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From Russia with Polyuria

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Abstract

Introduction: Polyuria is a sign for many disease processes, including diabetes mellitus and diabetes insipidus. Urine osmolarity helps distinguish osmotic diuresis caused by diabetes mellitus from water dieresis induced by diabetes insipidus. Case Presentation: We report a case of a 48-year-old woman who presented with polyuria, polydipsia, nocturia, and weight loss after a return from a visit to Russia, during which she received a five-day course of antibiotic Demeclocycline, a tetracycline derivative for dental treatment. She recovered from all clinical manifestations by 8 weeks. Conclusion: Manifestation of transient nephrogenic diabetes insipidus is induced by Demeclocycline.

Keywords

Polyuria, Urine Osmolarity, Nephrogenic Diabetes Insipidus, Demeclocycline

1. Introduction

Polyuria, urine production of more than 3 L/d, results from excretion of non-absorbable solutes (osmotic diuresis) or over-excretion of water (water diuresis) [1]. Osmotic diuresis ensues due to elevated urine osmolality usually >300 mosm/l on collection of large amounts of solutes in the renal tubules, major solutes being glucose in diabetes mellitus and mannitol and radiocontrast media administered exogenously [1]. In contrast, water diuresis occurs secondary to central diabetes insipidus caused by inadequate secretion of antidiuretic hormone (ADH) or nephrogenic diabetes insipidus due to failure of renal tubules to respond to circulating ADH with excretion of extremely dilute urine with osmolality < 250 mosm [1]. In this report, we describe a rare occurrence of nephrogenic diabetes insipidus triggered by administration of antibiotic, demeclocyline.

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2. Case Presentation

Forty eight year old woman was referred to endocrine clinic for polyuria and nocturia several times a day as well as polydipsia and 5 - 6 kg weight loss, vague abdominal pain, dry mouth, and tongue turning black and furry over two weeks' duration. She denied chest pain, heart racing, heat/cold intolerance, diaphoresis, shortness of breath, nausea, vomiting, diarrhea, headache, and visual changes. She denied recent head trauma One week prior to the onset of symptoms, she had undergone a tooth implant in Russia and was given a five day prophylactic antibiotic course. Her past medical and surgical histories were unremarkable. She is a non-smoker and did not use alcohol, illicit drugs, or over-the-counter herbals or supplements and has no known allergies. Family history was non-contributory.

Physical examination showed blood pressure, 116/72 mmHg; pulse rate, 68/min; respiratory rate, 12/min; body temperature, 98˚C; and weight, 62 kg. She was alert and oriented, and in no acute distress. The rest of the exam was unremarkable. Urine specific gravity was extremely low, 1.001 at this visit. Therefore, she was asked not to drink any fluids starting 7:00 pm that day and return following morning for further laboratory testing including "water deprivation test". At the follow up encounter at 4 weeks, the patient was free from all clinical manifestation including polyuria, polydypsia as well as black furry tongue and all the laboratory tests were repeated.

Complete blood count, liver enzymes, free T_4 and thyroid stimulating hormone were normal at both visits. Pertinent metabolic panel data reveal hypokalemia and metabolic alkalosis indicative of dehydration at initial visit with restoration of hydrated status at visit 2 as reflected by lower serum creatinine, urea nitrogen and resolution of hypokalemia and metabolic alkalosis (**Table 1**).

Results from water deprivation tests demonstrate presence of nephrogenic diabetes insipidus as documented by low urine osmolality with elevated serum ADH levels and lack of rise in urine osmolality on administration DDAVP at initial visit (**Table 2**) with remission at visit 2 confirmed by normalization of urine osmolality and serum ADH concentrations (**Table 3**). Changes in plasma renin and aldosterone concentrations confirm the presence of dehydration at initial visit and adequate hydrated state at visit 2 (**Table 2** and **Table 3**). The subject has remained free of the symptoms on 2 subsequent visits at 3 and 6 months.

3. Discussion

We report a rare case of polyuria secondary to nephrogenic diabetes insipidus induced by a broad-spectrum tetracycline antibiotic, Demeclocycline prescribed prophylactically following a dental procedure by the dentist during a visit to Russia. Complete recovery of clinical manifestations following normalization of both serum ADH concentration and its effect on urine osmolality during repeated water deprivation test confirms the transient and reversible nature of the disorder on discontinuation of Demeclocycline. Our observation is consistent with the data in the literature [2]-[6]. Moreover, occurrence of black furry tongue on administration and its remission following discontinuation of Demeclocycline noted in our patient is also previously documented [6].

Table 1. Pertinent metabolic panel results.

Metabolic panel normal range	Visit 1	Visit 2
Serum urea nitrogen 5 - 20 mg/dl	21.0	12.0
Serum creatinine 0.6 - 1.2 mg/dl	0.9	0.6
Serum glucose 60 - 99 mg/dl	89	92
Serum sodium (Na^+) 135 - 145 mosm/l	140	140
Serum potassium (K^+) 3.5 - 5.0 mosm/l	3.3	4.1
Serum chloride (Cl^-) 95 - 110 mosm/l	101	104
Serum bicarbonate (HCO_3^-) 25 - 32 mosm/l	30	25

Table 2. Water deprivation test at initial visit.

Time (hr)	Serum osmolality mosm/l (285 - 295)*	Urine osmolality mosm/l (50 - 1100)*	Urine specific gravity (1003 - 1030)*	ADH pg/ml (1 - 5)*	Renin supine ng/ml/hr (0.2 - 2.3)*	Aldosterone supine ng/dl (3 - 10)*
0	302	258	1.003	22	4.56	16
1	306	260	1.003	20		
2	305	252	1.004	23		
3	308	258	1.002	26		
4	307	250	1.003	-		
6	310	253	1.002	-		

*Normal range.

Table 3. Water deprivation test at visit 2*.

Time (hr)	Serum osmolality mosm/l	Serum osmolality mosm/l	Urine specific gravity	ADH pg/ml	Renin supine ng/ml/hr	Aldosterone supine ng/dl
0	242	463	1.015	1.1	0.66	6
2	244	873	1.021	2.0		
4	247	909	1.026	3.9		
6	247	914	1.026	6.8		

*Normal ranges shown in **Table 2**.

The exact mechanism of induction of nephrogenic diabetes insipidus by Demeclocycline has not been fully elucidated. Demeclocycline apparently inhibits ADH induced generation of cAMP, an effective second messenger required for promoting ADH effect on renal tubules to reabsorb water resulting in profound diuresis [5]. Therefore, Demeclocycline has been utilized to inhibit ADH activity in subjects manifesting syndrome of inappropriate ADH secretion (SIADH) or inappropriate antidiuresis (SIAD).

4. Conclusion

Nephrogenic diabetes insipidus is an uncommon side effect of Demeclocycline use. There are limited reports of this finding, especially since the use of this drug has been largely replaced by other antibiotics. However, there are still areas around the world where this antibiotic is still being used. This case report suggests that Demeclocycline should be used with caution for renal failure and nephrogenic diabetes insipidus.

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