CASE REPORT

Catatonia as an internal medicine disease: infrequent or still underdiagnosed?

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SUMMARY

Catatonia is a motor and behavioural syndrome with multiple psychiatric, general medical and neurological aetiologies that might be simultaneously present. B₁₂ deficiency is a rare, treatable cause of catatonia, not always easy to rule out. The authors present a case of a woman with catatonia associated with severe cyanocobalamin deficiency, admitted to an internal medicine ward. The benign course was related to an adequate and early diagnosis.

BACKGROUND

An altered state of consciousness represents a challenge to the Internist, especially when it occurs in patients with a prior history of psychiatric disorders or a serious concomitant medical illness. Catatonia can occur in both these settings and needs to be considered in the differential diagnosis, since timely treatment of the syndrome and the underlying cause is essential to a favourable outcome. Awareness of the syndrome and the multiplicity of underlying causes can lead the clinician to the identification of an organic cause.¹

Catatonia, a psychomotor syndrome unrelated to physical incapacity, can be found in association with a broad spectrum of systemic medical diseases and responds readily to adequate treatment.^{1–3} The syndrome is grouped under three forms of presentation: retarded (characterised by mutism, rigidity, immobility, negativism, catalepsy, posturing and echophenomena), excited (with restlessness, impulsivity and aggressivity presenting as the main symptoms) and malignant catatonia, a life-threatening form of which fever and autonomic instability are the warning signs.^{1–2} The underlying cause is important since it strongly influences prognosis. It is more frequently associated with mood disorders than with schizophrenia,⁴ and it is commonly found among patients with general medical, neurological and toxic disorders.¹

Cyanocobalamin deficiency is a rare but treatable and long known cause of neuropsychiatric symptoms.^{5–6} It should be part of the medical work up in this group of patients.

CASE PRESENTATION

A 68-year-old Caucasian woman presented to our emergency department, with decreased alertness, immobility, mutism and refusal to eat. The symptoms had begun 3 weeks earlier, with loss of interest in daily activities prompting her to visit her psychiatrist. The patient's family reported that she had undergone a 20 kg weight loss. Two days

before admission, she had reported of abdominal discomfort. The patient's family shared medical records of hiatal hernia and depressive disorder in this patient. However, the psychiatric condition was brought to their knowledge only a few weeks earlier and they had never noticed signs of depression. She was not taking any medication. On physical examination, the patient was stuporous and verbal response was absent. She had dilated though reactive pupils and generalised muscle weakness affecting particularly the inferior limbs. Abdominal examination revealed no abnormalities.

INVESTIGATIONS

Complete blood count revealed: anisocytosis (red cell distribution width 24.3%) with neither anaemia (haemoglobin 14.7 g/dL) nor macrocytosis (mean cell volume 89.3 fL); low reticulocyte index (1.4), normal white cell count and thrombocytopenia (minimum of $94 \times 10^9/L$). Blood smear showed many target cells and presence of elliptocytes. The remaining laboratory results showed severe B₁₂ vitamin deficiency (<117 pmol/L), total bilirubin 1.76 mg/dL, conjugated bilirubin 1.02 mg/dL, lipase 966 U/L and negative C reactive protein.

Urinary sediment contained a high white cell count. A urinary tract infection was diagnosed and the patient started empirically on oral amoxicillin/clavulanate.

Drug screening was negative. Testing for antigastrophic parietal cell antibody was positive and negative for anti-intrinsic factor antibody.

Abdominal X-ray was unremarkable. Abdominal ultrasound was inconclusive due to gas interposition. Abdominal CT showed no alterations. Upper endoscopy revealed an enanthematous pangastritis with mild atrophy. Biopsies were not performed. MRI of the head showed small areas of chronic ischaemic changes within the frontal and parietal lobes, and discrete cortical cerebral and cerebellar atrophy.

DIFFERENTIAL DIAGNOSIS

The clinical course of refusal to eat, marked weight loss and abdominal discomfort associated with a rise in lipase values led to the suspicion of a possible inflammatory/malignant aetiology. However, radiological work up ruled out these hypotheses; there was clinical improvement after initiation of enteral nutrition and lipase values spontaneously subsided.

The patient was diagnosed with pernicious anaemia with consequent vitamin B₁₂ deficiency-related catatonia.

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A possible underlying factitious and/or personality disorder was also considered. The patient progressively started to speak but her responses were vague. The possibility that she was intentionally answering only those questions she wanted to answer was taken into account, since her answers were frequently uncommon, though this could be explained by mutism due to the catatonic syndrome. The attempt to avoid medical or psychological evaluation could be interpreted in the context of negativism but it could also have been voluntary. The hypothesis that she was deliberately producing her symptoms was further considered due to her progressive hostility every time she was being examined, however, this could be a sign of combativeness, which has been described as a severity predictor in catatonia.⁷ A possible intent to influence health professionals regarding her clinical situation was also considered during psychiatry consultation. No secondary gains other than her family's attention were identified.

Regarding her personality, though behaviour in her occupational setting seemed adequate, she appeared to be a different person at home, unwilling to share her personal information with her family throughout her life. The patient thought she could assume total responsibility for her own health and decide on adequate treatment. Her devotion to her profession emphasises the possible influence of retirement on the exacerbation of previously unrecognised personality traits.

TREATMENT

The patient was started on intramuscular cyanocobalamin supplementation 1 mg daily during the first week, then weekly for 1 month and monthly thereafter. Assuming the diagnosis of catatonia, lorazepam was prescribed at a dose of 4 mg divided into two daily administrations.

