

# A hypertensive emergency with acute visual impairment due to excessive liquorice consumption

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## ABSTRACT

Hypokalaemic hypertension is the classical presentation of primary hyperaldosteronism but may also result from other mineralocorticoid activity, such as liquorice ingestion. Onset of hypertension as well as serum renin and aldosterone levels are central for the diagnosis. Liquorice ingestion has been reported to induce hypertension, hypokalaemia and metabolic alkalosis due to inhibition of the enzyme 11- $\beta$ -hydroxysteroid dehydrogenase 2. Here, we report the case of a hypertensive emergency with acute visual impairment due to hypertensive retinopathy in clear conjunction with a considerable consumption of liquorice.

## KEYWORDS

Hypertensive emergency, pseudohyperaldosteronism, mineralocorticoid excess, glycyrrhizin, liquorice

## CASE PRESENTATION

A 57-year-old Caucasian male patient with an unremarkable medical history presented to the Emergency Department with acute visual impairment. Initial examination revealed hypertensive retinopathy grade IV on ophthalmological fundoscopy and a blood pressure of 250/110 mmHg. The examination was otherwise normal (heart rate 88 bpm, temperature 36.8°C, weight 75 kg, height 1.75 m). Laboratory testing showed a severe hypokalaemia of 2.07 mmol/l (*table 1*). Potassium chloride was administered and antihypertensive treatment immediately started using intravenous urapidil and sublingual glyceryl trinitrate, which finally

### What was known on this topic?

Hypertensive emergencies require immediate therapy and a thorough diagnostic approach to identify the underlying cause. While hypokalaemic hypertension is the classical presentation of primary hyperaldosteronism, liquorice ingestion inhibiting the enzyme 11- $\beta$ -hydroxysteroid dehydrogenase 2 and thereby inducing hypertension, is an important differential diagnosis.

### What does this add?

Chronic regular liquorice consumption, even of a famous and frequently sold German sweet manufacturer, should be viewed as a potential culprit for the development of hypertension including hypertensive emergencies. Chronic liquorice intake should always be considered in adult hypokalaemic hypertensive patients.

resulted in improved blood pressure levels. To identify a potential cause for the hypertensive emergency, further diagnostic procedures were initiated. Normal serum creatinine, urinalysis and an inconspicuous abdominal ultrasound and renovascular Doppler imaging ruled out renoparenchymous or renovascular hypertension. Endocrine testing (*table 1*) excluded hypertension due to hyperaldosteronism, hypercortisolism, pheochromocytoma and paragangliomas. However, suppressed plasma aldosterone and renin levels were suggesting pseudohyperaldosteronism. Further evaluation of the patient's habits disclosed a noticeable weekly consumption of at least three packs of liquorice (each 300 g) from a

**Table 1.** Laboratory findings on admission and on discharge as well as one month later at follow-up

| Laboratory tests                  | On admission            | On discharge | At follow-up | Reference values              |
|-----------------------------------|-------------------------|--------------|--------------|-------------------------------|
| Blood counts                      |                         |              |              |                               |
| • Haemoglobin                     | 14.4                    | 13.5         |              | 12.0-16.0 g/dl                |
| • Platelets                       | 222                     | 190          |              | 150-400 x 10 <sup>3</sup> /μl |
| • White blood cells               | 7.46                    | 5.57         |              | 4.0-9.5 x 10 <sup>3</sup> /μl |
| Electrolytes and renal parameters |                         |              |              |                               |
| • Sodium                          | 144                     | 140          | 139          | 133-146 mmol/l                |
| • Potassium                       | <b>2.07</b>             | 4.19         | 4.11         | 3.5-5.1 mmol/l                |
| • Chloride                        |                         | 108          |              | 133-146 mmol/l                |
| • Bicarbonate                     | <b>29.4</b>             |              |              | 22-28 mmol/l                  |
| • Creatinine                      | 99.3                    | 81.3         |              | 55-110 mmol/l                 |
| Hormonal parameters (serum)       |                         |              |              |                               |
| • TSH                             | 2.86                    |              |              | 0.27-4.20 mIU/l               |
| • Renin                           | < 1*                    |              |              | 3-16 ng/l                     |
| • Aldosterone                     | < 11*                   |              |              | 10-160 ng/l                   |
| • Cortisol                        | 652 / 80 <sup>‡</sup> * |              |              | 171 - 535 nmol/l              |
| • Adrenaline                      | <b>120</b> *            |              |              | < 85 pg/ml                    |
| • Noradrenaline                   | 325*                    |              |              | < 400 pg/ml                   |
| • Dopamine                        | < 30*                   |              |              | < 50 pg/ml                    |
| • Metanephrine                    | 40.9*                   |              |              | < 90 pg/ml                    |
| • Normetanephrine                 | 108                     |              |              | < 200 pg/ml                   |
| 24-hour urinary excretion         |                         |              |              |                               |
| • Potassium                       | 26                      |              |              | 30-100 mmol/day               |
| • Sodium                          | 260                     |              |              | 60-260 mmol/day               |
| • Adrenaline                      | 14.3*                   |              |              | ≤ 40 μg/day                   |
| • Norepinephrine                  | 42.8*                   |              |              | ≤ 80 μg/day                   |
| • Metanephrine excretion          | 47.6*                   |              |              | ≤ 80 μg/day                   |
| • Normetanephrine                 | 34.1*                   |              |              | ≤ 120 μg/day                  |

