Letter to the Editor

Prevalence, diagnosis and management of secondary pseudohypoaldosteronism

Erica **Memoli**[1] • Sebastiano A. G. **Lava**[2] • Mario G. **Bianchetti**[1,3] Carlo **Agostoni**[4,5] • Gregorio P. Milani[4,5] (il mio cognome va in grassetto)

[1] Pediatric Institute of Southern Switzerland, Ospedale San Giovanni, Bellinzona, Switzerland;
[2] Pediatric Cardiology Unit, Department of Pediatrics, Centre Hospitalier Universitaire Vaudois (CHUV), and University of Lausanne, 1010 Lausanne, Switzerland;
[3] Università della Svizzera Italiana, Lugano, Switzerland;
[4] Pediatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy;
[5] Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy.

Correspondence
Mario G. Bianchetti, MD, Faculty of Biomedical Sciences, Via Buffi 13, Lugano (Switzerland). Email: mario.bianchetti@usi.ch

Word count
- Manuscript: 427 words
- References: 9

Sir:

We congratulate Atmis and colleagues for the fascinating case of a ~~Turkish~~ 2½-month-old girl with an anomalous urinary tract and a febrile urinary tract infection in spite of antimicrobial prophylaxis, which was complicated by secondary pseudohypoaldosteronism [1,2]. Presentation and course of the case were very well documented both clinically and biochemically.

We would like to briefly address the prevalence and the diagnostic attitude (with our experience), the differential diagnosis and the management of secondary pseudohypoaldosteronism in infants with urinary tract infection.

Atmis and colleagues [1,2] ~~apparently~~ suggest that the condition is rare. Furthermore, the determination of renin, aldosterone, adrenocorticotropic hormone and cortisol seems to be required for diagnosis. It has been speculated that secondary pseudohypoaldosteronism is no rare among infants with a febrile urinary tract infection [3,4]. In clinical practice, the diagnosis is made in an infant affected by a symptomatic urinary tract infection or an anomalous urinary tract, who is found to have at least two of following abnormalities: hyponatremia, hyperkalemia and metabolic acidosis [3-5]. In our experience, secondary pseudohypoaldosteronism is common (table 1): among 96 infants ≥4 weeks to ≤12 months of age affected by acute pyelonephritis, features consistent with secondary pseudohypoaldosteronism were noted in 29 (30%).

Salt-wasting crises due to congenital adrenal hyperplasia may mimic the biochemistry of pseudohypoaldosteronism [6]. However, no more salt-wasting cases due to this condition are noted in most high-income countries, because an efficient neonatal screening has been established [6]. Trimethoprim, often with sulfamethoxazole, is widely prescribed to prevent urinary tract infections. Since trimethoprim functions as a potassium-sparing diuretic [7], it may cause hyponatremia, hyperkalemia and acidosis. Consequently, urinary tract infections, anomalies of the urinary tract and drugs [7]

nowadays account for almost all cases of this abnormal biochemical pattern in infancy.

In secondary pseudohypoaldosteronism, the mainstay of management of water and salt disturbance consists of fluid resuscitation with an isotonic solution [3]. Normosaline is preferred to repair hyponatremia and lactated Ringer to repair acidosis [8]. Hyperkalemia customarily contraindicates Ringer, because it contains potassium. However, the literature does not support this view [8]. Hyponatremia may be severe (≤120mmol/L) in secondary pseudohypoaldosteronism. Since it develops over ≥48hours, a rapid correction risks iatrogenic osmotic demyelination syndrome [9]. Most authorities currently recommend a ≤6mmol/L daily increase in sodium [9]. In pseudohypoaldosteronism, isotonic solutions correct not only volume depletion and hyponatremia but also hyperkalemia [3]. Consequently, treatment of hyperkalemia with ß-agonists, sodium bicarbonate, insulin, fludrocortisone or cation exchangers is unnecessary. Reduced responsiveness to aldosterone may persist for months after treatment of the underlying infection or repair of the urinary tract anomaly [3]. Hence, long-term supplementation with salt is occasionally required.

References

1. Atmis B, Turan İ, Melek E, Karabay Bayazit A (2019) An infant with hyponatremia, hyperkalemia, and metabolic acidosis associated with urinary tract infection: Questions. Pediatr Nephrol 34:1737. doi: 10.1007/s00467-019-04252-4.

2. Atmis B, Turan İ, Melek E, Bayazit AK (2019) An infant with hyponatremia, hyperkalemia, and metabolic acidosis associated with urinary tract infection: Answers. Pediatr Nephrol 34:1739-1741. doi: 10.1007/s00467-019-04254-2.

3. Bertini A, Milani GP, Simonetti GD, Fossali EF, Faré PB, Bianchetti MG, Lava SAG (2016). Na^+, K^+, Cl^-, acid-base or H_2O homeostasis in children with urinary tract infections: a narrative review. Pediatr Nephrol 31:1403-1409. doi: 10.1007/s00467-015-3273-5.

4. Milani GP, Grava A, Bianchetti MG, Lava SAG, Dell'Era L, Teatini T, Fossali EF (2017) Electrolyte and acid-base abnormalities in infants with community-acquired acute pyelonephritis: prospective cross-sectional study. Nephron 137:99-104. doi: 10.1159/000478054.
5. Delforge X, Kongolo G, Cauliez A, Braun K, Haraux E, Buisson P (2019) Transient pseudohypoaldosteronism: a potentially severe condition affecting infants with urinary tract malformation. J Pediatr Urol 15:265.e1-265.e7. doi: 10.1016/j.jpurol.2019.03.002.
6. Turcu AF, Auchus RJ (2015) Adrenal steroidogenesis and congenital adrenal hyperplasia. Endocrinol Metab Clin North Am 44:275-296.
7. Zietse R, Zoutendijk R, Hoorn EJ (2009) Fluid, electrolyte and acid-base disorders associated with antibiotic therapy. Nat Rev Nephrol 5:193-202. doi: 10.1038/nrneph.2009.17.
8. Santi M, Lava SA, Camozzi P, Giannini O, Milani GP, Simonetti GD, Fossali EF, Bianchetti MG, Faré PB (2015) The great fluid debate: saline or so-called "balanced" salt solutions? Ital J Pediatr 41:47. doi: 10.1186/s13052-015-0154-2.
9. Lavagno C, Milani GP, Uestuener P, Simonetti GD, Casaulta C, Bianchetti MG, Fare PB, Lava SAG (2017) Hyponatremia in children with acute respiratory infections: A reappraisal. Pediatr Pulmonol 52:962-967. doi: 10.1002/ppul.23671.