OUTCOME AND FOLLOW-UP

A progressive improvement of the level of consciousness, mobility and verbal responsiveness was observed within a few days of treatment. The patient was, however, always vague in her speech, voluntarily avoiding questions related to her previous history and presenting illogical reasons for her behaviour, though a normal conversation was conducted when it was not about her. A more aggressive attitude was also progressively noted, which did not resolve after lorazepam titration. Therefore, haloperidol 1 mg twice daily was initiated and titrated to a maximum of 4 mg daily with behavioural improvement and no adverse effects. During the 34-day hospital stay, she maintained stereotyped movements of the limbs and urinary retention requiring urinary catheterisation. It was later brought to our knowledge that the urinary symptoms had been present for several years, and that the patient had used several exercises and techniques to help bladder voiding.

Five days after beginning supplementation, doubling of the reticulocyte number was observed ($54 \rightarrow 109 \times 10^9/L$), which is consistent with response to treatment. B₁₂ levels were corrected with a favourable course, though urinary catheterisation was still necessary once or twice daily for voiding. This was interpreted in the context of neurogenic bladder due to a chronic deficit of B₁₂ vitamin and was solved in the first month after discharge. A lifelong monthly administration of intramuscular cyanocobalamin was recommended.

DISCUSSION

Catatonia is a systemic medical syndrome that in the past has been incorrectly associated uniquely with psychiatric disorders.³ Currently, the American Psychiatric Association's Diagnostic

Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) recognises catatonia as: a specifier of depressive, bipolar and psychotic disorders; as a separate diagnosis in the context of a general medical condition; and as unspecified catatonia.^{1 8} Mutism, catalepsy, posturing and rigidity, and stereotyped movements, are typical signs of the retarded form of catatonia, which is its most typical presentation.² Our patient presented with stupor, mutism and negativism, and exhibited stereotyped movements in the course of the disease. Hence, criteria for the diagnosis of catatonia were fulfilled (at least 3 of 12 features established in the DSM-5: catalepsy, waxy flexibility, stupor, agitation, mutism, negativism, posturing, mannerisms, stereotypies, grimacing, echolalia and echopraxia).⁸ The patient also exhibited opposition/hostility symptoms, which can be interpreted as combativeness, a sign of severity according to the Bush-Francis Catatonia Rating Scale.⁷ Even though intentionality of her actions could not be peremptorily excluded, the clinical manifestations were in favour and could be argued in the context of catatonia, as previously stated. Catatonia was the final diagnosis, further corroborated by improvement after appropriate treatment.

The multiplicity of medical, neurological and psychiatric conditions that can present in the origin of catatonia¹ makes the aetiological diagnosis challenging, particularly because anamnesis is impaired. Recognition of catatonia as a syndrome frequently non-related to schizophrenia is extremely important—in order to prevent physicians treating it as such, as doing so could provoke potential life-threatening complications resulting from use of antipsychotics, namely malignant catatonia and neuroleptic malignant syndrome.⁹ Internists in particular should be aware of it, since these are the specialists approaching patients with altered states of consciousness in the emergency room, but also because it is a frequent complication of metabolic, haematological, endocrine and immune diseases,¹ and, as expected, also more frequent in the elderly population.¹⁰

B₁₂ deficiency, a long known cause of a variety of neuropsychiatric symptoms inclusively in the absence of anaemia or macrocytosis,^{2 4 8 9} has been described as a cause of catatonia.¹ Identification depends on a high grade of suspicion, because it can even occur with normal B₁₂ levels.¹¹ Psychiatric symptoms related to lack of cyanocobalamin are considered rare, but this has been reported as the only identifiable cause.^{11–13} However, this relationship is difficult to establish. Even in patients without a previous history of psychiatric disease, there might be social factors, such as retirement or unemployment, acting as stressors and negatively influencing the patient's psychological status at that moment.¹⁴ On the other hand, several factors may interact simultaneously, and synergically dictate the severity of symptoms. The psychiatric picture described in presence of B₁₂ deficiency seems to be severe^{11–14} or even life-threatening.⁹ Our patient had a history of stable depressive disorder, and suddenly exhibited worsening and presented with a severe episode of catatonia without a clear exacerbating or disturbing factor. Retirement could have acted as an environmental psychological stressor contributing to her catatonic presentation, though it had occurred 3 years earlier. Work up led to identification of severe B₁₂ deficiency, which is the most likely cause of 'decompensation'. The causal role of cyanocobalamin is particularly emphasised by the presence of neurogenic bladder, a neurological manifestation that can occur due to its chronic deficiency.

Awareness of the association led to a prompt initiation B₁₂ supplementation, concomitantly with general treatment for catatonia, favourably influencing the course of disease. As in previously published cases, this precludes conclusions in which

medication is responsible for the benefit. However, delaying treatment could result in irreversible damage with increased morbidity and mortality.

The difficulty in establishing a definitive aetiological diagnosis, most likely due to the plurality of factors involved, requires multidisciplinary management. Even though it is considered a rare cause of catatonia, B₁₂ deficiency is reversible; easily sought and early treatment is crucial in preventing permanent damage.^{6 13} The association should always be kept in mind, because rarity can always be explained by underdiagnosis.

Learning points

- ▶ Neuropsychiatric manifestations associated with B₁₂ deficiency can occur in absence of haematological abnormalities and usually precede them.
- ▶ Cyanocobalamin deficiency is an easily sought and treatable cause of catatonia, though its identification is highly dependent on clinical suspicion.
- ▶ Catatonia is a systemic medical syndrome frequent in the elderly population and therefore it is necessarily an internal medicine diagnosis.
- ▶ Treatment of catatonia with antipsychotics can result in malignant catatonia or neuroleptic malignant syndrome.

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and interpretation, as well as the literature review and correlation with the presented cases.

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