Neutropenia in a patient with Very-Late-Onset-Schizophrenia-Like-Psychosis under Risperidone treatment – Case report

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ABSTRACT

This case report describes the clinical evolution of a 75-year-old man with no psychiatric history, hospitalized for psychotic anxiety, commentary and imperative auditory hallucinations, and multimodal delusions in the absence of an affective disorder or neurocognitive decline. He was diagnosed with very-late-onset-schizophrenia-like-psychosis after a complex differential diagnosis, including Alzheimer’s dementia with psychotic symptoms, delirium, Lewy-body dementia, and other psychiatric or general medical conditions. The patient received antipsychotic treatment (Risperidone up to 3 mg/day) with favourable clinical outcomes. However, the laboratory tests showed a low neutrophil count three weeks into treatment. The thorough interdisciplinary evaluation concluded that another cause of neutropenia other than the pharmacologic treatment was improbable. Risperidone was then progressively switched to Olanzapine up to 10 mg/day. Neutrophils returned to base levels after a few days. Unfortunately, the clinical course was unfavourable, and since the reoccurrence of psychotic symptoms was debilitating for our patient, the decision to rechallenge Risperidone was made, starting with low doses of 0.5 mg/day and slowly increasing to 2 mg/day. Despite normal neutrophil count and positive clinical results after seven days, neutropenia was noticed again after two weeks. Therefore, because of the patient’s vulnerability and the uncertainty of periodic outpatient assessment of complete blood count, he was discharged on Haloperidol with resolution of psychotic symptoms and without any side effects. This report’s primary purpose is to highlight a challenging differential in an elderly patient while presenting a rare but potentially harmful adverse effect of Risperidone treatment.

Keywords: risperidone, neutropenia, very-late-onset-schizophrenia-like-psychosis

INTRODUCTION

Very-late-onset-schizophrenia-like-psychosis (VLOSPL) is a psychiatric condition described in patients over 60 who experience positive symptoms, such as delusional beliefs and multimodal hallucinations, in the absence of negative symptoms and with no correlation to affective states or structural brain abnormalities. The delusions are usually persecutory and severely distressing. Another characteristic of VLOSPL is represented by “partition” delusions (the idea that walls, doors, ceilings, or other structures are no longer barriers for sounds, objects, and people, therefore, the patients feel harmed, followed, assaulted, or stolen from) [1].

Schizophrenia and other psychiatric disorders are usually treated pharmacologically with antipsychotics. Among these, Risperidone is a commonly prescribed atypical antipsychotic. Adverse reactions of antipsychotics can sometimes cause neutropenia, defined as an absolute neutrophil count (ANC) <1.5 ×10^9/L or even agranulocytosis (absence of circulating neutrophils, basophils, and eosinophils) suggested by an ANC <0.5×10^9/L. These are well-known side effects of clozapine, and clinical guidelines recommend monitoring complete blood count (CBC) for patients under clozapine treatment. However, various case reports describe antipsychotics-induced neutropenia following treatment with Risperidone, Paliperidone, Olanzapine, Aripiprazole, and others. Drug-induced neutropenia may be caused by either
peripheral destructions of neutrophils (also caused by infections, immune or metabolic diseases, or hypersplenism) or a decreased production of these cells (also seen in illnesses that infiltrate the bone marrow, vitamin deficiency, tumours, or myelodysplastic syndromes). A high risk of this adverse reaction consists of opportunistic infections that can have a lethal effect without appropriate diagnosis and management [2].

CASE REPORT

Our patient is a 75-year-old man with no psychiatric history and no general medical conditions besides arterial hypertension and chronic venous insufficiency. He has no family history of mental health disorders and denies substance abuse. He worked as a car service technician after completing primary education and as a driver for all his adult life. He has been retired for about 20 years. Ever since his wife died ten years ago, he has been living alone and taking care of himself – managing to grocery shop, cook, pay bills, and meet with an old friend every few days. He has two children live who live in the same city.

Before being taken to the psychiatric emergency room by ambulance, his daughter found him at a subway station far away from home, in a state of severe agitation, extremely anxious, holding a knife and saying he must “end the story” with his neighbours “they told me to meet here, I want to be a step ahead of them”. During the psychiatric examination, he is partially oriented in time “I do not care about this; I am in danger any second”, guarded and suspicious, and has a tense posture, displaying psychotic anxiety. His speech and thoughts are racing. He is focused on the delusions of persecution, prejudice, and partition (“the neighbours have a special machine that sends some radiation through the walls, they can see me in my apartment, and they try to burn my hair; I never get to see them, but they enter my apartment and I am sure they leave things around on purpose, to make sure I know they were inside the house”). He describes auditory hallucinations (“they threaten to murder my children and take my house; they know everything about me, even where I keep my money; they tell me stories about people I know”). He cannot shift his attention to any other task. He explains his psychotic behaviour that led to admission to the hospital “they told me to meet them at the subway station and talk about our problems”. When asked if he has ever met his neighbours, he states “they do not want to see me, I tried knocking at their door, and they did not open it, but they talk to me every day through the walls”.

