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Delirium as a Presenting Feature of Occult Malignancy: A Case Report

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Abstract

Background: Delirium is a psychiatric syndrome prevalent in elderly patients. According to the DSM-5-TR and ICD-11 it is characterized by a disturbance in awareness, orientation and attention. Treating delirium is difficult as the underlying medical conditions are not always apparent. Etiology is heterogeneous and can be attributed to infection, electrolyte imbalances, substance withdrawal or other factors disrupting homeostasis.

Aim: The aim of this case report is to highlight the importance of considering metastatic malignancy in the differential diagnosis of delirium in elderly patients. Furthermore, it underscores the value of interdisciplinary collaboration between psychiatrists and internal medicine specialists in the diagnosis and management of such cases.

Materials and methods: A narrative literature review was conducted using PubMed, the WHO ICD database, Oxford University Press, and The Lancet, including meta-analyses, case reports, systematic reviews, and international treatment guidelines published up to 2025.

Case presentation: This case presents an 82 year old woman admitted to the psychiatric hospital, with a preliminary diagnosis of organic mood disorder. Exhibiting visual hallucinations, suicidal thoughts, fluctuating disturbances of consciousness and delusions of persecution. During hospitalization laboratory findings revealed elevated C-reactive protein levels and leukocytosis. Broad spectrum antibiotic therapy was administered after the collection of blood and urine samples. Due to suspected somatic causes of delirium and ineffectiveness of antibiotic therapy, the patient was transferred to the internal medicine department. During further diagnostic workup, the patient was found to have metastatic cancer of idiopathic origin.

Conclusions: This case report presents delirium as a possible indicator of physiological imbalance, such as a tumor, providing insight into how psychiatric symptoms may act as markers of an underlying systemic disease.

Key words: Delirium; Cancer-related delirium; Elderly patients; Neuropsychiatric symptoms; Diagnostic challenges; Paraneoplastic syndrome; Case report

Introduction

Delirium is a neuropsychiatric syndrome known to occur in hospitalized, postoperative, terminally ill, and elderly patients, as well as in individuals discontinuing psychoactive substances, thus representing a result of a global disruption of homeostasis. It is associated with a significant increase in mortality, reported to be as high as 28.79% for patients within hospitals or emergency departments (1). According to DSM-5-TR and ICD-11 delirium is characterized by a disturbance in attention, orientation and awareness with transient symptoms that may fluctuate depending on the underlying etiology (2). The underlying cause of delirium is often difficult to determine. It can result from a variety of factors that dysregulate brain function, including infections, electrolyte imbalances, medications, trauma, hypoxia and other metabolic disorders. Cancer is a prime example of a disturbance in homeostasis. Research indicates that the occurrence of delirium in cancer patients ranges from 11% to 35% while in patients who suffer from advanced cancer, the

prevalence may reach up to 46.9% (3). Although it has been identified in literature as a potential cause of delirium - particularly in patients with predisposing factors such as surgical intervention, pharmacotherapy and comorbidities (4) - research remains limited on delirium presenting as the primary symptom of advanced cancer. This case report presents delirium as a potential indicator of an underlying malignant process in elderly patients.

Case description

Admission to the Psychiatric Hospital

An 82 year old woman was admitted to the psychiatric hospital due to the presence of suicidal thoughts, dysphoria with a tendency towards irritability, persecutory delusions and visual hallucinations. The patient has been under psychiatric care since 2009 due to previous depressive episodes which were treated with 75 mg of venlafaxine and 200mg of quetiapine daily. Past medical history outlined hypertension, coronary artery disease and a myocardial infarction in 2022. The patient was placed under inpatient care with a preliminary diagnosis of organic mood (affective) disorder.

Upon admission, the patient displayed fluctuating disturbances of consciousness and was disorientated in time, but oriented to place and person. Persistent persecutory delusions and visual hallucinations were present. The patient denied any suicidal ideation following hospitalisation. Her mood remained labile and there were no signs of aggressive behaviour. Notable cognitive impairments were also evident. Initial treatment was modified with a discontinuation of venlafaxine and quetiapine and replaced with 1mg of risperidone and 5mg of donepezil daily, the latter selected for its procognitive effects. Due to the change in treatment, mood stabilization was achieved along with the resolution of sleep disturbances; however, the patient continued to exhibit qualitative disturbances of consciousness. Due to the remaining symptoms, a search for the somatic cause of delirium began.

Physical examination revealed slight crackles at the base of the lungs and back pain. Vital signs were within normal limits. ECG revealed a prolonged QT interval. Laboratory findings showed elevated C-reactive protein levels (CRP) 5.76mg/dl, (reference: <0.5 mg/dl), leukocytosis 14.1 μ l

and anemia Hb 11g/dl. Urinalysis, sodium, potassium and glucose levels were unremarkable. Chest X-ray revealed no abnormalities. The coagulation profile was within normal limits. The increase in inflammatory markers suggested an underlying infection and indicated a potential somatic cause of the delirium.

