

Nephrogenic Diabetes Insipidus: A Rare Presentation in Multiple Myeloma

Mehdi Dehghani*, Vahid Mohammad Karimi

Shiraz University of Medical Sciences, Hematology Research Center, Shiraz, Iran

Abstract

We report a case of multiple myeloma that presented with anorexia, fatigue, high erythrocyte sedimentation rate, bone marrow plasmacytosis of more than 30%, polyuria, and low urine specific gravity. This unusual presentation was diagnosed as nephrogenic diabetes insipidus secondary to a proximal tubular dysfunction. The tubular functional disturbance appeared to be related to the presence of lambda-type light chains. The patient was treated with desmopressine without response. After one month of treatment with thalidomide and dexamethasone for myeloma there was a dramatic response with decreased urine output.

Keywords: Nephrogenic diabetes insipidus, Multiple myeloma, Lambda light chain, Amyloidosis

Introduction

Multiple factors impair renal function in multiple myeloma. Fanconi syndrome is an uncommon complication frequently associated with deposits of reabsorbed immunoglobulin light chains in the proximal renal tubular epithelium.¹ Amyloidosis with kidney involvement and nephrogenic diabetes insipidus (DI) are the other abnormalities that can be seen by light chain deposition in renal tubules in multiple myeloma.^{2,3} Kappa light chain deposition and amyloidosis may be systemic in multiple

myeloma; the kidney is the only organ to show both amyloid and light chain deposits and it may be seen in both tubules and collecting ducts. Nephrogenic DI may present a prodromal phase of multiple myeloma that has previously been reported as a kappa light chain. Our patient was referred with complaints of excessive urine production and low specific gravity.⁴

Other systemic diseases may present with nephrogenic DI, including Sjögren's syndrome, hypokalemia, hypercalcemia, chronic renal disease, drugs (lithium, demeclocycline), post-obstructive neuropathy, and solute

♦Corresponding Author:
Mehdi Dehghani, MD
Hematology Research Center,
Shiraz University of Medical
Sciences, Shiraz, Iran,
Tel: +98-9177158312,
Email: dehghanim@sums.ac.ir

Table 1. Urine protein electrophoresis.

Fraction	Percent	mg/dl	Reference range
β2-microglobulin	2.8	2.4	0.0-0.0
Light chain	11.6	9.7	0.0-0.0
α1-microglobulin	32.1	27.0	0.0-0.0
apoprotein A1	8.8	7.4	0.0-0.0
Albumin	23.7	19.9	0.0-5.0
Transferrin	2.8	2.4	0.0-0.0
IgG	1.9	1.6	0.0-0.0
IgM	0.8	0.7	0.0-0.0
Hemoglobin	15.5	13.0	0.0-0.0
Tamm-Horsfall	0.0	0.0	0.0-5.0
Total	100	84	0.0-10

washout from the renal medulla (e.g. diabetes mellitus).^{3,5,6}

Case Report

A 66-year-old man had complaints of nonspecific signs and symptoms such as intermittent fevers, anorexia, fatigue, and urinary dribbling for about six months. There was no history of diabetes mellitus, drug abuse, or psychiatric problems. One month before admission he suffered from dyspnea on exertion and generalized body pain. In laboratory tests he had a Hb of 6g/dl and erythrocyte sedimentation rate (ESR) of 96. A bone marrow study showed more than 30% plasma cells that favored plasma cell dyscrasia (Table 1). Protein and immune electrophoresis were normal, but urine electrophoresis showed the presence of lambda chains (Table 2).

A marrow plasmacytosis of more than 30%, lambda light chains in the urine, anemia, and high ESR confirmed the presence of multiple myeloma and the patient began treatment.

During hospitalization he suffered from excessive urination (polyuria >4000 ml/day) and low specific gravity (1.004). The tests gave the impression of DI, therefore desmopressin was started with no response. He had nephrogenic DI, and after 4-6 weeks of treatment with thalidomide and dexamethasone the patient improved and his urine output was decreased. Ultrasonography showed normal-sized kidneys but increased parenchymal echogenicity.

Discussion

We presented a case of multiple myeloma with polyuria and renal dysfunction caused by lambda light chains. Various known factors cause renal injury in multiple myeloma, including hypercalcemia, hyperuricemia, dehydration, plasma cell infiltration, infection, amyloidosis and tubular dysfunction caused by light chain (lambda and kappa) infiltration in proximal tubules.⁷

Many reports of impairment due to kappa light chain exist, but renal impairment and nephrogenic DI due to the lambda light chain is very rare. Tubulopathy and Fanconi's syndrome are predominantly associated with monoclonal kappa in the urine, however there have been some rare instances of Fanconi's syndrome caused by lambda light chains.⁷

Fanconi's syndrome is an uncommon complication that appears to be related to the deposition of light chains. It is characterized by diffuse failure in reabsorption at the proximal renal tubule resulting in glycosuria, generalized aminoaciduria, and hypophosphatemia. Evidence shows that incompletely digested monoclonal light chains in renal tubule lysosomes cause kidney damage.⁷ Clinical manifestations include slowly progressive renal failure, renal tubular acidosis, and bone pain caused by osteomalacia.

