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CASE REPORT

Status epilepticus caused by a myxoedema coma

H.J. Jansen[1*], S.R. Oedit Doebé[1], E.S. Louwerse[2], J.C. van der Linden[3], P.M. Netten[4]

Departments of [1]Intensive Care, [2]Neurology, [3]Pathology and [4]Internal Medicine, Jeroen Bosch Hospital, 's-Hertogenbosch, the Netherlands, [*]corresponding author: Kronenburgerplaats 16, 6511 AW Nijmegen, the Netherlands, e-mail: Henry_jansen@hotmail.com

ABSTRACT

The case of a 63-year-old woman who presented with status epilepticus, coma and hypoventilation is reported. A primary neurological cause was considered. Hypothermia led to further investigations and a diagnosis of severe hypothyroidism. The neurological complications of hyperthyriodism include alteration in mental status with slowness, decreased concentration and lethargy, headache, cranial nerve palsies, dysarthria, hoarseness, myopathy, neuropathy, reflex changes, ataxia, and psychotic episodes. Our patient suffered from a rare consequence of severe hypothyroidism presenting with status epilepticus and she died despite treatment. To our knowledge this is the second patient to be reported with myxoedema coma with this kind of presentation. Despite therapeutic options, there is a high mortality rate.

KEYWORDS

Myxoedema coma, severe hypothyroidism, status epilepticus

INTRODUCTION

Traditionally, status epilepticus is defined as 30 minutes of continuous seizure activity or a series of seizures without return to full consciousness between seizures.[1] In about one third of the cases, an exacerbation of an idiopathic seizure disorder is thought to be the cause. In anther third, the episode of status epilepticus represents the first onset of a seizure disorder. In both conditions the diagnosis is made by exclusion of a myriad of other diseases or disorders that may precipitate status epilepticus, including all conditions that might cause cortical structural damage (stroke, neoplasm, hypoxic injury, subarachnoid damage, trauma), intoxications, alcohol withdrawal, electrolyte abnormalities, infections of brain and/or meninges, and metabolic disorders such as hypoglycaemia, and hypothyroidism.

Myxoedema coma is a complication of long-standing untreated hypothyroidism. The term is largely a misnomer since most patients are not comatose. This condition is characterised by marked impairment of the central nervous system and of cardiovascular function.[2]

We report a patient with status epilepticus caused by severe hypothyroidism, who died despite treatment with thyroid hormone. To our knowledge there is only one other case report which describes a patient with myxoedema coma who also presented with status epilepticus, but that patient survived.[3]

CASE REPORT

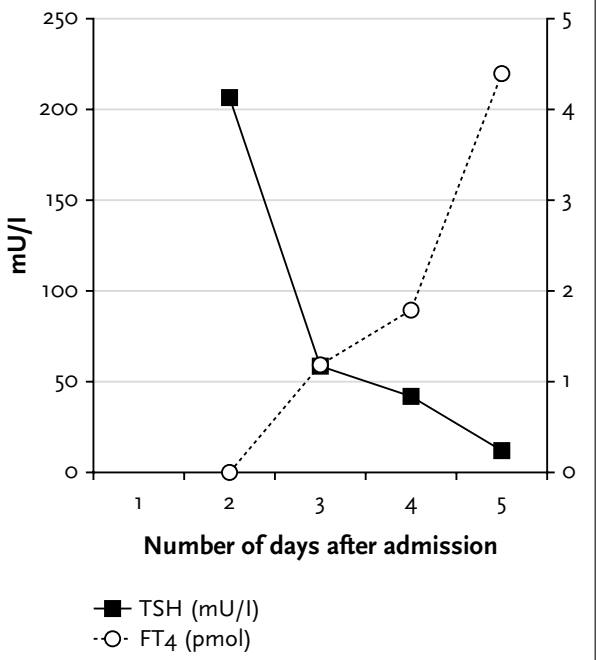
A 63-year-old female presented with convulsions and in coma. For six months she had been suffering from fatigue and lethargy. Five days before admission, she had developed problems with walking and muscle weakness. On the day of admission, she developed a seizure. Her medical history included hypertension and hypercholesterolaemia. On presentation, she had hypothermia of 34°C and a blood pressure of 160/110 mmHg. There were no signs of any infection at that time. She later developed hypotension (89/40 mmHg) with a heart rate of 100 beats/min. She had no peripheral oedema or oedema of her eyelids. Examination of the lungs, heart and abdomen revealed no abnormalities. Neurological examination showed a Glasgow Coma Scale score of $E_1M_1V_1$ and areflexia. Generalised tonic-clonic seizures were continuously observed.

