Acute Intermittent Porphyria Associated With Inappropriate ADH Secretion In A Hyperthyroid Patient

K Ashawesh, M Jones

Citation

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Abstract

Acute intermittent porphyria (AIP) is an autosomal dominant disease due to deficient Porphobilinogen (PBG) deaminase activity. Hyponatremia is found in approximately 20% of symptomatic AIP and often due to inappropriate ADH secretion (SIADH). The association between AIP and hyperthyroidism is not clearly established. Hyperthyroidism may have a role in exacerbation of previously latent porphyria. We describe a patient with AIP and SIADH who also presented with Graves' hyperthyroidism.

CASE REPORT

A 35-year-old lady with no significant past medical history was admitted to the gynaecology ward with lower abdominal pain. Physical examination was normal apart from tachycardia and small, diffuse goitre. Laboratory investigations revealed hyponatraemia, with serum sodium 120 meq/l, and mild leukocytosis (11.3 x 10^9/l). Abdominal laparoscopy was normal. Abdominal pain and hyponatraemia resolved over the next few days with no treatment, although the tachycardia persisted. Further investigations revealed Graves' hyperthyroidism, FT4 42 pmol/l (9-25), FT3 11.9 pmol/l (3.4-7.2) and TSH <0.03 mU/l (0.5-6) with a significant titre of thyroid peroxidase antibodies. She was treated with Carbimazole 20 mg twice daily. Eight weeks later, the patient was re-admitted with recurrent abdominal pain, nausea and vomiting. Physical examination was unremarkable and she was biochemically euthyroid on carbimazole 15 mg daily. Following treatment with metoclopramide and diclofenac, she again became Hyponatraemia with a serum sodium of 120 meq/l, and developed generalised weakness in all four limbs with significant respiratory muscle weakness. Bedside spirometry showed decreased forced vital capacity to 50% of predicted. Blood pressure was 80/40 mmHg. Inappropriate ADH secretion (SIADH) was found to be the cause of the hyponatraemia (serum osmolality 249 mOsm/kg, urine osmolality 770 mOsm/kg and urinary Na 107 mmol/l). The combination of SIADH and recurrent abdominal pain led to the diagnosis of Acute Intermittent Porphyria (AIP); Urinary PBG was 125 umol/l (normal < 10 umol/l), urinary total porphyrin 1677 nmol/l (normal 20-320 nmol/l) and Red Blood Cell PBG deaminase 20 mmol/h/ml (normal 24-67 mmol/h/ml). Family screening revealed that father and sister were affected, although both were asymptomatic. Following withdrawal of diclofenac and metoclopramide, treatment with IV 20% dextrose and rehabilitation, a marked improvement occurred with resolution of quadriparesis, respiratory muscle weakness and hyponatraemia. Four months later, she received an outpatient radioiodine therapy and remained euthyroid with no further AIP exacerbations during a four year follow up.

DISCUSSION

AIP is an autosomal dominant disease resulting from deficient PBG deaminase activity. Abdominal pain is the most common presenting symptom and usually persists for several days. Other common clinical features include: constipation (50%), nausea and vomiting (50%), tachycardia (40%), limb weakness (40%), hypertension (31%), urine discolouration (25%), delirium (22%), seizures (15%), and depression (8%).[1] Diagnosis of AIP is more difficult in those without family history when a high index of clinical suspicion is required.

Hyponatraemia, found in approximately 20% of patients with symptomatic AIP, is generally due to SIADH[1]. Hypothalamic damage, with neuronal loss in the supraoptic and paraventricular nuclei at the level of the median eminence, has been described in patients who died of AIP complicated by SIADH.[1,2,3] Damage to the hypothalamic hypophyseal tract during an exacerbation of AIP may therefore lead to an increase in circulating ADH. Other

causes of hyponatremia during symptomatic AIP include gastrointestinal and renal sodium loss. As the therapeutic approach is different, SIADH should be considered in a patient with AIP and hyponatraemia.

Hyperthyroidism shares many clinical features with symptomatic AIP including sinus tachycardia, muscle weakness, hypertension and nervousness. Diagnosis of hyperthyroidism can therefore be difficult in patients with symptomatic AIP. Persistent tachycardia and small diffuse goitre led to diagnosis of Graves' hyperthyroidism in our case.

The association between AIP and hyperthyroidism is not clearly established. Hyperthyroidism may aggravate the basic metabolic disturbance of AIP, possibly by further increasing hepatic 5-aminolaevulinate synthase activity[4]. Two previous case reports[5], [6] described an exacerbation of acute porphyria by hyperthyroidism and a marked improvement following antithyroid drug treatment. This is in agreement with our case in which the first episode of AIP was most likely precipitated by hyperthyroidism and there has been no recurrence of AIP since the euthyroid state was achieved.

CONCLUSION

Differential diagnosis of abdominal pain with concomitant hyponatraemia, particularly if caused by SIADH, should include symptomatic AIP. Development of hyperthyroidism in a patient with latent porphyria may precipitate an acute episode and increase the disease severity.

KEY POINTS

- AIP is rare, but can be fatal.
- Differential diagnosis of abdominal pain and hyponatraemia should include Symptomatic AIP.
- SIADH should be considered in patients with symptomatic AIP and hyponatraemia.
- Hyperthyroidism may have a role in exacerbation of previously latent porphyria.

CORRESPONDENCE TO

Dr Khaled Ashawesh Department of medicine: Princess Royal Hospital Telford, TF 6TF, UK Tel: 0044(0)1952641222 ext. 4791 Fax: 0044(0)1952243405 Email: k_ashawesh@yahoo.com

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Author Information

Khaled Ashawesh, MRCP
Department of Medicine, Singleton Hospital

M. Keston Jones, M.D., FRCP
Department of Medicine, Singleton Hospital