

Cognitive Challenges in Aging: Unmasking Malignancy-Related Altered Mental States in the Elderly

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Abstract: ***Background:** Altered Mental Status (AMS) is common in elderly ED patients with various potential causes, including structural, metabolic, infections, metastasis, primary central nervous system (CNS) malignancies, polypharmacy and rarely psychiatric causes. Malignancies should be considered as an important, often overlooked cause of AMS in the elderly. Age-related cognitive decline and various neurological presentations make malignancies a significant factor. **Case Summary:** A 70-year-old farmer arrived with worsening consciousness and decreased urine output. Despite normal initial tests, further investigations uncovered hypernatremia, renal impairment, and unremarkable NCCT head, ultimately unveiling an undisclosed renal malignancy with metastases. This underscores the significance of recognizing paraneoplastic causes when elderly patients with AMS present such symptoms. **Conclusion:** Altered Mental Status (AMS) in older adults with normal lab results and brain imaging can be misattributed to aging. This case underscores the need for heightened suspicion of occult malignancies, as AMS can precede cancer diagnosis. Vigilance in considering malignancies as a cause can improve outcomes and emphasizes comprehensive care for elderly patients.*

Keywords: Altered Mental Status, Elderly, Malignancies, AMS, Paraneoplastic causes

1. Introduction

Altered Mental Status (AMS) is a frequent concern among elderly ED patients, with 25-30% affected. The list of potential causes for AMS is exhaustive. Structural causes like CVA or space-occupying lesions also have significant contributions. Metabolic factors like hyponatremia, hypernatremia, hypercalcemia, Vitamin D toxicity, and hyperglycaemias contribute, alongside conditions like uremic, hepatic, and hypoxic encephalopathies in the geriatric population. Psychiatric disorders are rarely a cause of AMS^(1,2). This report presents a case study highlighting the significance of identifying malignancies as a potential cause of AMS in the elderly without the usual causes. As age advances, the incidence of various malignancies increases; however, there is also significant age-related cognitive decline. Malignancy has a wide range of neurological presentations. They frequently cause AMS, primary aetiologies being metabolic derangements like hypercalcemia or hyponatremia and metastatic lesions in the brain. It sheds light on the complex presentation of malignancies, which, despite being known for their physical symptoms, can also lead to subtle or profound cognitive alterations in older individuals. We aim to enhance understanding of mental status changes, assessment, and diagnostic methods in the elderly.

2. Case Report

We are reporting a case of a seventy-year-old elderly gentleman who presented to our ED with complaints of

progressive decline in sensorium over the last month associated with reduced urine output for a week. Our patient, hailing from a remote village in Madhya Pradesh, was a farmer with a reasonably active lifestyle till six months before the presentation. He had a medical history of hypertension for which he was compliant with his antihypertensive drugs. He became progressively sluggish and dull, so he was confined to his room until one month before admission to the hospital. His oral intake also reduced significantly, and he became bedridden last month. A week before the presentation, the caregiver reported a complete cessation of urine output and unresponsiveness to stimuli.

On presentation to the emergency, the patient had a GCS of E2V1M4 with a blood pressure of 100/50 mm of Hg and a respiratory rate of 29/min. B/L planters were mute, and pupils were reactive to light. He was intubated for airway protection, and preliminary workup for the altered sensorium, including blood sugar and NCCT head, was normal. ABG (Arterial Blood Gas) suggested a pH of 7.4 with lactates 2.4, bicarbonates -20, and pCO₂ -24. He had hypernatremia with a sodium of 151 mmol/L. After sending a blood culture, management was initiated for hypovolemic hypernatremia, and broad-spectrum antibiotics were started. Renal function was deranged with serum creatinine of 3.2 mg/dl and blood urea of 276 mg/dl. Liver enzymes were slightly deranged and with normal bilirubin and PT-INR.