Table 1 shows the most relevant laboratory investigations on presentation; no abnormalities were found despite a white cell count of 3.0 x 10^9/l, aspartate aminotransferase

Table 1. *Laboratory values on admission*

Variable	Value	Normal range
Haemoglobin (mmol/l)	8.5	7.5-10.0
Platelet count (x 10^9/l)	161	150-400
White-cell count (x 10^9/l)	3.0	4.0-10.0
Sodium (mmol/l)	140	135-145
Potassium (mmol/l)	4.0	3.5-5.0
Aspartate amino-transferase (U/l)	94	0-40
Alanine amino-transferase) (U/l)	98	0-45
Creatinine (umol/l)	96	50-100
Glucose (mmol/l)	7.9	4-7.7
Lactate dehydrogenase (U/l)	733	0-450
C-reactive protein (mg/l)	<1.0	0-6.0
Thyroid stimulating hormone (mE/l)	206	0.15-6.0
Free thyroxin (pmol/l)	<1.0	12.0-22.0
Arterial blood gas analysis		
Ph	7.14	7.36-7.44
pCO_2 (mmHg)	13.2	4.4-6
pO_2 (mmHg)	14.3	10.7-14.7
Bicarbonate (mmol/l)	33	22-29
Base excess (mmol/l)	0.6	-3.0-3.0

Figure 1. *TSH/FT4 curve (treatment was started two days after admission)*



94 U/l, and alanine aminotransferase 98 U/l. A thyroid-stimulating hormone (TSH) level of 206 mU/l and a free thyroxine (FT4) level of <1.0 pmol/l were determined two days after admission. An electrocardiogram (ECG) showed a sinus rhythm of 75 beats/min and some artefacts due to jerking of the extremities. There were no ECG signs of hypothermia such as an Osborn or J wave. Chest X-ray was normal. Brain CT scan and cerebral spinal fluid (CSF) examination revealed no abnormalities.

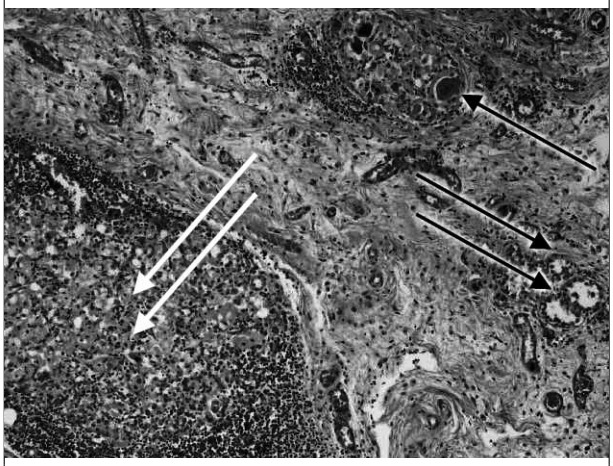
Because of hypoventilation, she was mechanically ventilated. She was treated with active re-warming using a hot air blanket and inotropic agents. Initially, convulsions were treated with diazepam 10 mg. Subsequently, intravenous phenytoin was started. Despite optimal antiepileptic treatment the seizures continued uninterruptedly and an EEG showed epileptic activity. Thiopental narcosis was induced for a period of three days.

Two days after admission, suppletion of thyroxine (T4) was started at a daily dosage of 100 µg and subsequently 150 µg daily, and triiodothyronine (T3) was given at 12.5 µg twice daily. *Figure 1* shows values of thyroid hormone after starting treatment. Because of the possibility of hypocortisolism, we administered hydrocortisone 100 mg intravenously every eight hours. After a few days, the patient developed a ventilator-associated pneumonia of her right lung. She was treated with cefuroxim 750 mg every eight hours intravenously.

Unfortunately, the patient showed no neurological improvement. She remained comatose with a Glasgow Coma Score of $E_1M_1V_{tube}$. After 14 days, we decided to stop the treatment because of a lack of improvement. Autopsy was performed. On histological examination the thyroid revealed complete atrophic follicles and an area of chronic inflammation with lymphocytes. The surrounding tissue showed fibrosis (*figure 2*).

Histological examination of the brain and the pituitary gland revealed no abnormalities.

Figure 2. *Thyroid tissue showing complete atrophic follicles (black arrow) and an area of chronic inflammation containing lymphocytes (white arrow)*



Between the area of inflammatory cells and atrophic follicles, fibrotic tissue is seen. (magnification 200 x)

DISCUSSION

Our patient suffered from severe primary hypothyroidism with status epilepticus, coma and hypoventilation as presenting symptoms. For several months she complained of fatigue and lethargy. On admission she had hypothermia, hypotension and was comatous with areflexia. Generalised tonic-clonic seizures with status epilepticus were observed.

