Black urine

PAUL ALTMANN
M.B., B.S.

MARTIN A. MANSELL
M.B., M.R.C.P.

Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ

Summary

A patient is described in whom spontaneous blackening of the urine, due to melanin formation, resulted from treatment with α -methyl dopa. The colour change became apparent only after the correction of a severe postoperative hyponatraemic alkalosis, once the urinary pH had become alkaline, as melanin formation in acid urine is very slow.

Introduction

Black urine may be caused by the presence of methaemoglobin or phenols, or may follow the ingestion of pyrogallol (Frankel, Reitman and Sonnenwirth, 1970). Blackening of the urine on exposure to light is characteristic of homogentisic acid, due to alkaptonuria and may also result if melanogens are present. These are substances which spontaneously polymerize to form melanin, which may be found in the urine of patients with disseminated malignant melanoma, Addison's disease or long-standing intestinal obstruction (Davidsohn and Henry, 1969). Normal metabolism of α -methyl dopa also produces a variety of melanogens, of which the best defined is α -methyl dopamine (Buhs *et al.*, 1964). Spontaneous melanin formation in the urine of patients taking α -methyl dopa, without contact with bleach, does not appear previously to have been reported.

Case report

A 63-year-old woman underwent cholecystectomy for repeated attacks of biliary colic. Her previous medical history was unremarkable apart from essential hypertension, diagnosed 7 years before, for which she was taking methyl dopa 2 g/day, and bendrofluazide 5 mg every morning. Routine pre-operative blood count, electrolytes and urea and chest X-ray were normal.

Surgery was uneventful and her hypotensive therapy was re-started on the first postoperative day, together with i.v. dextrose-saline and small amounts of oral fluids. However, her conscious level deteriorated steadily during the next 48 hr and she became

semi-comatose. On examination she was afebrile, with a normal pulse and BP and, apart from the depressed level of consciousness, no abnormality was found in the CNS. The rest of the physical examination was similarly unremarkable, apart from a small area of crackles at the right base of the lung, compatible with postoperative atelectasis.

Investigations showed that the plasma sodium and potassium were very low (109 mmol/l and 1.7 mmol/l respectively) while the bicarbonate was elevated at 30 mmol/l. She was alkalotic, with a pH of 7.56, a normal P_{CO_2} (4.5 kPa, 34 mmHg) and a diminished P_{O_2} (7.4 kPa, 55 mmHg). The blood count was normal and chest X-ray showed a modest degree of bilateral basal collapse. 'Spot' measurements of urinary sodium and potassium were 64 mmol/l and 57 mmol/l respectively.

A diagnosis of symptomatic hyponatraemia was made and she received 2 litres of 2N saline and 280 mmol of potassium i.v. during the next 24 hr. Despite a reasonable urine output she developed signs of hypervolaemia during this time which responded to 40 mg of frusemide.

By the next day she was fully awake and orientated with a plasma sodium of 123 mmol/l and potassium of 3.0 mmol/l. The i.v. fluid was changed to normal saline and by the 6th postoperative day she had made a complete clinical and biochemical recovery.

However, at about this time it was noted that the urine when freshly passed had a greyish tinge and that it turned jet black after standing in the light for a few hours. The urine gave positive reactions with ferric chloride and nitroprusside (black and blue/green colorations respectively), although reducing substances were absent, excluding the presence of homogentisic acid. These reactions are characteristic of melanogens, substances which polymerize to form melanin in the presence of light and oxygen.

The hypotensive therapy was changed to oxprenolol and hydralazine and within 5 days the appearance of the urine had returned to normal. The patient left hospital on the 15th postoperative day with no residual abnormalities.

Discussion

Whilst postoperative hyponatraemia is not uncommon it is rarely of this degree, so that other factors may have been important. In the first 2 post-operative days she received 5 litres of dextrose-saline, which contains only 30 mmol of sodium/l, so that some of the observed depression of plasma sodium was dilutional. Although thiazides by themselves rarely produce hyponatraemia, urinary sodium loss is increased by the accompanying metabolic alkalosis which, in turn, is aggravated by profound hypokalaemia (Schrier, 1976). Acute symptomatic hyponatraemia is a medical emergency, demanding treatment with hypertonic saline (Arieff and Guisado, 1976), as irreversible brain damage may occur within 12 hr if the plasma sodium falls below 125 mmol/l (Lipsmeyer and Ackerman, 1966).

Colour changes, varying from red to black, have been noted in the urine of patients taking methyl-dopa (Cardwell, 1969), or L-dopa (Deveraux and Mancall, 1974), although only after contact with lavatory bleach. The spontaneous formation of melanin from melanogen, as occurred in this patient, requires a urine pH of 7 or more. The authors found that urine samples, made alkaline, from patients receiving methyl-dopa or L-dopa turned black on exposure to light in 85% and 40% of the samples respectively, suggesting that the phenomenon is more common than the literature would suggest.

Presumably in this patient the alkalosis associated with thiazide therapy would have been accompanied by the production of an acid urine, in which the formation of melanin is very slow. Only after vigorous re-salination did the urine pH increase into the range where melanin formation occurred quickly

enough to be detected in the urine samples awaiting collection from the ward.

The occurrence of hyponatraemia and melanuria in this patient prompted investigation for ectopic hormone production by an occult neoplasm. The only abnormality found was a solitary, non-functioning thyroid nodule which was excised surgically and found to be benign.

Acknowledgments

We thank Mr A. G. Cox, M.D., F.R.C.S., for his permission to report this case and Dr H. Worth and Mr D. J. Wright (Department of Clinical Chemistry) for help in identifying the urinary pigment.

References

- ARIEFF, A.I. & GUISADO, R. (1976) Effects on the central nervous system of hypernatremic and hyponatremic states. *Kidney International*, **10**, 104.
- BUHS, R.P., BECK, J.L., SPETH, O.C., SMITH, J.L., TRENNER, N.R., CANNON, P.J. & LARAGH, J.H. (1964) The metabolism of methyl-dopa in hypertensive human subjects. *Journal of Pharmacology and Experimental Therapeutics*, **143**, 205.
- CARDWELL, J.B. (1969) Red urine associated with methyl-dopa treatment. *Lancet*, **ii**, 326.
- DAVIDSOHN, I. & HENRY, J.B. (Ed.) (1969) *Clinical Diagnosis by Laboratory Methods*, 14th Edn, p. 40. W. B. Saunders and Co., Philadelphia.
- DEVERAUX, M.W. & MANCALL, E.L. (1974) Brown urine, bleach and L-dopa. *New England Journal of Medicine*, **291**, 1142.
- FRANKEL, S., REITMAN, S. & SONNENWIRTH, A.C. (Eds.) (1970) *Clinical Laboratory Methods and Diagnosis*, 5th Edn, p. 1046. C. V. Mosby Co., St Louis, Missouri.
- LIPSEMEYER, E. & ACKERMAN, G.L. (1966) Irreversible brain damage after water intoxication. *Journal of the American Medical Association*, **196**, 286.
- SCHRIER, R.W. (1976) *Renal and Electrolyte Disorders*, 1st Edn, p. 101. Little, Brown and Co., Boston.