ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: www.ijmacr.com

Volume – 4, Issue – 1, January - February - 2021, Page No. : 128 – 132

Nephrogenic Diabetes Insipidus : A New Clinical Case

[1,2]Mariam Akhrif , [1]Mouna Sabib, [1]Toufik Meskini, [1]Nezha Mouane

[1]Department of Pediatric Hepatology Gastroenterology and Nutrition, Rabat Children's Hospital, Morocco

[2]Faculty of Medicine and Pharmacy, Morocco

Corresponding Author: Mariam Akhrif, Department of Pediatric Hepatology Gastroenterology and Nutrition, Rabat Children's Hospital, Morocco

How to citation this article: Mariam Akhrif , Mouna Sabib, Toufik Meskini, Nezha Mouane, "Nephrogenic Diabetes Insipidus : A New Clinical Case", IJMACR- January - February - 2021, Vol – 4, Issue -1, P. No. 128 – 132.

Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

Introduction: Nephrogenic diabetes or nephrogenic diabetes insipidus is a rare entity of diabetes insipidus, it is a clinical syndrome due to a defect or resistance of the renal tubules to concentrate urine, stimulating normal or even high plasma concentrations of AVP. It may be acquired or secondary caused by electrolyte imbalances, renal or extrarenal disease and medications.

Materials and Methods: the authors report the case of an 11 month old male infant with no pathological history, admitted in our service for chronic diarrhoea, dehydration. The history of his illness goes back to the age of 4 months, with post-prandial food vomiting, then at the age of 7 months the association of liquid diarrhoea > 4 with weight stagnation, , the evolution was marked by the persistence of vomiting and the appearance of thirst episodes, especially at night. The clinical examination found an infant: apyretic, conscious and malnourished, pale with dehydration folds, with a delayed weight gain, The patient benefited from rehydration regimen, during hospitalization He presented a polyuria polydipsia syndrome. He had Polyuria with Diurese: 10cc/KG/H. Calculated osmolarity: 286.51 mOSm; effective osmolarity: 283.19 mOSm, and a negative glucose test .Blood Ionogram did not show hydroelectrolytic disorders. Urine Ionogram was; without abnormality the thyroid test did not show any abnormalities. The antidiuretic hormone dosage was increased to 38.40 pmol/l (NV :< 13) , the diagnosis of nephrogenic diabetes insipidus was retained, treatment with indometacine was started.

The objective of this work is to know how to evoke this rare pathology in order to start an adequate treatment to avoid complications.

Keywords: Nephrogenic diabetes insipidus; Polyuria ; vasopressin (AVP), genetic disease

Introduction

Diabetes insipidus is a rare disease characterised by the elimination of large volumes of highly diluted urine. This disorder is caused by the inability of the neuro-pituitary

gland to secrete sufficient amounts of vasopressin (VPA), also known as the antidiuretic hormone (neurogenic or central diabetes insipidus), or by the inability of the kidney to respond to circulating VPA (nephrogenic diabetes insipidus NDI). [1]. Nephrogenic diabetes insipidus is a clinical syndrome resulting to a defect or resistance of the renal tubules to concentrate urine, stimulating normal or even high plasma concentrations of AVP.[2]. NDI is classified as primary or secondary. The primary or congenital form is hereditary. The secondary form is that which is observed in the various kidney diseases.[2]

Case Report

We report the case of an 11 month old male infant, the only one in his family from a followed pregnancy, carried to term, delivery by the vaginal route, with a birth weight of 2600g, he was breastfed until the age of 1 month, then artificially with the diversification of his diet at the age of 4 months. he had a good psychomotor development, there is no inbreeding. admitted in our service for chronic diarrhoea, dehydration. The history of his illness goes back to the age of 4 months, with post-prandial food vomiting, then at the age of 7 months the association of liquid diarrhoea > 4 with weight stagnation, , the evolution was marked by the persistence of vomiting and the appearance of thirst episodes, especially at night. The clinical examination found an infant: apyretic, conscious and malnourished, pale with dehydration folds, with a delayed weight gain: 6,10: (-3DS). Height: 68 cm (-2DS), Cranial perimeter: 44.5 cm. The rest of the clinical examination was unremarkable. The patient benefited from rehydration regimen, during hospitalization he presented a polyuria polydipsia syndrome.

Blood Ionogram did not show hydroelectrolytic disorders: Natremia: 135; Kalaemia: 4.4; Chlor: 105; Blood urea: 0.15 creatinemia: 3.8 triglyceride: 2.91; Cholesterol Total: 1.27 ; Calculated osmolarity: 286.51 mOSm; effective osmolarity: 283.19 mOSm, and a negative glucose test .Urine Ionogram was; without abnormality. the thyroid test did not show any abnormalities: TSH: 2.439 uIU/ml; T3: 1.62pg/ml; T4: 0.90 ng/dl. He had Polyuria with Diurese: 10cc/KG/H. The urine strip was normal, he did not have hyperglycemia. Kidney ultrasound showed small kidneys with regular thickening of the bladder wall. the antidiuretic hormone dosage was increased to 38.40 pmol/l (NV :< 13) , the diagnosis of nephrogenic diabetes insipidus was retained, treatment with indometacine was started.

