Clinical Reports

Reversible coma in Wernicke's encephalopathy

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Summary: A case of coma due to Wernicke's encephalopathy complicated by respiratory failure is described. Ventilation and thiamine administration lead to recovery, although Korsakoff's psychosis and ataxia persisted. A review of similar cases of coma emphasizes the absence of diagnostic features, but that if structural disease is excluded the presence of pupillary and ocular signs may support a diagnosis of Wernicke's encephalopathy. The response to thiamine may be diagnostic as in 8 of these patients who received it, but the long-term morbidity remains high.

Introduction

The Wernicke-Korsakoff syndrome is a common but underdiagnosed acute, subacute or chronic condition that occurs in thiamine-depleted alcoholic and non-alcoholic individuals (Harper, 1983). Coma due to acute Wernicke's encephalopathy is considered rare though Wernicke's may co-exist in coma due to hepatic encephalopathy, hypoglycaemia, drug overdose, infection, seizures or subdural haematoma. It is thought to represent an advanced stage of the condition with a high mortality (Victor *et al.*, 1971; Campbell & Russell, 1941). We report a patient who presented in coma, required ventilatory support and improved with thiamine administration.

Case report

A 42 year old man had not been seen by neighbours for three days and was found unconscious in his flat. He was known to drink 15 pints (8.5 l) of beer daily.

On admission he was in coma and deeply cyanosed with inadequate respiratory movements. His temperature was 37.2°C, heart rate 120 beats/min, blood pressure (BP) 100/60 mm Hg. The pupils were of equal size in mid-position but non-reactive to a bright light. His eyes maintained a conjugate forward gaze and there were no spontaneous or doll's-eye movements. The corneal reflexes were depressed and gag reflex impaired. There was arm withdrawal to pain but

reflexes and plantar responses were unobtainable.

Arterial gases on 24% inspired oxygen were; pH 7.17 P_{O_2} 10 kPa, P_{CO_2} 8.3 kPa, standard bicarbonate (HCO_3) 18 mmol/l, base excess -9.5 mmol/l, O_2 saturation 86%. He was intubated and ventilated. Gastric lavage showed an empty stomach. Investigations including plasma urea and electrolytes, glucose, prothrombin time ratio and chest radiograph were unremarkable. Cerebrospinal fluid (CSF) was clear, under normal pressure and contained 5 white cells/mm³, 20 red cells/mm³, protein 0.36 g/l and glucose 4.7 mmol/l. No drugs or alcohol were detected in the blood. Other investigations requested at the time of admission showed a mean corpuscular volume of 102 fl, creatine kinase 410 IU/l (normal 0–150), albumin 30 g/l (35–53), gamma glutamyl transpeptidase 142 IU/l (8–50), and aspartate transaminase 71 IU/l (7–40). A subsequent electroencephalogram showed generalized wave slowing and a computed tomographic brain scan showed cortical and cerebellar atrophy. Because a diagnosis of Wernicke's encephalopathy was considered, thiamine (250 mg) was administered intravenously, and continued daily thereafter.

The following day he was extubated but remained drowsy with a fixed conjugate forward gaze. On the third day he responded to commands and there were dysconjugate eye movements with first degree horizontal and vertical nystagmus. On the seventh day he showed amnesia with confabulation, horizontal and upbeat nystagmus, vertical gaze palsy, areflexia, marked truncal and mild limb ataxia.

Oral thiamine was continued but 6 months later confusion, confabulation, occasional urinary incontinence and moderate truncal ataxia persisted.

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Accepted: 18 October 1984

Table 1 Coma in Wernicke's encephalopathy

Ref.	Age (y)	Features noted before	Hypothermia (35°C) rectal	Hypotension (systolic 90 mm Hg)	Sluggish pupils	Absent doll eye or calorics	Effect of thiamine	Outcome
RCP (1979)	83		+		-		Not given	†
Devaltrasan & Koh (1982)	32	confusion, ataxia - acute			+		Improved	poor memory, nystagmus
Donnan & Seeman (1980)	62	ataxia, nystagmus-2 weeks	+				Improved	ataxia, nystagmus, neuropathy
Donnan & Seeman (1980)	60	confusion, ataxia - 3 weeks	+				Improved	ataxia, nystagmus neuropathy
Harper (1980)	50			+	Fixed in coma	+	Not given	†
Harper (1980)	71		+	+	+	+	Not given	†
Harper (1980)	65			+			Not given	†
Harper (1981)	45		+		+	-	Not given	†
Kearsley & Musso (1980)	53		+	+		+	Improved	†
Lonsdale (1978)	57				-	-	24 mg/d	†
Mancall & McEntee (1965)	18	ophthalmoplegia, ataxia. - acute			Fixed in coma		Not given	†
Nadel & Burger (1976)	78			-	-	-	Not given	†
Nadel & Burger (1976)	61			+	-	-	Not given	†
Wallis <i>et al.</i> (1978)	63	dementia, ophthalmoplegia, ataxia - 3 y	+	+	-	+	Improved	confusion, nystagmus
Wallis <i>et al.</i> (1978)	52	dementia - 7 y	-	-	-	+	Improved	†
Wallis <i>et al.</i> (1978)	59	ataxia - 1 y	+		-	+	Improved	†
Wallis <i>et al.</i> (1978)	63	dementia, ataxia - 3 y				+	Improved	confusion, ataxia, nystagmus, neuropathy

