Persisting Delirium as a Presenting feature of Myeloproliferative Neoplasm in Elderly

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Abstract

A 71 year old female presented with an unusually long course of persisting delirium and a rapid downhill functional decline. She presented with progressive symptoms over a course of year with confused behaviour, sleep disturbances, irrelevant talk and restlessness followed by difficulty in walking, falls, speech disturbances, generalized weakness of six months duration and decreased appetite with urinary and stool incontinence of 2 week duration. Her lab reports had shown consistently abnormal blood counts for 4 years before hospitalization. The abnormalities from peripheral blood smear and (GBP) general blood picture showed elevated platelet count, total leucocyte count, decreased red blood cell count, and hemoglobin level. Specific work up for myeloproliferative neoplasm (MPN) showed JAK mutations on qualitative (RT-PCR) Reverse transcription-polymerase chain reaction test, and excessive megakaryocytes in bone marrow biopsy suggestive of essential thrombocythemia. Patient was started on chemotherapy with oral hydroxyurea 500 mg to normalize the blood counts along with anti-platelet and hypolipidemic agents as prophylaxis against stroke. This patient was regularly followed up in the OPD with periodic checks on blood counts. She responded well to medication and her haemoglobin level and blood counts (RBC, TLC and Platelet Count) were gradually normalised over subsequent visits, and she continued to remain asymptomatic for more than six months in her follow-up period.

INTRODUCTION

Myeloproliferative neoplasms (MPN) are a heterogeneous group of disorders characterized by cellular proliferation of one or more haematological cell lines in the peripheral blood. The clinical picture is of fatigability, fever, abdominal discomfort, loss of appetite and weight loss, and the peripheral blood smear is dominated by excessive white and red blood cell precursors and giant platelets. These patients are also at an increased risk of both thrombotic and embolic complications like stroke, myocardial infarction, easy bruising and bleeding.

Delirium in older adults usually lasts from a few hours to days, and common underlying causes are infections, dehydration, anemia, metabolic disturbances, hypoglycaemia, or acute neurological, vascular events like stroke. The symptoms of delirium disappear once the underlying cause is successfully treated.
Case Presentation

A 71-year-old female presented with varied symptoms over the previous year before consultation at our unit: confused behavior, sleep disturbances, irrelevant talk, and restlessness for a year; difficulty in walking, falls, grinding of teeth, speech disturbances, a generalized weakness for 6 months (diagnosed as Idiopathic Parkinson's disease); and decreased appetite with urinary and stool incontinence of 2 weeks duration. Levodopa and Carbidopa combination was prescribed for the treatment of Idiopathic Parkinson's disease elsewhere which led to body stiffness, and involuntary movements of hands, jaw, and head. Her medical history included diabetes mellitus, coronary artery disease, cerebrovascular disease, successfully treated pulmonary tuberculosis twice, and a traumatic fracture of the left forearm. She was a lady of thin build, pallor, resting tremors of hands, lower jaw and head, and an enlarged liver spanning 5–6 cm below the right costal margin. Mental status examination revealed an unkempt, disoriented patient with increased psychomotor activity and irrelevant speech.

Lab reports showed persistently elevated platelet (14 lac cells/mm$^3$) and leucocyte (36000 cells/mm$^3$) and decreased RBC (upto 2.82 million cells/mm$^3$) counts, and persistently low haemoglobin (6.9 gm/dl) in the preceding 4 years. General blood picture showed microcytic hypo-chromic anemia, and neutrophilia with large platelets, serum ferritin (566 ng/mL), S. CRP (11.73 mg%) and S. LDH (1403 U/L) were also found to be elevated. Serum liver function tests (LFT), renal function tests (RFT), serum uric acid, serum vitamin D3 and B12 levels, viral markers (HIV, HBsAg, HCV, and VDRL), blood and urine culture and sensitivity and chest X-ray were found to be unremarkable. Ultrasound abdomen revealed mild to moderate hepatosplenomegaly. Plain CT brain showed diffuse cerebral atrophy with periventricular ischemic demyelination. X-ray left forearm revealed fracture of distal 1/3rd Ulna. For bruxism, a temporary POP cast was placed for fracture stabilisation of left forearm and Silicon occlusal splint. All her previous medications were tapered and stopped. She received blood transfusion, antibiotics, insulin, IV fluids, oral melatonin and quetiapine. An acute episode of shortness of breath with derangement of vitals was managed with intravenous hydrocortisone, frusemide, calcium gluconate and external oxygen support.

