THE SYNDROME OF LETHAL CATATONIA

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ABSTRACT

Lethal catatonia (LC) is a life-threatening neuropsychiatric syndrome associated with a host of psychiatric, neurologic and medical conditions. The clinical picture is characterised by fragmented psychotic symptoms, catatonic phenomena particularly alternating stupor and agitation, altered consciousness, hyperthermia and other autonomic disturbances. A case of LC in a 19-year-old Chinese woman showing a dramatic response to lorazepam and bromocriptine is described and a brief overview of the contemporary literature is provided.

Keywords: lethal catatonia, bromocriptine, benzodiazepines

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INTRODUCTION

Lethal catatonia (LC) is a rare and potentially fatal neuropsychiatric syndrome which is associated with a wide variety of medical and psychiatric conditions[1]. Typically the clinical presentation starts with a non-specific prodromal phase lasting up to 2 weeks characterised by insomnia and anxious and irritable mood. The next stage consists of a period of rapidly emerging extreme anxiety, agitation, perplexity, fragmented delusions and hallucinations. This is followed by stupor, mutism and a variety of catatonic symptoms including rigidity, waxy flexibility and occasional active resistance to attempts to mobilise her. Autonomic disturbances especially high fever, tachycardia, labile blood pressure, urinary retention or incontinence, constipation and acrocyanosis are always present. Insomnia, anorexia and dehydration also accompany the florid psychosis. In most cases predisposing or precipitating factors cannot be unequivocally identified.

LC is sometimes mistakenly equated with certain psychiatric disorders like schizophrenia. It is, therefore, important to understand that LC is essentially an acute catatonic psychotic syndrome of diverse aetiologies and not a disease entity per se.

Since LC may occur in any medical setting and its management involves subspecialties other than psychiatry, a basic knowledge of the concept of LC and the principles of its management is essential for all medical professionals.

LC has been widely discussed under different terms (eg Bell's mania, fatal catatonia, psychotic exhaustion syndrome) in the psychiatric literature since its first description by Calmeil in 1832[2]. Stauder's series[3] published in 1934 revived the interest in LC among psychiatrists but the syndrome has remained largely unknown to other specialities. There have been numerous case reports and a few retrospective series of Caucasian patients with LC[1]. We describe a case of LC in a Chinese patient. In the Chinese literature neuroleptic malignant syndrome (NMS), a variant of LC, has been frequently reported[4,5] since 1979 while LC has not been comprehensively discussed.

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CASE REPORT

Ms M, a 19-year-old, single clerk, was admitted to the medical ward of a University teaching hospital presenting with low-grade fever, flu-like syndromes and diarrhoea for a week. She behaved oddly, talked irrelevantly at times and appeared muddled in thinking. Previously she had been healthy without medical or psychiatric problems. There was no family history of psychiatric illness.

On admission (Day 1) physical examination revealed no focus of infection while psychiatric consultation found a perplexed, mildly anxious young woman who was disorientated in time, place and person. She answered questions briefly with much hesitation but no hallucinations, delusions or thought disorder was detected. A provisional diagnosis of acute organic brain syndrome was made although subsequently the results of investigations including full blood count, plasma electrolyte, urea and creatinine, glucose and arterial blood gas analysis were all normal except for mildly raised white blood cell count and liver enzymes. Bacteriological, virological and fungal studies of CSF were negative and CT of the brain and EEG showed no abnormality either. Despite these negative findings, an early phase of viral encephalitis was suspected. Intravenous acyclovir was therefore started from Day 2 but was stopped on Day 4 because the relatives insisted on discharge against medical advice.

The family brought Ms M to a shaman who performed exorcism. This did not bring relief and her condition deteriorated further. Her anxiety and odd behaviour increased, her occasional utterances were incoherent. On her second admission at Day 12, examination revealed a high spiking fever (up to 40°C), tachycardia, muscle rigidity in the neck and limbs and coarse tremor of the extremities. She had faecal impaction and urinary incontinence. She was found stuporous, her eyes were mostly closed, she was mute and unresponsive apart from actively resisting any attempts to move her limbs or offer her food and drink. On Day 14, the immobility was suddenly interrupted by a bout of purposeless agitation which subsided after intramuscular administration of 5 mg haloperidol. This was the only time during her illness when she received antipsychotic medication. She was subjected to a more extensive range of investigations including immunological tests (antinuclear antibody, rheumatoid factor, viral serology and serum ceruloplasmin) in addition to repeating the ones mentioned earlier. An MRI scan of the brain was also performed. The results were all normal except for increased liver

enzymes (alanin amino transferase 413 IU/L [normal<58 IU/L], hypoalbuminaemia (27g/L [normal 36-48 g/L]) and serum creatinine phosphokinase (CPK) which peaked on Day 21 with 8840 U/L.