During the hospital course, the patient showed improvement in labs (Table I) without any improvement in sensorium. On day 5 of hospitalization, RFT (Renal Function Test) normalized with adequate urine output, normal sodium

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values, no fever, and minimal ventilatory support, but his sensorium remained the same. A thorough evaluation for other possible causes of the poor sensorium, including hypercalcemia, hypothyroidism, hyperammonaemia, meningitis, pneumonia, infective endocarditis, UTI (Urinary Tract Infection.), and tropical fever, was done, which all turned out to be negative. These findings helped us eliminate specific infectious causes and continued our diagnostic journey to identify the underlying cause of the Patient's AMS. A tracheostomy was done for prolonged airway protection. TT aspirate was sterile, and CBNAAT (Cartridge-based nucleic acid amplification test) for PTB (Pulmonary tuberculosis) was negative (was advised due to the high prevalence of Tuberculosis in India). Brain MRI was expected, and EEG did not suggest any epileptic activity. CECT abdomen and thorax was done to look for any solid organ abscess or malignancy, which ultimately showed a distinctive, heterogeneously enhancing exophytic multi-lobulated soft tissue mass originating from the lower pole of the left kidney, extending into the left perinephric space, likely of primary neoplastic origin.

Additionally, osteolytic bone lesions, hypodense lesions in the liver, and focal heterogeneously enhancing nodular opacities in the right lung raised suspicion of metastasis. Our imaging indicated a renal neoplasm with metastases to the liver, lungs, and bones. At the same time, no central nervous system (CNS) involvement was evident.

Altered sensorium in the patient was the first manifestation of an occult malignancy in our patient, which was long ignored, considering it an age-relative cognitive decline or metabolic/septic encephalopathy. A high index of suspicion for AMS as a paraneoplastic presentation, even in the absence of metabolic or imaging abnormalities, could help in the early diagnosis of such cases.

Table I: Lab Reports of the Patient

Investigation	DAY 1	DAY 5
Hemoglobin	12.6	11.5
RBC Counts	4.57	4.23
Hematocrit	40.7	38.2
Platelet counts	316	250
White blood cells	12.20	6.37
Neutrophils	79.2	77.9
Lymphocytes	17.5	19.3
Eosinophils	0.1	0.3
Monocytes	3	2.5
Basophils	0.2	0.0
RFT		
Serum Creatinine	3.67	0.76
Blood Urea	276.84	33.16
LFT		
Total Bilirubin	0.79	0.59
AST	57	26
ALT	26	20
ALP	128	140
GGT	41.3	41.8
Total Protein	7.19	5.14
Serum Albumin	3.13	2.03
Blood Culture	Sterile after 48 hours	-
Urine Culture	Sterile after 48 hours	-
CSF Parameters		Within Normal Range
CRP	63.2	5.7

3. Discussion

With a growing global population, advances in healthcare, and increased life expectancy, the number of geriatric patients seeking medical attention has risen significantly, especially in developing countries like India. In the United States alone, approximately 18 million patients aged 65 and older visit the Emergency Department⁽²⁾. Physicians often use the term Altered Mental Status (AMS) to encompass a range of symptoms, such as confusion, restlessness, stupor, coma, etc⁽²⁾. The management of AMS in the elderly presents formidable hurdles. This complexity arises from a myriad of potential causes, including iatrogenic factors.

Consequently, prompt and accurate assessment is crucial, requiring consideration of various diagnostic pathways to ensure effective treatment. AMS is underdiagnosed in the elderly and attributed to age-related cognitive decline. In countries with limited resources, timely diagnosis is much more difficult.

When assessing a patient in the emergency department who presents with an abrupt alteration in consciousness, as seen in our case, it is crucial to explore a wide range of potential etiologies. These include metabolic factors such as vitamin deficiencies, uraemia, and vitamin D toxicity, as well as electrolyte imbalances like hyponatremia, hypernatremia, and hypercalcemia. Infections, toxic exposures, hypoxemia, and psychiatric conditions should also be considered. Age-related conditions such as dementia (including Alzheimer's and frontotemporal dementias), vascular events, hypertensive encephalopathies, normal pressure hydrocephalus (NPH), traumatic injuries, seizures, polypharmacy, malignancies, and Paraneoplastic syndromes should all be part of the differential diagnosis.^(2-6,8) This comprehensive approach ensures that no potential causes are overlooked when determining the underlying reason for the altered sensorium.

Our Patient presented with a Glasgow Coma Scale (GCS) score of 7, evaluating cognitive function using the Mini-Mental State Examination (MMSE) challenging. We considered septic and metabolic encephalopathy common causes of Altered Mental Status (AMS) in the elderly. Despite the absence of fever, we kept sepsis and meningitis in our differential diagnosis, as they can manifest without elevated body temperature.⁽⁷⁾ The Patient had no history of surgery, no medication allergies, and did not use alcohol, tobacco, or illicit drugs. Given the profound cognitive changes, we initiated a non-contrast head computed tomography (CT) scan, which revealed age-appropriate normal results, ruling out conditions like normal pressure hydrocephalus, stroke, primary CNS malignancies, metastasis, and infectious brain lesions. To rule out cardiac causes of AMS, particularly important in the elderly, we conducted an electrocardiogram (ECG), which also served as a baseline for monitoring QT prolongation, a potential side effect of certain drugs, although we had not established a psychiatric cause in this case.