Abnormal values are depicted in bold. \*Endocrine tests in serum, plasma and urine were obtained following initial blood test on admission. †Cortisol obtained 1 hour after administration of 1 mg dexamethasone. TSH = thyroid-stimulating hormone.

German sweet manufacturer for the last three to four months. Since this nutritional behaviour was considered to be likely related to the patient's hypertension, the liquorice consumption was stopped. Initially, antihypertensive medication comprising seven different drugs was required to lower the blood pressure below 140/70 mmHg (*table 2*), finally resulting in substantial improvement of eye vision at the time of discharge. One month later, his blood pressure (160/80 mmHg) had already improved with the need for only two antihypertensive drugs (*table 2*). While the hypertension was not yet satisfactorily controlled, laboratory tests showed a normal potassium value at that time (*table 1*). After three months, with the patient still not eating any liquorice and having treatment with the same two antihypertensive drugs, a normal blood pressure was achieved (*table 2*).

## DISCUSSION

Hypertension associated with hypokalaemia is the classical presentation of primary hyperaldosteronism. However, the present patient's laboratory testing showed suppressed aldosterone and renin levels with

a normal aldosterone-to-renin-ratio. While the clinical picture resembled hyperaldosteronism, the hormonal profile showed hyporeninaemic hypoaldosteronism. Liddle's syndrome is a hereditary hypertension with hypokalaemia due to gain-of-function mutations in the gene encoding the renal epithelial sodium channel.<sup>1</sup> However, this disorder is rare and the age of onset is in childhood; thus, Liddle's syndrome was considered very unlikely to be present in this case. Another form of low-renin hypertension associated with low aldosterone and hypokalaemia is apparent mineralocorticoid excess (AME), a congenital defect in 11-β-hydroxysteroid dehydrogenase 2 (11-β-HSD2).<sup>2,3</sup> Since 11-β-HSD2 converts the biologically active cortisol to inactive cortisone, the defect allows cortisol to act as a ligand for the mineralocorticoid receptor, thereby resulting in sodium retention and volume expansion. However, as with Liddle's syndrome, AME is a disorder of the young, starting in early childhood. A much more common cause of hypertension due to pseudohyperaldosteronism in the adult is excessive liquorice consumption, with its ingredient glycyrrhizin being responsible for a mineralocorticoid effect. Previous reports showed that glycyrrhizin

**Table 2.** Antihypertensive medication on admission, discharge and at follow-up after one and three months, respectively

| Antihypertensive drugs | On admission | On discharge | 1 month later | 3 months later |
|------------------------|--------------|--------------|---------------|----------------|
| Metoprolol             | ∅            | 95 mg qd     | ∅             | ∅              |
| Urapidil               | ∅            | 90 mg tid    | ∅             | ∅              |
| Ramipril               | ∅            | 5 mg bid     | 5 mg qd       | 5 mg qd        |
| Hydrochlorothiazide    | ∅            | 25 mg qd     | ∅             | ∅              |
| Triamterene            | ∅            | 50 mg qd     | ∅             | ∅              |
| Amlodipine             | ∅            | 5 mg bid     | 10 mg qd      | 10 mg qd       |
| Spironolactone         | ∅            | 50 mg qd     | ∅             | ∅              |

qd = daily; bid = twice daily; tid = three time a day.