Discussion

Nephrogenic diabetes or nephrogenic diabetes insipidus (NDI) is a rare entity of diabetes insipidus, the prevalence of diabetes insipidus is estimated at 1:25,000, 90% of which is represented by central diabetes insipidus while nephrogenic diabetes insipidus is less common [3]. Restricted definition: NDI includes only states of resistance to the antidiuretic hormone. Extended definition: NDI also includes the following states pathological conditions characterised by the impossibility of establishing a corticomedullary osmolar gradient associated or not with resistance to the antidiuretic hormone [4]. clinical manifestations are dominated by Polyuria, Polydipsia , Family history of NDI. In the first few months after birth, polyuria and polydipsia may not be noticed immediately; As in the case of our patient, polyuria was diagnosed at 11 months of age .infants with NDI are usually poor feeding, underweight and irritable [5] . Polyuria is defined by: 150 ml/kg/day in newborns, 100e110 ml/kg/day in children up to 2 years of age and 40e50 ml/kg/day in older children. [6]. our patient had polyuria with a diuresis of 10cc/Kg/h equivalent to 240cc/kg/day.

The diagnosis must be based on the measurement of volume, osmolarity and glucose collected while the patient is eating and drinking normally and is not taking any medication that may interfere with or cause diuresis. In an adult or child over 2 years of age, a volume greater than 40 ml/kg body weight, an osmolarity less than 300 mosms/L and a negative glucose test constitute a diagnosis of ID our patient had Calculated osmolarity: 286.51 mOSm and effective osmolarity: 283.19 mOSm and a negative glucose test . In infants or children under 2 years of age, the upper limit of normal for urine volume is slightly higher due to the higher water content of their diet [7].

As previously mentioned, diabetes insipidus is a clinical syndrome due to a defect oresistance of the renal tubules to concentrate urine, stimulating normal or even high plasma concentrations of AVP [1]. It is classified as primary or secondary. The primary or congenital form is hereditary. The secondary form is that seen as part of the clinical picture of various nephropathies.[1]. Approximately 90% of patients with congenital nephrogenic diabetes have an X-linked mode of inheritance. These patients have inactivating mutations in the gene encoding the V2 receptor of AVP (AVPR2) [1] ; this gene has been located in the Xq28 region. These mutations lead to intra-cellular entrapment of the receptor and the inability to reach the cell membranes in contact with the plasma So far, more than 220 different mutations of the gene encoding AVPR2 have been described. [8]. In this variant, all patients are male. In women who present the AVPR2 mutation, the phenotypic expression of the defect may be absent, partially present or complete.[9]. Approximately 10% of patients have an autosomal recessive inheritance.

In these cases, mutations in the gene coding for the action of aquaporin 2 (AQP2) have been observed, which conditions the lack of response of the main cells of the nephron collecting tubules to the action of AVP.[9].

In patients with primary tubulointerstitial nephropathies, anatomical alterations are frequently observed in the renal marrow that modify the osmolar gradient depending on the action of the countercurrent multiplication mechanisms and condition the development of polyuria[1]. Thus, nephrogenic diabetesinsipidus has been described in patients with juvenile nephronoptisis (before the development of chronic renal insufficiency), in patients with polycystic renal disease, distal renal acidosis, Fanconi syndrome, hypercalciuria idiopathic and renal amyloidosis [10].

The method used for differential diagnosis varies according to clinical presentation and available resources. In the rare patient with an abnormal elevation of plasma/sodium osmolarity, primary polydipsia as well as partial pituitary and partial nephrogenesis can be excluded and the remaining possibilities, severe pituitary DI or severe nephrogenic DI can be differentiated simply by determining the effect on urinary osmolarity of the injection of standard test doses of AVP (0.05 units of aqueous Pitressin) or desmopression. [11]. A new approach that eliminates the need for fluid deprivation offers a simpler but equally reliable way to differentiate between the three main types of ID, regardless of the severity of the underlying defect. It is based on two observations: firstly, basal plasma VAP is always normal or elevated in nephrogenic DI s, but low or undetectable in pituitary DI s and primary polydipsia; secondly, the hyperintense signal ("bright spot") normally emitted by the posterior pituitary gland on T-1-weighted brain MRI is absent or abnormally low in pituitary DI s, but present or

abnormally high in primary polydipsia. Thus, the three types of DI can be differentiated in two steps.

The first consists of measuring basal plasma DVT and simultaneous urine osmolarity under conditions of unrestricted fluid intake. If the plasma DVT is normal or high (>2.5 pg/mL) when urinary osmolarity is low, then the first step is to measure the basal plasma DVT and urine osmolarity at the same time. [11].