+ sign present; - sign absent; blank indicates sign not documented; † died.

Discussion

Coma is an important, but unusual feature of acute Wernicke's encephalopathy. It has frequently been precipitated in susceptible patients by naso-gastric or intravenous feeding without vitamin supplements. Nine such patients are reported (Mancall & McEntee, 1965; Nadel & Burger, 1976; Lonsdale, 1978; Demonstration, 1979; Harper, 1980, 1981) in whom the diagnosis was made at autopsy when the pathological features of Wernicke's encephalopathy were found. In a further 4 described cases coma was reversed by thiamine administration (see Table I) (Wallis *et al.*, 1978; Donnan & Seeman, 1980).

There are reports of 4 patients who presented in coma due to acute Wernicke's encephalopathy (Wallis *et al.*, 1978; Kearsley & Musso, 1980; Devathanan & Koh, 1982). All improved with thiamine although 2 died later from other causes (Kearsley & Musso, 1980). In addition, encephalopathy (Kearsley & Musso, 1980) and seizures (Devathanan & Koh, 1982) may have been contributory causes of coma. Our patient presented in coma with a mixed respiratory and metabolic acidosis which may have contributed to the coma. Acute Wernicke's encephalopathy has a high mortality (26 of 245 in one series; Victor *et al.*, 1971), the cause of which is frequently respiratory failure due to involvement of vital brainstem centres (Harper, 1980) or bronchopneumonia (Harper, 1979). We believe ours is the first patient reported to have improved with ventilatory support and thiamine.

A high index of suspicion is required if cases of coma due to acute Wernicke's encephalopathy are not to be overlooked. The clinical triad of confusion, ophthalmoplegia and ataxia are classical features but these may be absent. A history of alcohol abuse, Korsakoff's psychosis or specific clinical features may not be available particularly in the patient who presents in coma. Of the 17 patients cited here (see Table I), 12

were known either to have had a predisposing cause of Wernicke's encephalopathy or one or more features of the triad. The diagnosis must therefore be considered in the absence of a standard history of alcohol abuse or the triad of Wernicke's encephalopathy. Other clinical features are hypothermia (8/17), sluggish pupils (5/17) and absent oculocephalic or oculovestibular reflexes (7/17) (Koeppan *et al.*, 1969). Coma is due to diencephalic or periaqueductal lesions, hypothermia has been attributed to hypothalamic involvement, sluggish or fixed pupils to midbrain lesions and absent oculocephalic and oculovestibular reflexes principally to lesions of the vestibular nuclei. In diffuse metabolic coma pupillary light reflexes are usually preserved and, except when coma is deep, caloric stimulation produces conjugate deviation of the eyes. Pupillary abnormalities and ophthalmoplegia in the coma of Wernicke's encephalopathy could lead to confusion with structural disease. These features are characteristic of the focal accentuation of the effects of thiamine deficiency and if structural disease is excluded they may provide support for the diagnosis. Blood transketolase or pyruvate levels may confirm thiamine deficiency but do not necessarily establish it as a cause of coma or assist in the immediate management. Conclusive evidence requires the use of thiamine to reverse coma, as in 8 cases given adequate doses (100–500 mg/d) (Lonsdale, 1978).

Thiamine should therefore be given before glucose to all cases of undiagnosed coma and to susceptible patients in coma; it should accompany all naso-gastric or parenteral feeding or fluid regimens longer than 2 weeks or so in duration (Ziporin *et al.*, 1965). Nevertheless our patient's outcome is representative of acute Wernicke's encephalopathy in that four-fifths suffered from persistent Korsakoff's psychosis and more than half from incomplete recovery of gait (Victor *et al.*, 1971).

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