

How the systematic detection of delirium may help physicians avoid a misdiagnosis of acute myocardial infarction: two case reports

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A 93-year-old female and an 81-year-old female presented to the Emergency Department (ED) with hypoactive delirium. In both cases, a quite common delirium-precipitating factor was initially thought to be found by the ED physicians. However, a proactive searching for all medical reasons potentially underlying delirium enabled the physicians of our Acute Geriatric Unit to unveil a diagnosis of acute myocardial infarction. These cases illustrate the complexity of detecting delirium and its etiology, especially in frail patients. We suggest that a systematic diagnostic workup should be performed in all patients presenting with delirium, including an EKG and enzymes measurement even in the absence of typical cardiovascular symptoms.

Key words: Delirium, Myocardial infarction, Underdetection, Older

INTRODUCTION

Delirium is a common and serious disorder of cognition, usually resulting from an underlying medical condition¹. According to the DSM-5, key diagnostic features include an acute onset and fluctuating course of symptoms, inattention, impaired level of consciousness, and disturbance of cognition indicating disorganization of thought¹. Delirium is associated with several negative outcomes, including worsening of cognitive and functional status, increasing patients' and caregivers' burden and elevated mortality in the middle to long term^{2,3}. Despite the toll of these negative outcomes, delirium is frequently undetected in clinical practice and its diagnostic still remains a critical area of need⁴. Here, we report two cases of old females in whom the diagnosis of acute myocardial infarction was obtained after a process of active searching of the underlying causes of delirium.

CASE PRESENTATION N°1

A 93-year-old Caucasian female was admitted to the Emergency Department (ED) of our hospital because

of an altered level of consciousness. On admission, her caregiver reported a subtle though progressive and significant impairment of patient's baseline mental and motor status occurring in the last week. The patient was reported fully dependent in all the activities of daily life, except for self-feeding which was still preserved. She had a history of major tobacco consumption (one packet/day since she was very young). Despite a history of falls, for which she underwent hip-surgery about ten years before, she was still able to walk at home with assistance until the previous week. She had no relevant disease but an uninvestigated cognitive impairment with behavioral disorders, for which she was prescribed low dosage of benzodiazepines and haloperidol. In the last few days, her caregiver also noticed foul-smelling urine. General practitioner was called home and suggested bringing her to the hospital.

At ED presentation, the patient was lethargic, with temperature as high as 36.7°C, blood pressure (BP) was 95/60 mmHg, heart rate (HR) 110/min, respiratory rate (RR) 30 breaths/min while arterial oxygen saturation was normal. Cardiovascular, thoracic and abdominal

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examinations were unremarkable. Laboratory investigations revealed elevated levels of leucocytes (17.800/mm³, with 78% of neutrophils), elevated C-reactive protein (21.71 mg/dl), and creatin-kinase (589 U/l), whereas the chest X-ray did not find pneumonia but mild pleural effusion. Intravenous fluid therapy and empiric antibiotic therapy with ceftazidime were started, soon after urine and blood cultures collection and, on the same day of ED arrival, the patient was transferred to our Acute Geriatric Unit (AGU) with a suspected diagnosis of urinary tract infection.

On admission to the AGU, she was still difficult to wake, scoring -3 at the modified Richmond Agitation and Sedation (m-RASS) ⁵, and she was unable to direct, focus and sustain attention. Accordingly ⁵, a diagnosis of hypoactive delirium was made, and soon the underlying causes of delirium were actively searched. To this aim, an electrocardiogram (EKG) was run, showing QS and RS complexes with persistent ST-segment elevation in the anterior and septal leads (V1-V4). Cardiac enzymes were elevated - TroponinT-hs (TnT-hs) 3852 ng/l, creatin-kinase-mb-isoenzyme (CK-MB) 33.94 ng/ml – and an echocardiography showed a complete apical and septal akinesia (LVEF 25-30%) in addition to moderate mitral valvular regurgitation. ST-Elevation Myocardial Infarction (STEMI) was then diagnosed and both antiplatelet and beta-blocker were started. Moreover, antibiotic therapy was shifted to Ampicillin/Sulbactam, as urine culture resulted positive for *Enterococcus Faecalis*.

Patient's arousal gradually improved and delirium finally resolved on third day after AGU admission. There was a progressive normalization of the EKG pathologic findings and a corresponding decline of troponin and CK-MB serum levels. A return to pre-hospital health conditions was achieved over the next fortnight and the patient was discharged home with stable clinical conditions and normal arousal.

CASE PRESENTATION N°2

An 81-year-old Caucasian female affected by severe Alzheimer's disease (AD) was admitted to the ED of our hospital because of trauma due to a fall occurring at home. According to her caregiver's report, there was a progressive impairment of patient's baseline mental status starting in the last few days before admission. The patient was fully dependent in all the activities of daily life; except for AD, the only remarkable disease was a type 2 diabetes mellitus. No drug was prescribed at home.

