to the patient, expense incurred, and the possibility of repeated venepunctures having an adverse propaganda effect on the rubella immunisation programme it seems unjustified and unnecessary to extend the programme to include follow-up after vaccination. No harm seems to have been done to the potency of the vaccine by the patient keeping the ampoule in her handbag for many hours, but on the general principles of vaccine storage this should be discouraged. The time spent checking on patients has now eliminated the hitherto regular instances of worry for patients and doctors on alleged rubella contact in pregnancy.

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Polycythaemia vera and central sleep apnoea

Secondary polycythaemia is a widely recognised complication of longstanding sleep apnoea.¹ It may be distinguished from polycythaemia vera by the absence of leucocytosis, thrombocytosis, and splenomegaly. In several cases sleep apnoea has occurred with neurological diseases and systemic illnesses known to have pathophysiological effects on central nervous system functioning.¹ While various neurological manifestations have been described in 56% to 78% of patients with polycythaemia vera, sleep apnoea has not been among them.² We recently studied a patient with polycythaemia vera and a subacute organic psychosis in whom central sleep apnoea responded to phlebotomy.

Case report

A 39-year-old man presented with a well-documented seven-year history of polycythaemia vera which had been confirmed by increased chromium-51 red blood cell volume, erythroid hyperplasia and absent iron stores in bone marrow, leucocytosis, raised leucocyte alkaline phosphatase activity, and normal arterial oxygen saturation. Initial clinical manifestations had been confined to malaise, headaches, phethora, and mild splenomegaly. During the last two years, however, he had had epistaxis, episodes of confusion on awakening, progressive difficulty in concentrating, and excessive daytime somnolence. During the month before admission to hospital his packed cell volume (PCV) had rapidly increased from 54% to 65%, accompanied by gross disorientation, memory loss, perseveration, and prominent delusions of guilt and annihilation. Bilateral papilloedema was present, although the remainder of the neurological examination was normal. Cerebrospinal fluid pressure was 280 mm H₂O. An exhaustive neurological and medical evaluation found no additional cause for these abnormalities, and waking respiratory function was normal. Polysomnography was performed both before phlebotomy and after reduction of his PCV to 48.8%. During this 10-day interval the confusional psychosis and papilloedema receded dramatically. Baseline studies had shown that frequent microarousals and decreased sleep efficiency were attributable to 52 episodes of central sleep apnoea, none of which occurred during rapid eye movement (REM) sleep. Apnoea occupied 14.1 minutes or 5% of total sleep time, with an average episode length of 16.3 seconds. Apnoea index (number of episodes per hour of sleep) was 8.9, compared with a published mean value for normal controls of 0.5.³ There was no evidence of an upper airway obstructive component to the sleep apnoea nor was it accompanied by cardiac arrhythmias. Follow-up sleep studies disclosed total disappearance of central sleep apnoea after phlebotomy. The patient has now remained free of neuropsychiatric symptoms and disordered sleep for one year with maintenance phlebotomy as his only treatment.

Comment

Although narcolepsy has been described in a few cases of primary polycythaemia,² we believe that this is the first reported case of central sleep apnoea complicating unequivocally diagnosed polycythaemia vera. Recognition of this potentially reversible cause of sleep apnoea is important, especially since it may be mistaken for the more commonly associated secondary polycythaemia. We further hypothesise that polycythaemia vera may lead to sleep apnoea through decreased cerebral blood flow to diencephalic respiratory centres. A similar mechanism has been proposed for other reversible neurological dysfunction described in this disorder.² Moreover, significant diminution of cerebral blood flow occurs even at PCV values often considered acceptable in the management of polycythaemia vera.⁴ The reason that apnoea never occurred during REM sleep may be that cerebral blood flow is increased during this stage of sleep.⁵

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Massive arterial thrombosis and oral contraception

The relationship between oestrogen-containing contraceptives and venous thrombosis is well known. We report a case of widespread arterial thrombosis in a woman using a combined oral contraceptive pill.