blocks 11- $\beta$ -HSD<sub>2</sub>, thereby mimicking AME and resulting in hypertension, hypokalaemia and alkalosis at any age.<sup>4</sup> Due to the blockage of 11- $\beta$ -HSD<sub>2</sub> the active cortisol binds to the aldosterone receptor. Via this mechanism the serum concentration of renin and aldosterone is low in affected patients. In fact, consumption of a considerable amount of liquorice explained the hypertension which probably developed gradually in the present patient, finally resulting in a hypertensive emergency. In addition, the elevated bicarbonate level indicated alkalosis, which perfectly complements the laboratory findings. While liquorice-induced hypertension is a well-known entity and liquorice is coming more and more into discredit,<sup>5,7</sup> a hypertensive emergency with acute visual impairment in terms of retinopathy due to liquorice in sweets has not yet been reported. Liquorice ingestion has been described to be a possible cause of posterior reversible encephalopathy syndrome (PRES), which could induce visual disturbance.<sup>8</sup> MRI or at least CT scan of the brain might have been useful for differential diagnosis in our case. However, because of the hypertensive retinopathy proven by fundoscopy and the triad of hypertension, hypokalaemia and alkalosis PRES was unlikely to be the underlying reason. Further investigations in the present case revealed that the glycyrrhizin content per kg ingested liquorice was about four grams. Since the patient stated an average consumption of approximately 1 kg liquorice per week, his intake resulted in approximately 500 mg glycyrrhizin per day. Recently, a Swedish study with healthy volunteers revealed a linear dose-response relationship of liquorice ingestion and hypertension starting at a daily intake of 75 mg glycyrrhizin for two weeks.<sup>9</sup> In addition, in 2006, Sigurjonsdottir et al. described that the aldosterone effect of liquorice might be gender specific and males may be more susceptible.<sup>10</sup> This might have even increased the effect of the liquorice ingestion in the present case. Of note, the hypertensive effect may prevail for some time despite stopping ingestion of liquorice, as observed in the

present case. Thus, patients should be monitored for some time after stopping liquorice intake, Sigurjonsdottir and colleagues recommend a period of up to four months until the renin suppression is overcome.<sup>9</sup> In the present case, effective control of blood pressure over time with only two antihypertensive drugs underlines that prior excessive liquorice consumption had been at least partly responsible for the hypertensive emergency in this patient. However, a potential effect of additional essential hypertension cannot be excluded. In conclusion, regular liquorice consumption should clearly be viewed as a culprit for the development of hypertension including hypertensive emergencies and liquorice intake should always be considered in hypokalaemic hypertensive patients.

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#### DISCLOSURES

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#### REFERENCES

- Warnock DG. Liddle syndrome: genetics and mechanisms of Na<sup>+</sup> channel defects. *Am J Med Sci.* 2001;322:302-7.
- Ferrari P. The role of 11 $\beta$ -hydroxysteroid dehydrogenase type 2 in human hypertension. *Biochim Biophys Acta.* 2010;1802:1178-87.
- Ulick S, Levine LS, Gunczler P, et al. A syndrome of apparent mineralocorticoid excess associated with defects in the peripheral metabolism of cortisol. *J Clin Endocrinol Metab.* 1979;49:757-64.

4. Ferrari P, Sansonnens A, Dick B, Frey FJ. In Vivo 11 -HSD-2 Activity: Variability, Salt-Sensitivity, and Effect of Licorice. *Hypertension*. 2001;38:1330-6.
5. Sontia B, Mooney J. Pseudohyperaldosteronism, Licorice, and Hypertension. *J Clin Hypertens*. 2008;10:153-7.
6. Ruiz-Granados ES, Shouls G, Sainsbury C, Antonios T. A salty cause of severe hypertension. *BMJ Case Rep*. 2012;2012.
7. Kormann R, Languille E, Amiot HM, Hertig A. Dying for a cup of tea. *BMJ Case Rep*. 2012;23087275.
8. Van Beers E, Stam J, van den Bergh W. Licorice consumption as a cause of posterior reversible encephalopathy syndrome: a case report. *Crit Care*. 2011;15:R64.
9. Sigurjónsdóttir HA, Franzson L, Manhem K, Ragnarsson J, Sigurdsson G, Wallerstedt S. Licorice-induced rise in blood pressure: a linear dose-response relationship. *J Hum Hypertens*. 2001;15:549-52.
10. Sigurjónsdóttir HA, Axelson M, Johannsson G, Manhem K, Nyström E, Wallerstedt S. The licorice effect on the RAAS differs between the genders. *Blood Press*. 2006;15:169-72.