Simultaneously, we promptly initiated broad-spectrum antibiotics and secured the Patient's airway. His basic metabolic panel indicated abnormal serum creatinine levels

and euvoletic hyponatremia, excluding other causes of AMS. Elevated C-reactive protein levels led us to investigate infectious etiologies further. After 48 hours, blood culture results returned negative for bacterial growth. Subsequently, we performed a lumbar puncture,⁽⁷⁾ analyzing cerebrospinal fluid (CSF) for biochemical markers, cell count, viral panel, mycology stains, aerobic culture, and Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) for tuberculosis, and results came to normal.

By the fifth day of admission, our Patient improved his Basic Metabolic Panel (BMP) with normalized C-reactive protein (CRP) levels and serum creatinine values as described in Table I. However, his consciousness remained unaltered. To explore other potential causes, we opted for an electroencephalogram (EEG), even though no family history of seizures existed. Non-convulsive status epilepticus (NCSE) needs consideration as it can be a factor when the origin of acute altered sensorium remains elusive.⁽⁵⁾ Fortunately, the EEG results came back normal, effectively ruling out NCSE. Intending to investigate the underlying cause further, we proceeded with the magnetic resonance imaging (MRI) scan of the brain. The results showed regular age-appropriate changes and no signs of infective lesions. Despite the improvements in laboratory values, the persistence of altered consciousness prompted a thorough investigation into the paraneoplastic syndrome as a potential cause, underscoring the intricate and multifaceted nature of the Patient's condition.

Subsequently, we ordered a contrast-enhanced computed tomography (CECT) of the abdomen and thorax, which showed a left renal mass with multiple metastatic lesions in the liver, bones, and lungs. Considering these findings, we began to suspect a paraneoplastic syndrome as a cause of the Patient's altered sensorium. Systemic cancers can lead to non-metastatic complications, encompassing toxic metabolic encephalopathy, cerebrovascular issues, immunocompromised infections, and paraneoplastic neurological syndromes (PNS).⁽⁸⁻¹²⁾

In comparison, metabolic encephalopathy is the most common non-metastatic complication of systemic cancer.⁽⁴⁾ Amongst these, PNS pose the highest diagnostic difficulty. In 60% of patients, the neurologic symptoms precede the cancer diagnosis.⁽¹³⁾

PNS encompasses a range of conditions, including encephalitis, encephalomyelitis, cerebellar involvement, myopathies, and more. The diagnosis of PNS primarily relies on detecting onconeural antibodies such as Anti-CRMP5 and Anti-Hu in the serum or cerebrospinal fluid (CSF).^(13,14) However, it is essential to note that only 60-70% of individuals with PNS possess these antibodies, making them less reliable as standalone diagnostic tests. Furthermore, magnetic resonance imaging (MRI) findings in PNS cases tend to be non-specific. CSF studies typically reveal mild to moderate pleocytosis, elevated protein levels, and varying presence of oligoclonal bands. Interestingly, in our Patient's case, CSF findings were within the normal range, adding to the diagnostic challenge.⁽¹³⁾

Our elderly Patient experienced a progressive cognitive decline over a month, diagnosed belatedly even after seeking tertiary care. Initial assessments for altered mental status yielded no clues. Despite improved vital signs, persistent cognitive impairment led to considerations beyond infection or metabolism. Malignancy evaluation was delayed due to inconclusive radiological findings unrelated to PNS.

4. Conclusion

AMS in older adults, when accompanied by normal laboratory results and brain imaging, can be mistakenly attributed to age-related cognitive decline. However, our experience in this case highlights the importance of maintaining a higher suspicion of occult malignancies to ensure early diagnosis and intervention. Indeed, AMS can manifest as an early symptom of systemic cancer, often preceding its formal diagnosis. By remaining vigilant and considering malignancies as a potential cause of AMS, we can make a profound impact on the well-being and outcomes of elderly patients, emphasizing the need for comprehensive care that extends beyond routine assessments.

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