Case report

A previously fit 33-year-old housewife was admitted to a local hospital after two grand mal fits. She smoked 40 cigarettes daily and had used oral contraception (Eugynon-30) for at least five years. Four days before admission she complained of headaches, upper abdominal pain, and vomiting. On examination she was drowsy, obese, had right hypochondrial tenderness, and a blood pressure of 220/140 mm Hg. Heart size and optic fundi were normal. Investigations: haemoglobin 14.7 g/dl, white blood count $24.3 \times 10^9/l$ ($24\,300/mm^3$), alanine aminotransferase 78 IU/l, lactate dehydrogenase 1319 IU/l, glucose 9.8 mmol/l (176 mg/100 ml), urea 3.0 mmol/l (18 mg/100 ml), amylase 60 IU/l. Radiographs of chest, skull, and abdomen were normal. Over the next few days her drowsiness cleared but a small right pupil, nystagmus, incoordination of right arm and leg, and impaired sensation over the left leg were noted. Tendon reflexes were absent in both legs. Cerebrospinal fluid and computed tomography of the head were normal. On day 3 the patient was anuric with absent femoral pulses. Blood pressure was now 140/90 and urea 19.5 mmol/l (117 mg/100 ml). On day 6 she was transferred to Withington Hospital in acute renal failure. Both legs were cold and pulseless. Bowel sounds were absent. Investigations: blood urea 40 mmol/l (240 mg/100 ml), creatinine 1.30 mmol/l (14.7 mg/100 ml), potassium 6.7 mmol(mEq)/l, haemoglobin 10.9 g/dl with fibrinogen degradation products of 19 mg/l (normal 6 mg/l), prothrombin time 15 s, thrombin-fibrinogen time 19 s, platelets $166 \times 10^9/l$ ($166\,000/mm^3$). Abdominal x-ray picture showed dilated loops of small bowel. Bilateral retrograde pyelograms were normal. A translumbar aortogram was unsuccessful, but an approach through the left axillary artery showed complete occlusion of the aorta to the level of T11. Mesenteric and renal arteries could not be filled. The electrocardiogram showed sinus rhythm with T-wave inversion in all chest leads. The patient remained anuric and died eight days after admission. Necropsy showed thrombus in the left ventricle with no evidence of myocardial infarction and healthy coronary arteries. The abdominal aorta was

occluded by thrombus from the bifurcation to the coeliac axis. Both renal arteries, the superior mesenteric, and the right vertebral arteries were thrombosed with the kidneys, small bowel, and part of the cerebellum infarcted. No venous thrombosis was present. The patient also had gall stones.

Comment

Oestrogen-containing contraceptives are well known to cause abnormalities of coagulation¹ and venous thromboembolic disorders.² Arterial thrombosis is less often encountered, though cerebral,² coronary,² mesenteric,³ and vertebral artery thromboses⁴ are described. But these events are relatively rare and usually occur singly. Our patient is unusual in that she experienced widespread large artery thrombosis without venous involvement, leading to ischaemia of the legs, infarction of kidneys and small bowel, and the lateral medullary syndrome. In the absence of other known factors influencing coagulation the oral contraceptive use is thought to be significant. Enhancing her susceptibility to oestrogen-associated thromboses would be her smoking habit, age of 33 years, and taking the pill for over five years.³ Two further adverse factors were obesity and hypertension.⁵ Massive arterial thrombosis is unusual and represents another major complication of oral contraception. It further emphasises the dangers of oestrogen-containing pills in women in the high-risk group defined by the Royal College of General Practitioners' report.³

We thank Mr D Charlesworth for allowing us to report this case.

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Postpartum cranial diabetes insipidus

Cranial diabetes insipidus is uncommon and is rarely associated with Sheehan's syndrome.¹ Isolated impairment of posterior pituitary function in the face of entirely normal anterior pituitary function is most unusual after postpartum haemorrhage. We here describe a patient with such abnormalities.