Nephrogenic diabetes insipidus nephrogenicus is a rare disease that requires special treatment. Unfortunately, as is the case with rare diseases, the diagnosis of Nephrogenic diabetes insipidus nephrogenicus requires special treatment can be either missed or misunderstood, leading to dangerous abuse. Although the pathophysiology and molecular diagnosis of congenital polyuric states is well established [12]. The standard treatment consists of symptomatic relief by reducing dietary sodium intake and replacing urine fluid loss, inhibiting tubular sodium reabsorption with thiazide diuretics and administering a prostaglandin synthetase inhibitor, most commonly indomethacin [13]. Indomethacin, a non-selective cyclo-oxygenase inhibitor, antagonises prostaglandin synthesis, resulting in increased water reabsorption in the proximal tubules and a 25-50% greater reduction in UOP than with thiazide diuretics alone [14]. In general, these treatments reduce the volume of urine by about 30-70% [13].

Conclusion

Polyuria, polydipsia and tubular resistance to arginine-vasopressin are the characteristics of the NDI. The mutations with loss of function of AVPR2 or AQP2 give a classic pure NDI with exclusive water loss.the NDI treatment is based on non-specific measures to reduce the amount of water presented to the collecting channel and to avoid dehydration and volume contraction.

References

1. Velásquez JL. Alteraciones hidroelectrolíticas en Pediatría.México: Editorial Prado; 2010. p. 53.
2. Berl T, Verbalis J. Fisiopatología del metabolismo de agua. En:Brenner BM, editor. Brenner y Rector. El ri˜nón. Tratado de Nefro-logía. Madrid: Elsevier; 2005. p. 857---919.
3. Kalra S, Zargar AH, Jain SM, Sethi B, Chowdhury S, Singh AK, Thomas N, Unnikrishnan AG, Thakkar PB, Malve H. Diabetes insipidus: The other diabetes. Indian J Endocrinol Metab. 2016 Jan-Feb;20(1):9-21. doi: 10.4103/2230-8210.172273. PMID: 26904464; PMCID: PMC4743391.
4. Bichet DG. Diabètes insipides néphrogéniques [Nephrogenic diabetes insipidus]. Nephrol Ther. 2006 Nov;2(6):387-404. French. doi: 10.1016/j.nephro.2006.07.010. Epub 2006 Sep 25. PMID: 17081961.
5. Knoers N, Lemmink H. Hereditary Nephrogenic Diabetes Insipidus. 2000 Feb 12 [Updated 2020 Feb 27]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020.
6. Sperling M. Pediatric endocrinology. 4 ed. Philadelphia, PA: Elesevier; 2014.
7. Robertson GL. Diabetes insipidus: Differential diagnosis and management. Best Pract Res Clin Endocrinol Metab. 2016 Mar;30(2):205-18. doi: 10.1016/j.beem.2016.02.007. Epub 2016 Feb 18. PMID: 27156759
8. Armstrong SP, Seeber RM, Ayoub MA, Feldman BJ, Pfleger KD.Characterization of three vasopressin receptor 2 variants: anapparent polymorphism (V266A) and two loss-of-function muta-tions (R181C and M311V). PLoS One. 2013;8:e65885.

9. Wesche D, Deen PM, Knoers NV. Congenital nephrogenic dia-betes insipidus: the current state of affairs. Pediatr Nephrol.2012;27:2183---204.
10. Patra S, Nadri G, Chowdhary H, Pemde HK, Singh V, Chandra J.A case report of nephrogenic diabetes insipidus with idiopat-hic Fanconi syndrome in a child who presented with vitamin Dresistant rickets. J Pediatr Endocrinol Metab. 2014;27:573---5.
11. Robertson GL. Diabetes insipidus: Differential diagnosis and management. Best Pract Res Clin Endocrinol Metab. 2016 Mar;30(2):205-18. doi: 10.1016/j.beem.2016.02.007. Epub 2016 Feb 18. PMID: 27156759.]
12. Bockenhauer D, Bichet DG. Pathophysiology diagnosis and management of nephrogenic diabetes insipidus. Nat Rev Nephrol 2015; 11:576–588. Detailed description of AVPR2 and AQP2 mutations, diet recommendations including osmotic load and common treatments.
13. Schernthaner-Reiter MH, Stratakis CA, Luger A. Genetics of Diabetes Insipidus. Endocrinol Metab Clin North Am. 2017 Jun;46(2):305-334. doi: 10.1016/j.ecl.2017.01.002. Epub 2017 Feb 28. PMID: 28476225
14. Dabrowski E, Kadakia R, Zimmerman D. Diabetes insipidus in infants and children. Best Pract Res Clin Endocrinol Metab. 2016 Mar;30(2):317-28. doi:10.1016/j.beem.2016.02.006. Epub 2016 Feb 27. PMID: 27156767