At ED presentation, the patient was lethargic, with normal BP, HR and RR values. Cardiovascular, thoracic and abdominal examinations were unremarkable. Laboratory investigations revealed nothing but elevated

CK values (298 U/l), which was initially considered consequence of recent fall, and the EKG did not reveal abnormal findings. On the same day of ED arrival, she was transferred to our AGU for observation and treatment. On admission to the AGU, she was lethargic, with m-RASS scoring -3, and unable to direct, focus and sustain attention. A diagnosis of hypoactive delirium was done in this case as in the previous one ⁵, and the somatic causes underlying delirium were actively searched. To this aim, laboratory investigations were re-checked and an important elevation of CK (2840U/l) was found. Thus, specific cardiac enzymes were collected, finding elevation of TnT-hs and CK-MB values (TnT-hs 8647 ng/l and CK-MB 75.68 ng/ml, respectively). A new EKG showed T-wave inversions in the infero-posterior and lateral leads, associated with ST depressions in the anterior leads. Therefore, a diagnosis of Non-ST-Elevation Myocardial Infarction (NSTEMI) was done and both antiplatelet and beta-blocker treatment was started.

In the following days, there was a progressive reduction of Tn-T-hs and CK-MB serum levels and a corresponding normalization of the EKG pathologic findings. Patient's arousal gradually improved and delirium resolved. The patient was discharged home with stable clinical conditions and normal arousal.

DISCUSSION

Delirium is a multifactorial disorder, depending on complex interactions between predisposing and precipitating factors ^{1 2}. Infections, metabolic derangements, drugs, dehydration and immobility are commonly accepted delirium precipitating factors. Predisposing factors include baseline cognitive impairment or dementia, multimorbidity and older age ². A recent systematic review and meta-analysis has also shown that frailty significantly predisposes to subsequent delirium, contributing to the individual's susceptibility towards various negative outcomes ⁶. From a geriatric perspective, delirium may therefore be considered as one of the syndromic presentations of an individual's underlying condition of frailty ⁶.

Since cardiac diseases as well as other conditions can present with atypical signs/symptoms including delirium ⁷⁻⁹ in older people, all patients at risk (i.e., the frail patients) should undergo a systematic assessment of delirium to detect especially the hypoactive subtypes ¹⁰. In fact, although many clinicians think of patients with delirium as being agitated, hyperactive delirium represents only 20% of cases, with the others having hypoactive ("quiet") delirium ^{10 11}. Importantly, hypoactive delirium is associated with a significantly worse prognosis at short-term than hyperactive or no delirium ³. Many

screening tools have been validated in recent years¹², but their use is still missed in clinical practice. However, without detecting delirium, many acute clinical conditions may go under-recognized in clinical practice. Once delirium is detected or suspected, a proactive searching for possible causes is imperative to guide diagnostic investigations and to avoid risk of missed diagnosis. Since an acute change in the level of consciousness is often the first clue of delirium, patient's baseline mental status and a prior diagnosis of dementia must be assessed from an adequate interview with caregiver, which information is not always easy to gather (delirium superimposed on dementia has significant prognostic implications if compared with dementia alone)^{1,2}.

To the best of our knowledge, only few studies and a small number of case-reports have been published on the association between delirium and acute myocardial infarction (AMI), which is one of the most common causes of death worldwide, particularly among the older population¹³. For example, Grosmaître et al. retrospectively reviewed 255 patients aged 75 years and older with ST-Elevation Myocardial Infarction, finding that delirium and impaired general conditions were the main presenting symptoms in nearly 12% of all patients⁷. Anyway, the method to detect delirium in this study is not reported and it is likely that a standardized assessment with proper tools has not been done. Another retrospective study including patients aged 90 years and older, reported delirium or agitation being present in more than a quarter of AMI hospitalized patients⁸; this finding was probably an underestimation of the true prevalence since stupor and coma were not always classified as possible manifestations of delirium⁸. Atypical symptoms are even much more frequent among patients with pre-existing cognitive impairment or communication difficulties, since these symptoms seem to be associated with vulnerability criteria such as dementia, functional dependence and impaired communication skills^{7,9,11,13}.

The importance to detect atypical presentation (and then delirium) in older patients with AMI is evident. Based on data from the NRMI-2, Canto et al. have shown that patients with atypical symptoms are at risk of delayed diagnosis, incorrect management and inappropriate discharge, and are less likely to receive reperfusion therapy^{9,13}. According to a recent editorial¹⁴, age discrimination in the management of acute coronary syndrome is still present in clinical practice, whereas current evidence suggests older people with AMI should normally be referred to an interventional cardiologist for consideration of invasive treatment. The After Eighty Study¹⁵ also remind that there is no place for discriminatory clinical practices based on age alone, stressing the need for individually tailored approach.

In conclusion, a systematic detection of delirium should be done in all frail patients once they arrive at an ED. The detection of delirium may rapidly enable clinicians to start a diagnostic workup including an EKG and enzymes measurement, even in the absence of cardiovascular symptoms.

Summarizing, the goal of this report is to highlight the critical importance of 1) detecting delirium systematically in older patients on ED arrival, 2) proactively searching for delirium causes and 3) underscoring the critical gaps existing in knowledge of the relationship between delirium and AMI. Future research is needed to advance in this field.

CONFLICT OF INTEREST

The Authors declare to have no conflict of interest.

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