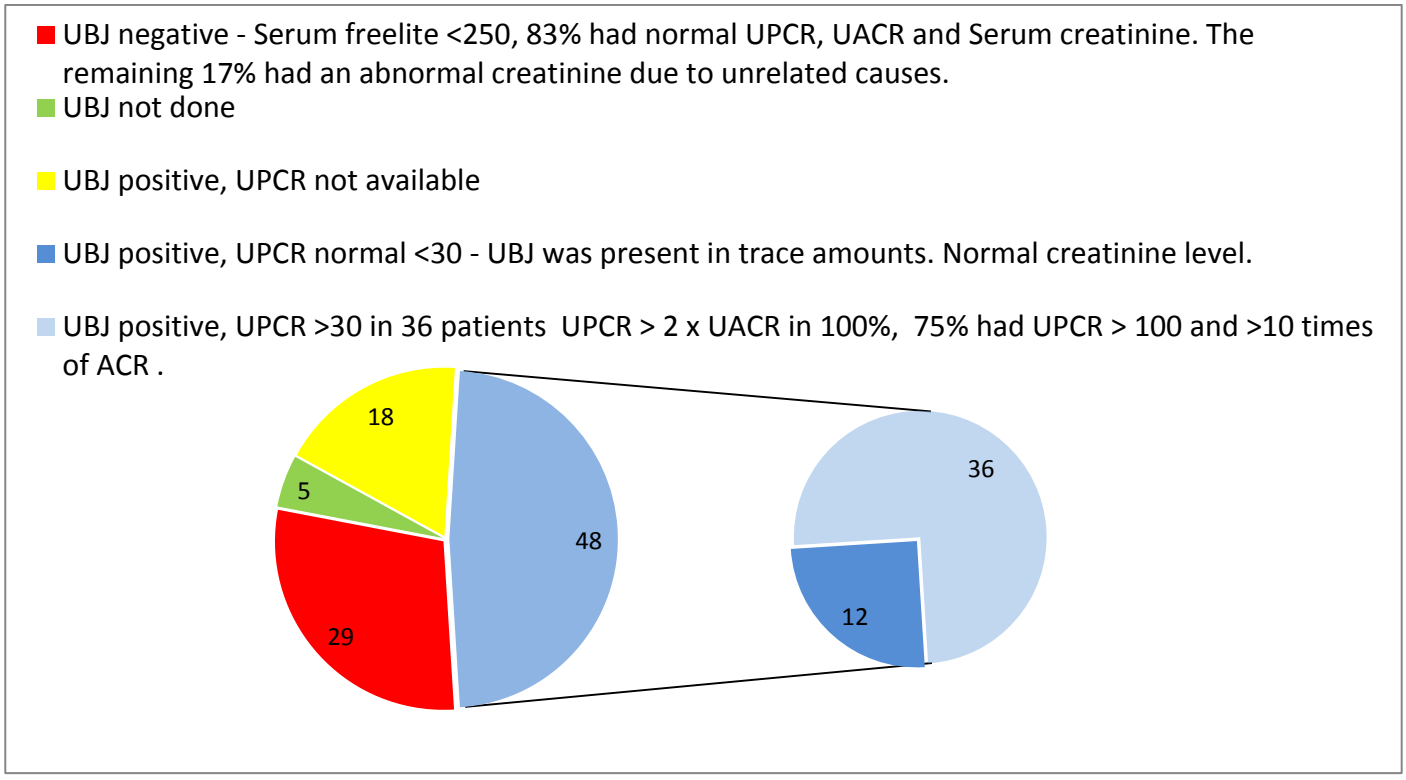
Normally particles with a molecular mass of >60kDa cannot filter through the glomerular basement membrane (GBM) and hence albumin which is 66.5 kDa is not filtered though the glomerulus unless there is a structural damage to the glomeruli such as in diabetic nephropathy

Immunoglobin molecules are made up of heavy and light chains; the light chain molecules are small (κ~25kDa and λ~50 kDa) and hence can pass through GBM. Normally the kidneys have the ability to reabsorb these light chains in the proximal tubule so that they are not excreted in the urine. In myeloma, the light chain production may exceed that of reabsorption resulting in appearance of light chains in the urine (also called Bence Jones proteinuria BJP).

Presence of Light chains (UBJ) protein in the urine is the most common cause of renal failure in myeloma in addition to sepsis, hypercalcaemia, NSAID use and amyloidosis. Urinary free Light chains precipitate when they come in contact with Tams Horsfall protein and form an intratubular cast causing obstruction at nephron level leading to renal failure.



We correlated Urine PCR and ACR, Urine BJ positivity, serum freelite levels and the presence or absence of renal impairment at diagnosis in 100 patients with myeloma who presented from July 2014 to July 2016.



Out of 66 patients who were positive for urine BJP, urine PCR was done in 48 of them and was abnormal i.e. >30 mg/mmol in 36 patients. PCR was >100 mg/mmol in 29 patients.

Patients with significantly abnormal and discordant Urine PCR compared to ACR (i.e more than 10 times) had a relatively higher serum freelite value >1000mg/L and were at maximum renal risk.

In 14 patients, PCR was >30 and 2 x ACR value several months prior to diagnosis. PCR was 10 x ACR in 8 of these patients indicating that myeloma could have been diagnosed many months earlier as shown in examples above.

The above study was conducted to emphasise the need to interpret the results of Urine PCR and ACR correctly and to request screening tests for myeloma i.e. urine Bence Jones protein early. Earlier diagnosis of myeloma will eventually result in reduced rates of complications, reduced morbidity and improved overall survival.

Biochemistry department will insert a comment from now on
"If PCR is raised i.e. >30 mg/mmol and ≥ twice the value of ACR, please send a urine sample to immunology for Bence Jones (light chains) proteinuria"

We hope that you have found the essay useful and would be grateful for your comments.
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