Given the patient's age, comorbidities and disturbances of consciousness, a broad spectrum antibiotic (Ceftriaxone) was administered at 2g/day iv. Blood and urine cultures were obtained prior to the start of the antibiotics. The results showed sterile blood cultures, while the urine cultured identified an E. coli infection, sensitive to the antibiotics listed in the antibiogram. After 4 days of antibiotic therapy a slight decrease in CRP levels was observed. However, after 7 days the CRP levels rose to 7.1mg/dl and leukocytosis presented at 15 μ l. Repeat urinalysis showed no abnormalities. A follow-up chest X-ray was also unremarkable. A neurology consultation was requested, during which no signs suggestive of a central nervous system infection were observed. Due to the suspected somatic cause of delirium and ineffectiveness of antibiotic therapy, it was decided that the patient should be transferred to the internal medicine department.

Following Admission to the Internal Medicine Department

Further diagnostic workup revealed elevated tumor markers, borderline elevated calcium levels (12.5 mg/dl, with normal PTH levels and correct vitamin D levels), and decreased hemoglobin and albumin levels. Abdominal CT revealed multiple bone metastases, bladder wall thickening, aortic atherosclerotic changes, suspected nephrolithiasis, and renal cysts. Echocardiography showed moderate mitral regurgitation, mild aortic stenosis, and features of left ventricular outflow tract narrowing. The patient received intensive fluid therapy, loop diuretics, glucocorticosteroids, and intravenous zoledronate, resulting in a reduction of serum calcium levels. Due to decreased hemoglobin, without signs of gastrointestinal bleeding, a total of 3 units of packed red blood cells were transfused.

Given the patient's poor general condition, medical history, inability to provide informed consent, and advanced malignancy of unknown origin, a joint decision was made along with the family to discontinue further invasive diagnostic and therapeutic, procedures. The patient died following admission into palliative care.

Table 1. Electrolytes and CRP levels during the first five days of hospitalization (Internal Medicine Department)

<i>Parameter</i>	<i>Results</i>	<i>Reference range</i>
Sodium	141 mmol/l	135–145 mmol/l
	137 mmol/l	
	144 mmol/l	
	140 mmol/l	
	136 mmol/l	
Potassium	3.7 mmol/l	3.5–5.1 mmol/l
	3.6 mmol/l	
	3.4 mmol/l	
	3.9 mmol/l	
	4.2 mmol/l	
Calcium	12.0 mg/dl	9–11 mg/dl
	12.5 mg/dl	
	11.7 mg/dl	
	8.0 mg/dl	
	7.8 mg/dl	
Phosphorus	3.9 mg/dl	2.5–4.5 mg/dl
	3.7 mg/dl	
	3.6 mg/dl	
	3.4 mg/dl	
	3.5 mg/dl	

<i>Parameter</i>	<i>Results</i>	<i>Reference range</i>
CRP	85 mg/l	<8mg/l
	76 mg/l	
	106 mg/l	
	180 mg/l	
	118 mg/l	
Creatinine	0,65 mg/dl	0,6–1,2 mg/dl
	0,81 mg/dl	
	0,80 mg/dl	
	0,85 mg/dl	
	0,75 mg/dl	

Discussion

Etiology and pathophysiology of delirium in cancer

This report exemplifies the significant challenges that occur during diagnosis and treatment of delirium associated with metastatic cancer. Even with high prevalence in the available data, early detection still remains low. As suggested by Yamamoto. K *et al.* (2023) onset of delirium may depend on the cancer type, with most common being pancreatic cancer, oropharyngeal cancer and lymphoma compared to patients with gastric cancer. Delirium risk appears to be significant in patients with cancers close to the central nervous system particularly brain or oropharynx (4).

The variation in prevalence of delirium across different types of cancer may be due to the difference in screening, detection, medication and immunological mechanisms behind oncogenesis. For instance, during tumor lysis, a release of different chemical mediators can lead to elevated levels of proinflammatory factors, including, interleukin (IL)-1- β , IL6 (linked to hyperactive delirium), IL-8, tumor necrosis factor (TNF- α) and prostaglandin E2 (EP1-4)(5). These factors are proven to contribute to both delirium and cancer progression. Furthermore, a

significant increase in CRP levels may indicate an inflammatory cause of delirium, as CRP elevation is largely driven by increased interleukin-6 (IL-6) activity.

During the search for the somatic cause of delirium, the most common underlying causes were taken into consideration. Sodium and glucose levels were within normal range, excluding hypo/hyponatremia, as well as hypoglycemia as the primary contributor to delirium. One of the factors that may contribute to the development of delirium is medication. Particularly by agents such as benzodiazepines, anticholinergics, opioids and tricyclic antidepressants (4,12). As these medications are commonly used within elderly and cancer populations, their effects may lead to misinterpretation of the underlying etiology of delirium. In the case presented, the patient was adequately hydrated and was not taking any medication known to induce delirium (quetiapine, venlafaxine). These factors further support the fact that underlying malignancy was most likely responsible for the cause of delirium.