The onset of auditory hallucinations, followed by delusions, severe anxiety, and psychotic behaviour, was about two months before arriving at the hospital and gradually increased in severity. Three days before this episode, the patient’s daughter called him and discovered he had moved to a hotel. Upon her arrival, she saw a towel covering the air conditioning installation while he whispered, “I can hear them anywhere I go; they are following me on the street, in the park, and here; they will find a way to get rid of me”. She tried to convince him to see a psychiatrist. However, because of the low insight into the pathology, the patient denied any kind of medical evaluation, and further evolution led to hospitalization three days later.

Neurological examination shows no abnormalities, and his cerebral CT scan has no sign of acute vascular events. However, his cerebral MRI scan shows a few isolated chronic punctiform demyelinating lesions in the frontal lobe (probably microvascular ischemic brain disease), mild global cortical and cerebellar atrophy, and higher-grade bilateral atrophy of the medial temporal lobe. The patient neuropsychological evaluation results (Mini-Mental State Evaluation – 24/30, Addenbrooke’s Cognitive Examination – 77/100) did not correlate with cognitive impairment when adapted to the patient’s age and educational level [3].

A thorough differential diagnosis between VLOSLP, delirium, Alzheimer’s Dementia with Psychotic symptoms (ADP), Lewy Body Dementia (LBD) and other psychiatric and general medical conditions was conducted by a multidisciplinary team. Considering the patient’s clinical presentation, imagistic findings, and neuropsychological examinations, he was diagnosed with very late-onset schizophrenia-like psychosis (VLOSLP).

Following treatment with oral Risperidone up to 3 mg/day, the clinical evolution of symptoms was favourable. However, three weeks into treatment, the laboratory results showed a low ANC, and antipsychotics-induced neutropenia was suspected. Risperidone treatment was switched to Olanzapine, up to 10 mg/day. Despite the significant improvement in the ANC, which returned to base values after a few days, the clinical outcome was negative. The patient was found during the morning rounds covered under his blanket, with psychotic anxiety, complex verbal hallucinations, and delusions “I heard them saying that they killed my son last night; you need to call him and see that I am right; now they want to come after me, they can see me, and they will poison me today”. Given the patient’s severe distress, the decision to rechallenge Risperidone was made with careful monitoring of the CBC, particularly ANC. Risperidone was started at low doses of 0.5 mg/day and gradually increased to 2 mg/day. ANC was regular seven days later, but neutrophils fell again out of the normal range after another week. Because of the patient’s vulnerability and the uncertainty of periodic outpatient assess-
ment of complete blood count, he was discharged on 4 mg/day of Haloperidol, with resolution of psychotic symptoms and without any side effects.

**DISCUSSIONS**

The particularities of this case regard not only the treatment’s adverse reaction but also the controversial diagnosis. The onset of a first psychotic episode in a 75-year-old patient with no psychiatric history required a thorough differential diagnosis of general medical conditions and various psychiatric disorders. Delirium was first excluded since the patient’s symptoms did not fluctuate during the day, and there was no identifiable organic cause to explain the symptomatology. Various medical evaluations ruled out vitamin deficiencies and endocrinological or metabolic disorders. The differential diagnosis between VLOSLP, ADP, and LBD required a careful phenomenological approach. Hallucinations were the primary phenomenon which led to further delusions. They were intense and involved clear, verbal, threatening voices. In ADP, perceptual phenomena appear subsequently to the delusions and consist of noises or indistinct babbling, while in LBD, they are usually visual. Delusions appeared soon after the onset of the episode, unlike LBD, where they correlate with a more advanced phase of the disease. The presence of partition delusion supported the VLOSLP diagnosis since they are primarily described in VLOSLP (36.8% vs <15% in ADP) [4,5].

Our patient had normal CBC at the time of admission into the hospital, and he was naive to any psychotropic medication. Neutropenia was managed conservatively by switching to a different antipsychotic. However, due to the severity of his psychotic symptoms after two weeks on Olanzapine, a second Risperidone trial was made to improve his clinical outcome. After another drop in the level of neutrophils, the diagnosis of drug-induced neutropenia was almost certain. Due to immediate management, he has never reached severe neutropenia (lowest ANC being 0.89×10⁹/L) during his stay in the hospital. This decision was made considering the age of our patient and the life-threatening risk of a potentially severe infection. Experts’ opinions and various case reports share the recommendation for younger patients to continue treatment if it is essential for clinical remission and if the patient has no signs of an active infection, if the neutrophil’s level is above 0.5-0.7×10⁹/L and if continuous haematological supervision is available [6].

**CONCLUSION**

VLOSLP is a rare diagnosis which should be considered in elderly patients presenting with psychotic symptoms and normal neurocognitive function. However, it represents a diagnostic and a therapeutic challenge and requires an extensive differential diagnosis. Data regarding the mechanisms underlying psychotic disorders and recommendations for treating the elderly are continuously improving. In this case, the correlation between clinical presentation and the rare adverse reaction of antipsychotic treatment is questionable. However, atypical antipsychotics have been linked to various haematological abnormalities in patients of all ages and with various disorders. Further research could identify potential risk factors that may lead to blood dyscrasias during antipsychotic treatment.

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**REFERENCES**