With viral encephalitis remaining a diagnostic option despite negative CSF findings, Ms M was given iv acyclovir and ceftazidine, 2 g/day of each, from Day 12 to Day 22 and Day 25 respectively. Symptomatic treatment aimed at decreasing the fever and correcting the fluid and electrolyte imbalance and hypoalbuminaemia, which were regarded as consequences of malnutrition. Subcutaneous heparin (5,000 units/day) was also administered to prevent thromboembolism from prolonged immobility.

Despite vigorous treatment Ms M's condition remained unchanged until Day 21 when treatment with lorazepam (2 mg tds given through Ryle's tube) was commenced. The rigidity, tremor and negativism noticeably decreased after the first dose. She seemed to recognise her sister and managed to whisper a few words. By Day 22 CPK dropped from 8840 to 5431 U/L. On Day 22 and 23 she produced coffee-ground vomit. A stress ulcer was provisionally diagnosed and iv ranitidine (150 mg/day) was given for a week. At this point psychiatric opinion was sought. Symptoms of intermittent agitation, perplexity, irrelevant speech alternating with period of mutism, negativism, muscular rigidity and tremor were found and the syndromal diagnosis of lethal catatonia of uncertain origin was made. Further improvement was observed after bromocriptine (2.5 mg tds) was started on Day 24. She gradually became more alert and responsive. Muscle rigidity gradually diminished as demonstrated by the serial CPK values:1407 U/L on Day 26, 87 U/L on Day 41. From Day 41 she was afebrile.

Ms M was transferred from the medical to the psychiatric ward on Day 27 for close observation and rehabilitation. Despite being cooperative, she lacked motivation and interest, and was emotionally blunt and sluggish in response. No delusions, hallucinations, thought disorder or depressive mood could be elicited. She had only vague recollection of events in the previous 5-6 weeks and could not give a coherent account of her subjective experiences during that period. Cognitive examination was otherwise normal.

Further recovery proved to be rapid and uneventful. By Day 38 Ms M was ambulatory and able to attend to her own personal hygiene. She gradually regained her initiative and emotional participation. She was discharged on Day 65 on lorazepam 2 mg bd and bromocriptine 5 mg tds which were gradually tapered off over the subsequent month. On discharge she was physically fit and all the laboratory tests were normal. She resumed her original clerical job on Day 90. On Day 115, apart from mild impairment in attention and concentration, she was free from any psychiatric symptoms. By Day 200 she fully recovered and returned to her premorbid level of functioning.

DISCUSSION

In this case, as frequently occurs[1], signs of frank psychosis, being fragmented and of fluctuating intensity, were inconspicious, particularly in the beginning. Otherwise the clinical manifestations, ie the acute onset, autonomic disturbances, perplexity, anxiety and initial, albeit short-lived, agitation, followed by stupor, mutism, rigidity and active negativism, corresponded well to the classical description of LC. Prolonged agitation does not necessarily precede the stuporous phase[6]. Autonomic disturbances and a reduction in the level of consciousness accompanied the clinical picture. Elevated CPK and leucocytosis are always present[1] while liver enzyme abnormalities are occasionally reported[7,8]. Despite a wide range of investigations no underlying somatic cause of the LC syndrome was found and not even a non-organic psychiatric disorder could be diagnosed. The only dose of haloperidol was given when the LC had already been progressing, therefore the diagnosis of a neuroleptic malignant syndrome (NMS) can confidently be excluded. The prompt reversal of the progressively downhill course following the introduction of lorazepam and bromocriptine speaks in favour of the effectiveness of these drugs. The patient's physical and psychological health was restored after this severe bout of LC, except for a mild impairment in attention and concentration which was temporary.

The diagnosis of LC is fairly straightforward if clinicians are familiar with the concept. The only differential diagnostic option is NMS which is also characterised by fever, rigidity, altered consciousness and autonomic disturbances[9]. Cross-sectionally NMS is virtually indistinguishable from LC. In fact, many authors[10] regard NMS as a neuroleptic drug induced subtype, ie an iatrogenic variant of LC. In most instances the differentiation between LC and NMS is an academic question since the management of the two conditions is nearly identical.