Case report

A 23-year-old Yemeni woman, gravida 5, para 3, ruptured her uterus during delivery of her fourth child at term, when she had a severe uterine haemorrhage and hypotension which required emergency hysterectomy. Postoperatively she developed sudden severe thirst, polydipsia, and polyuria. She was unable to establish lactation but her child thrived. During the next 12 months she lost 5 kg in weight, continued to pass 7-8 l urine/24 h, but took no medication. Physical examination showed no signs of hypopituitarism. She was clinically euthyroid; blood pressure was 120/75 mm Hg. Milk could not be expressed from her breasts. Urine output was 6.5 l/24 h with no glycosuria. Radiograph of sella turcica, perimetry of visual fields, and computerised tomography scan of head were all normal. Serum calcium, glucose, and electrolytes were within normal limits, as was thyroid function (thyroxine 112 nmol/l (8.7 µg/100 ml), triiodothyronine uptake 106%). Anterior pituitary stimulation by insulin-induced hypoglycaemia, thyrotrophin releasing hormone (TRH), and luteinising hormone-releasing hormone (LHRH) were entirely normal (table) and basal prolactin (230 mU/l) was not raised. But despite fluid restriction, which resulted in a 4.5% weight loss, and an increase in plasma osmolality of 10 mmol/kg there was little decrease in urine flow rate or increase in urine osmolality (table). Intranasal DDAVP (synthetic vasopressin analogue) 40 µg caused a prompt rise in urine osmolality. Furthermore, immunoreactive plasma vasopressin² was low (2.3 pg/ml) and failed to rise after osmotic stimulation with hypertonic saline which increased plasma osmolality by 23 mmol/kg. All the patient's symptoms were controlled with intranasal DDAVP 10 µg daily.

Results of anterior and posterior pituitary stimulation tests in case of postpartum cranial diabetes

	Time (min)	Glucose (mmol/l)	Cortisol (nmol/l)	GH (mU/l)	LH (U/l)	FSH (U/l)	TSH (mU/l)
Anterior pituitary	0*	5.2	290	5	12	7	2.3
	30	1.7	—	15	30	—	10.7
	60	2.3	730	14	14	—	8.4
	90	3.2	510	8	—	—	—
	120	4.5	510	7	—	—	—
	Time (h)	Weight (kg)	Plasma osmolality (mmol/kg)	Urine flow (ml/min)	Urine osmolality (mmol/kg)		
Posterior pituitary	0	39.8	293	—	70		
	1.5	—	—	8.9	73		
	2	38.9	299	9.5	107		
	3.5	38.2	—	3.9	190		
	5†	38.0	303	3.4	275		
	8	—	—	0.6	611		
	23	40.2	289	0.2	753		

*Soluble insulin 6 U, LHRH 100 µg, TRH 200 µg given intravenously at time 0.

†DDAVP 40 µg given intranasally at 5 h and patient allowed free fluids.

GH = growth hormone; LH = luteinising hormone; FSH = follicle-stimulating hormone; TSH = thyroid-stimulating hormone; LHRH = luteinising hormone releasing hormone; TRH = thyrotrophin releasing hormone.

Conversion: SI to traditional units—Glucose: 1 mmol/l ≈ 18 mg/100 ml. Cortisol: 1 nmol/l ≈ 0.32 µg/100 ml. Osmolality: 1 mmol/kg = 1 mosmol/kg.

Comment

This patient had clear evidence of cranial diabetes insipidus from the results of fluid restriction and subsequent response to DDAVP and also from the lack of vasopressin response to osmotic stimulation by hypertonic saline. Yet there was no suggestion of anterior pituitary dysfunction on either clinical or biochemical grounds. From the history the abnormalities apparently dated from the immediate postpartum period after uterine rupture. We were unable to find any other possible cause for the diabetes insipidus—particularly pituitary and suprasellar tumours that occasionally result in isolated diabetes insipidus. To our knowledge only one similar case has been reported³ and in that instance plasma vasopressin concentrations were not measured.

Pituitary dysfunction after postpartum haemorrhage usually affects only the anterior part of the gland. Nevertheless, despite the lack of clinical evidence of cranial diabetes insipidus, most patients with longstanding Sheehan's syndrome have neuronal degeneration of the supraoptic and paraventricular nuclei of the hypothalamus with associated changes in the posterior pituitary.⁴ Therefore other hypothalamic disorders might be expected with Sheehan's syndrome. Persistent hyperprolactinaemia and galactorrhoea in association with cranial diabetes insipidus but preserved anterior pituitary function have been described in only two patients.⁵ Why the posterior pituitary and hypothalamus, in contrast to the anterior pituitary, are so rarely affected by postpartum haemorrhage is not clear. The explanation may be due, in part, to a difference in blood supply, since the adeno-hypophysis is supported by the superior hypophyseal artery, whereas the neurohypophysis and hypothalamus are supplied by the inferior hypophyseal artery and branches from the circle of Willis. Whatever the explanation, our patient presents an unusual syndrome of isolated cranial diabetes insipidus with preserved anterior pituitary function after postpartum haemorrhage.

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