Myeloproliferative neoplasm (MPN) was suspected and a bone marrow aspiration, trephine biopsy and MPN reflex panel showed normal granulocytic (55%) and erythroid (35%) lineage, myeloid to erythroid ratio of 1.3:1, increased megakaryocytes with hyperlobulated forms, lymphocytes (3%), plasma cells (2%), and nucleated blasts (< 2%). Genetic mutations were positive for JAK 2 v617F and negative for BCR-ABL, CALR, MPL, and JAK 2 Ex12 on qualitative RT-PCR. A diagnosis of essential thrombocythemia was made and cytotoxic chemotherapy with oral hydroxyurea 500 mg was started. The patient responded well to chemotherapy and her antineoplastic drug dosage was titrated according to the haemoglobin levels and blood counts done periodically in subsequent follow-ups over the next six months. Stroke prophylaxis in the form of oral anti-platelet and lipid lowering drugs were simultaneously prescribed, as the risk of thrombo-embolism is usually higher in patients with MPN. Hydroxyurea drug holiday was advised for 1–2 weeks whenever the blood counts go subnormal as a preventive measure against bleeding and infection. The blood counts fluctuated initially in the first 2–3 months of chemotherapy but ultimately attained stability by six months. The patient continued to maintain clinical remission for the same period.

Discussion

Systematic Review of Literature

A literature search for similar cases was carried out on electronic databases (PubMed Central, PsycINFO, Embase, Index Medicus, Scopus, Web of Science, Google Scholar, Cochrane Database of Systematic Reviews, Medknow and Blood). The key parameters were: age > 60 years, publication year 1980 to 2022, and no language restriction. Subject and MeSH terms of “delirium”, “myeloproliferative”, “elderly”, “geriatric”, “old”, “essential thrombocythemia (ET)”, and “essential thrombocytosis”, alone and in combination, yielded only 3 relevant case reports (Table 1).
Table 1: Summary of Case Reports Published

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<th>Author(s)</th>
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<td>Kristine et al.</td>
<td>Delirium in 76 year old female undergoing rehabilitation after hip replacement with newly diagnosed primary hyperparathyroidism but stable calcium level and new onset ET. Lab reports revealed elevated platelet count (10 L/µL). BMB revealed hyper-cellular marrow with increased megakaryocytes with hyperlobated forms and erythroid precursors. Abdominal CT scan revealed massive splenomegaly. No response on lorazepam or haloperidol. She improved with anti-platelet cytotoxic chemotherapy.</td>
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<td>Chawla et al.</td>
<td>Delirium in 65 year old female underlying (PRV) Polycythemia Rubra Vera. She had a past history of two depressive episodes. Lab reports revealed elevated Hb 18.9 gm%, RBC 6.6 million cells/mm3, WBC 18<em>10^9 per L, PLTC 1090</em> 10^9 per L. Following venesection, the patient recovered completely but relapsed with psychotic mania 2 weeks later. Definitive management for PRV with oral allopurinol and IV radioactive phosphorus.</td>
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<td>Sutar et al.</td>
<td>Delirium in 87 year old male underlying myelodysplastic syndrome (MDS), associated with hyponatremia, hypertension and haemorrhoids. Lab reports showed persistently increasing WBC counts (8k, 17k, 22k per mL) and falling haemoglobin (9.5, 9.2, 7.3 gm%) and platelet count (1.67 L, 1.27 L and 58K per µL). Past history of 2 similar presentations. BMB revealed dyserythropoiesis and megakaryopoiesis. PBS revealed monocytosis (14% blasts). Treatment was deferred in view of complex treatment regimen, advanced age, comorbid conditions and patient’s inability to take self care. Patient was discharged on tablet Quetiapine 25 mg. This case highlighted the importance of screening all geriatric patients attending neuropsychiatric units.</td>
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This case presented with a prolonged course of delirium underlying an undiagnosed myeloproliferative neoplasm. Instead, this lady was misdiagnosed elsewhere as idiopathic Parkinson’s disease and was treated with levodopa/carbidopa combination, and antipsychotic drugs for ten months leading to the origin of drug induced extrapyramidal side effects. MPNs are usually diagnosed after 50 years with a median age of 67. In various MPNs, fatigue is the most common complaint. Approximately 1/3rd of patients require assistance in activities of daily living and 11% report MPN-related medical disability. Falls, insomnia, and fatiguability are common early presenting features of MPN which can be mistaken as symptoms of depressive disorder, but not delirium, which is rarely reported. Around one in six elderly with unexplained blood counts have findings consistent with MDS/MPN disease spectrum. The median survival was 59 weeks in one study, with unidentified haematological malignancy and varied clinical presentations leading to death. A case report described delirium in two young patients (< 60 years) with promyelocytic leukaemia on induction chemotherapy and other in an elderly patient with Myelodysplastic Syndrome.

The goal of treatment was cytoreduction and prevention of clinical thrombotic episodes, as per NCCN (National Comprehensive Cancer Network, 2.0) clinical practice guidelines in Oncology. Our patient received oral hydroxyurea 500 mg (antineoplastic, antimetabolite class agent) with a periodical review every two weeks for early detection of blast transformation and bleeding tendencies. Oral anti-platelet and hypolipidemic therapy was initiated to prevent future thrombotic events. The patient completely recovered from delirium with near normalisation of blood counts and has remained in remission. The overall prognosis of ET in the absence of any unusual events is good with a median survival of 20 years for those above 60 years of age having a comparable life expectancy to that of healthy controls.

Conclusion
This case highlights the importance of basic laboratory workup in older adults.

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Nil

Conflict of Interest
None

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Delirium in Myeloproliferative Neoplasm of Elderly


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