Hypercalcemia is a recognized contributor to neuropsychiatric symptoms. In early or mild cases hypercalcemia can cause mood and cognitive disturbances, while in cases with high severity it may cause psychosis including, auditory hallucinations, paranoia and persecutory delusions, stupor or coma (6). The most common causes are: primary hyperparathyroidism (parathyroid adenoma), tertiary hyperthyroidism, lithium toxicity, thiazide diuretics and bone metastases (7). As PTH levels remained within normal limits, and hyperthyroidism was excluded, malignancy-associated hypercalcemia could have been one of the causes of delirium, likely due to increased osteoclast activity and enhanced bone resorption (7). However, calcium levels did not exceed 12.5 mg/dl, suggesting that delirium was more likely due to other potential causes, where mild hypercalcemia may have acted synergistically alongside the inflammatory process.

Differential diagnosis and challenges

When discussing this case, it should be noted that Lewy Body Dementia (LBD) remains a possible clinical consideration, as visual hallucinations, fluctuating cognition and psychotic features may occur in both delirium and LBD. Typically dementia is characterized by a gradual and progressive cognitive decline, whereas delirium underlies other medical conditions; however, distinguishing between these two conditions remains challenging. As previously mentioned, sleep disturbances,

visual hallucinations, delusions and depressive symptoms were present, all of which may be observed in both conditions. However, no movement disorders or extrapyramidal symptoms, features characteristic of LBD, were identified. Additionally, LBD is often associated with antipsychotic hypersensitivity. In this case, treatment with risperidone was beneficial and did not result in the exacerbation of symptoms. However, late-life depression is known to increase the risk of dementia (9); therefore, the possibility of delirium being superimposed on dementia cannot be discounted.

Secondary brain tumors should not be overlooked in the differential diagnosis, particularly as CT imaging was restricted to the abdominal region and did not include the brain. This is significant, as changes in intracranial pressure may lead to vascular and neuroinflammatory interference, disrupting normal brain function (13). Delirium is more common in patients with secondary brain tumors (31%) than those with primary tumors (17%) (13). Furthermore, fronto-temporal tumors are associated with higher incidence of delirium (13), which is consistent with their roles in attention and emotional processing. The absence of neuroimaging represents a limitation due to the scarce information about the neuropathology that may have developed, affecting management decisions and diagnostic certainty. It should be noted that performing a CT scan may be challenging in patients with delirium, as this procedure requires the patient to remain still and follow instructions.

During literature review, certain paraneoplastic syndromes, such as Trousseau syndrome and stroke secondary to its hypercoagulability, were noted as important considerations in the differential diagnosis of patients with atypical or sudden-onset delirium (8). In a case reported by Yamaguchi, J. *et al.*, delirium was the sole clinical manifestation of a serious cancer-related complication, as no focal neurological signs (e.g., paralysis) and metabolic causes were observed; the patient only developed delirium and speech impairment (8). This example illustrates how delirium is frequently attributed to more common etiologies, especially in patients with a previous medical history of delirium, potentially leading to delays in appropriate treatment and diagnosis. This is consistent with the findings presented in our case report.

Other diagnostic challenges can be attributed to clinical presentation. Delirium may occur in two forms, or a combination of both, hypoactive: characterized by psychomotor slowing and apathy, and hyperactive, marked by agitation and aggressive behaviour (15). Hypoactive and mixed delirium are more common among the elderly and palliative population, accounting for 45-65% (10-11); yet, hypoactive delirium is often underdiagnosed due to its subtle clinical manifestation, which delays appropriate treatment (10). The screening tools recommended by NICE (National Institute for Health and Care Excellence), 4AT, CAM-ICU and ICDSC (14), still demonstrate limited sensitivity in detecting hypoactive delirium, portraying another challenge in delirium diagnosis amongst the elderly population. In the present case, the patient exhibited features consistent with a mixed subtype.

Conclusions

This case demonstrates the need to re-evaluate and expand the differential diagnosis in patients presenting with delirium, particularly when common etiologies have been excluded, and with high risk due to predisposing factors such as advanced age, surgery, medications, low albumin levels and infections. Initial management should not be purely symptom-based, but also must focus on identifying the underlying cause. Malignancy should be considered in patients with elevated inflammatory markers without a clear source, unexplained anemia and hypercalcemia. This case provides insight into how psychiatric symptoms may represent potential paraneoplastic manifestations, bridging the fields of psychiatry, oncology and internal medicine, while portraying the need for an interdisciplinary approach, as effective management required collaboration between psychiatry and internal medicine. There is an ongoing debate about the appropriate setting for the treatment of delirium. Single-specialty psychiatric hospitals may not be equipped with diagnostic tools needed for further assessment. This can pose a significant challenge, especially in patients who are less cooperative and suffering from hyperactive delirium. This issue should be addressed through closer collaboration between psychiatric and general medical hospitals. The final aspect to consider is the prospective new research, as there remains limited information about diagnosis and management of delirium associated with metastatic cancer.

Disclosure

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Declaration of the Use of Generative AI and AI-assisted technologies in the Writing Process

During the preparation of this manuscript, the authors used ChatGPT for the purpose of language improvement, readability enhancement, and text formatting. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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