Progression into myxoedema coma occurs when a hypothyroid patient's homeostatic mechanisms are disrupted (for example in the winter months). Multiple factors can precipitate myxoedema coma.[4,5] The more common precipitating factors include infection, particularly pneumonia, (uro)sepsis and cold exposure. In addition, several drugs may also precipitate myxoedema coma, including amiodarone, β-blockers, diuretics, narcotics (such as oxazepam), and lithium. In our patient, clear precipitating factors were not evident.

The neurological complications of myxoedema coma include alteration of mental status with slowness, decreased concentration and lethargy, headache, cranial nerve palsies, dysarthria, hoarseness, myopathy, neuropathy, reflex changes, ataxia and psychotic episodes.

Hypothyroidism and convulsions can occur in two different ways. First, late-onset epilepsy has been described in several patients who were later found to be hypothyroid and in whom convulsions stopped permanently when thyroid hormone was given.[6] In contrast, when convulsions accompany myxoedema coma they are usually preterminal. All nine patients reported in the literature with seizures who had myxoedema coma died,[7-9] except for one patient.[3]

The cause of epileptic seizure activity in hyperthyriodism is unknown. The electroencephalogram (EEG) in patients with hypothyroidism usually shows low-voltage alpha activity.[10] However, even pronounced hypothyroidism can exist with a normal EEG. It has been postulated that convulsions may be due to cerebral oedema secondary to expansion of the extracellular fluid volume. This may be related to inappropriate antidiuretic hormone (ADH) secretion and hyponatraemia, and hypoventilation with postanoxic encephalopathy. However, in our patient brain autopsy revealed no abnormalities.

The optimal mode of thyroid hormone therapy in patients with myxoedema coma is controversial, largely because the condition is so rare that there are no clinical trials comparing the efficacy of different treatment regimens. While fast increase of serum thyroid hormone concentrations carries some risk of precipitating myocardial infarction or atrial arrhythmias, this risk must be accepted because of the high mortality of untreated myxoedema coma. Some authors favour administration of T_3, because its biological activity is greater and its onset of action is more rapid than T_4. Others prefer T_4 because high serum T_3 concentrations during treatment have been correlated with mortality.[11]

It should be given intravenously because gastrointestinal absorption may be impaired.[12] The first dose of T_4 should be large – 200 to 400 µg – with the exact dose dependent on the patient's weight and age and the likelihood of complications such as myocardial infarction or arrhythmia. Thus, the dose should be reduced in lighter and older patients and those at risk of cardiac complications. For T_3 the same can be concluded. We decided to treat our patient with both T_3 and T_4. Because of the possible cardiac complications no loading dose of T_4/T_3 was given.

Hypothermia is a cardinal feature of myxoedema coma and is noted in approximately 80% of the patients. Correction of hypothermia requires external warming with blankets or a Bair hugger. However, one should be aware of hypotension because of the vasodilatory effect of rewarming. Sometimes inotropic support may be necessary. The susceptibility to vasodilatation is further aggravated by heart failure. Hypothyroidism may lead to decreased cardiac contractility, resulting in a reduction of stroke volume and cardiac output.

Electrolyte disturbances are common in myxoedema coma. The most common electrolyte abnormality is hyponatremia and it is usually due to impairment of free water excretion due to an inappropriate excess vasopressin secretion (SIADH) or impaired renal function.[13]

Hypoglycaemia may reflect underlying adrenal dysfunction. Patients with myxoedema coma are generally treated with stress dose corticosteroids. To rule out adrenal insufficiency, a random cortisol level can be obtained before initiation of therapy, or a rapid ACTH stimulation test can be performed.

Finally, supportive measures are extremely important in the treatment of myxoedema coma. These measures include treatment in an intensive care unit, mechanical ventilation if necessary, administration of intravenous fluids including electrolytes and glucose, correction of the hypothermia previously mentioned, and the treatment of any underlying infection.

The syndrome of myxoedema coma and convulsions represents the most extreme form of complicated hypothyroidism, and despite the best contemporary intensive medical care, is associated with substantial mortality ranging from 30 to 60%.[14] Factors associated with poor prognosis include advanced age, bradycardia, persistent hypothermia and the degree of consciousness (Glasgow Coma Scale).[15]

In our case there had been a delay of two days before starting thyroid suppletion. The most important elements in the treatment of myxoedema coma are early recognition, presumptive thyroid hormone replacement, corticosteroids and appropriate care.

This case showed us that if a patient suffers from status epilepticus associated with lethargy, fatigue and

hypothermia, myxoedema (coma) should be included in the differential diagnosis. Rapid determination of TSH, T4 and T3 must be performed and thereafter early institution of therapy.

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