Diabetes insipidus is characterized by the passage of large volumes of dilute urine (polyuria). Excessive urine production is defined as greater than 3 l/24 h. However, in severe cases output can be as high as 20 l/24 h. Three pathogenetic

Table 2. Blood and urine laboratory results.

cCBC		Blood chemistry		Serum protein electrophoresis	
Hb	6g/L	Serum Cr	2.3	Albumin	3.8g/L(53%)
WBC	5600	Na	139	α 1	0.2g/L(2.4%)
Platelet	221000	K	3.9	α 2	1g/L(13.3%)
ESR	96	Ca	8.5	β 2	0.5g/L(7.2%)
PH	7.45	P	3.2	gamma	1.8g/L(24.1%)
HCO ₃	17.7	blood sugar	146	Serum immune electrophoresis	
PCO ₂	25	Urine analysis		Normal range	
PO ₂ :	91	BLOOD	trace	IgG:2.94 g/L	(6.56-18.37)
O ₂ SAT	94%	RBC	4-5	IgA:0.18g/L	(0.71-3.6)
Blood chemistry		WBC	8-10	IgM:0.24g/L	(0.40-2.63)
BUN	28	protein	1+		
		specific gravity	10.04		

mechanisms are responsible for polyuria:5 i) lack of vasopressin secretion (central DI), ii) absence of kidney response to adequate circulating vasopressin (nephrogenic DI), and iii) excessive consumption of water (dipsogenic diabetes or insipidus primary polydipsia). In nephrogenic DI the plasma concentration of vasopressin is appropriate for plasma osmolality, but it fails to act on the renal tubules because of receptor dysfunction.⁵

Patients with nephrogenic DI have the same presenting symptoms as cranial DI; these symptoms depend on their thirst mechanism and adequate fluid intake to maintain plasma tonicity. The plasma sodium is normal unless the patient is denied access to water. Urine osmolality is inappropriately low in relation to plasma vasopressin.⁵

Causes of nephrogenic DI are both familial and acquired. Familial nephrogenic DI arise from either an X-linked recessive inheritance or an autosomal recessive inheritance, whereas acquired nephrogenic DI may be the result of drugs (lithium, demeclocycline), metabolics (hypokalemia, hypercalcemia), postobstructive uropathy, chronic renal disease, or solute washout from the renal medulla (diabetes mellitus).⁵

There was a report of IgA-kappa multiple myeloma diagnosed with bone pain, anemia, and high ESR with DI. The patient had a considerable amount of urine (4-6 l/day) output with low specific gravity and hardly controllable thirst.

Nephrogenic DI presents as the prodromal phase of multiple myeloma. In this report, the light chain was kappa, however this type of tubular damage also occurs with the lambda light chain. The patient was responsive to myeloma treatment.⁴

In the hereditary form of DI, substitution of arginine-137 of the vasopressin type 2 receptor for histidine leads to nephrogenic DI, whereas substitution of the same residue to cysteine or leucine causes the nephrogenic syndrome of inappropriate antidiuresis.⁸

Central nervous system involvement in multiple myeloma is uncommon, with extremely rare signs and symptoms. In the literature there are reports of this rare presentation in multiple myeloma. There is a report of two patients with multiple myeloma involving the central nervous system, one case with obstructive hydrocephalus ten years after the initial diagnosis of multiple myeloma and the second with hypopituitarism and DI one year after diagnosis.⁹ These rare complications add new information about the wide spectrum of clinical and laboratory manifestations of multiple myeloma. In our case the lack of response to desmopressine and elevated lambda light chain favored nephrogenic DI. Descriptions of additional cases are required to better understand the mechanisms of light chain nephrogenic DI in multiple myeloma patients.

Conclusion

Lambda light chains are a cause of proximal

tubular disturbance in myeloma and nephrogenic DI.

References

1. Minemura K, Ichikawa K, Itoh N, Suzuki N, Hara M, Shigematsu S, et al. IgA-kappa type multiple myeloma affecting proximal and distal renal tubules. *Intern Med* 2001;40(9):931-5.
2. Jacquot C, Saint-Andre JP, Touchard G, Nochy D, D'Auzac de Lamartinie C, Oriol R, et al. Association of systemic light-chain deposition disease and amyloidosis: A report of three patients with renal involvement. *Clin Nephrol* 1985;24(2):93-8.
3. Kirkpatrick CJ, Curry A, Galle J, Melzner I. Systemic kappa light chain deposition and amyloidosis in multiple myeloma: Novel morphological observations. *Histopathol* 1986;10(10):1065-76.
4. Goranov S, Hristova I, Pencheva K. Nephrogenic diabetes insipidus-prodromal phase of multiple myeloma. *Folia Med (Plovdiv)* 1994;36(2):63-6.
5. Peter H Baylis. Diabetes Insipidus. posterior pituitary. *Medicine. The Medicine Group (Journals) Lt.* 1997 (9-11).
6. Martin A, Shearn MD, Wu-Hao Tu. Nephrogenic diabetes insipidus and other defects of renal tubular function in Sjögren's syndrome. *Am J Med* 65;39(2):312-8.
7. Lacy MQ, Gertz MA. Acquired Fanconi's syndrome associated with monoclonal gammopathies. *Hematol Oncol Clin North Am* 1999;13(6):1273-80.
8. Rochdi MD, Vargas GA, Carpentier E, Oligny-Longpré G, Chen S, Kovoov A, et al. Functional characterization of vasopressin type 2 receptor substitutions (R137H/C/L) leading to nephrogenic diabetes insipidus and nephrogenic syndrome of inappropriate antidiuresis: Implications for treatments. *Mol Pharmacol* 2010;77(5):836-45. Epub: 2010 Feb 16.
9. Pontikoglou C, Fragos C, Kolyvaki E, Samonis G, Eliopoulos GD, Papadaki HA. Multiple myeloma involving the central nervous system: A report of two cases with unusual manifestations. *Leuk Lymphoma* 2005;46(5):737-41.