The prevalence of LC among acute psychiatric admissions has been reported to be between 0.13% and 0.5% subject to admission policy, diagnostic practice and many other factors[11,12]. It is assumed that in many cases the diagnosis is missed and patients with LC are treated in medical or intensive care units as "Non-specific encephalitis"[1,6]. In Mann et al's[1] meta-analysis of LC based on 292 cases collected from the world literature between 1960 and 1986, two-thirds of the patients were female and two-thirds of them were under 40 years of age. Introduction of electroconvulsive treatment (ECT) and better general medical care notwithstanding, the mortality is still about 60%[1]. Cardiovascular exhaustion, renal insufficiency due to dehydration and rhabdomyolysis and thromboembolism are the most frequent causes of death. However, if LC arises in the context of a functional psychosis like schizophrenia or mania, autopsy revcals only non-specifc findings not sufficient to account for the cause of death.

The aetiology and pathomechanism of LC is not known. It is associated with a variety of psychiatric, medical and neurologic conditions such as functional psychiatric illness (eg schizophrenia, affective disorder), cerebrovascular thrombosis, brain tumours (eg glioma of the third ventricle), head trauma, infections (eg viral encephalitis, bacterial septicaemia, typhoid fever), status epilepticus (petit mal), endocrine and metabolic disorders (eg hyperthyroidism, Cushing syndrome, uraemia), drug-induced and toxic conditions like NMS, tetraethyl lead poisoning[1]. However, whether these associations are causative or coincidental is debatable. Based on the similarities in clinical presentation and treatment response between LC and the neuroleptic malignant syndrome, it has been speculated that dysregulation of dopaminergic transmission in the diencephalon and the extrapyramidal system might explain the autonomic and motor symptoms[1]. The involvement of adrenergic and cholinergic neurotransmitter systems has also been hypothesised[13]. To date there is little evidence in terms of clinical and postmortem studies to support the dopaminergic hypothesis of LC. Ferro et al[14] reported elevated cortisol plasma levels in one case which normalised after the resolution of LC. In another case study the 24-hour urinary output of free cortisol and norepinephrine increased, while the urinary excretion of dopamine significantly decreased[15]. Reduced activity of the brain dopaminergic system was found at autopsy in two patients who died of "fatal catatonia"[13]. The paucity of biological investigations is understandable since patients with LC are rarely available for clinical research.

The term "lethal catatonia" is a misnomer because early recognition and vigorous treatment may prevent a fatal outcome. The importance of high-quality medical and nursing care cannot be overemphasised. Supportive measures are directed towards the correction of fluid and electrolyte imbalance, stabilisation of cardiorespiratory functions and lowering hyperthermia. Otherwise the treatment is more a matter of clinical wisdom and experience than scientifically sound guidelines. Corticosteroid hormones, favoured 30-40 years ago, are not recommended by modern literature[1]. There is consensus that ECT is still the treatment of choice[1,10,16]. Recent detailed case studies suggest that ECT may be life-saving in the very advanced stage of LC[7,17], even in the presence of Cheyne-Stokes respiration, decerebrate posturing and bilateral Babinski signs[15]. Postulating that LC and NMS share a common neurochemical basis, the majority of writers caution against the use of neuroleptics and advise to withdraw them immediately if LC is suspected[8,10,13]. Recently, sodium dantrolene alone[18] or in combination with ECT[7], ECT and benzodiazepines[8], and ECT, benzodiazepines and bromocriptine[17], were successfully employed in the treatment of LC. All these drugs and ECT have also been effective in NMS thus providing indirect evidence for a common pathophysiology. Since dantolene may cause liver damage, we opted for bromocriptine in our patient who had slightly elevated liver enzymes.

This case report illustrates several important practical issues in the management of LC. Good collaboration among different subspecialties is essential as soon as LC is suspected. Such patients require aggressive supportive treatment, high-quality nursing care, close monitoring of somatic and psychiatric status and a painstaking search for any potentially reversible aetiological factors. The critically ill LC patients can be best managed in an intensive care unit. Mobilisation should begin at the earliest possible stage to prevent complications owing to prolonged immobility and rigidity.

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