

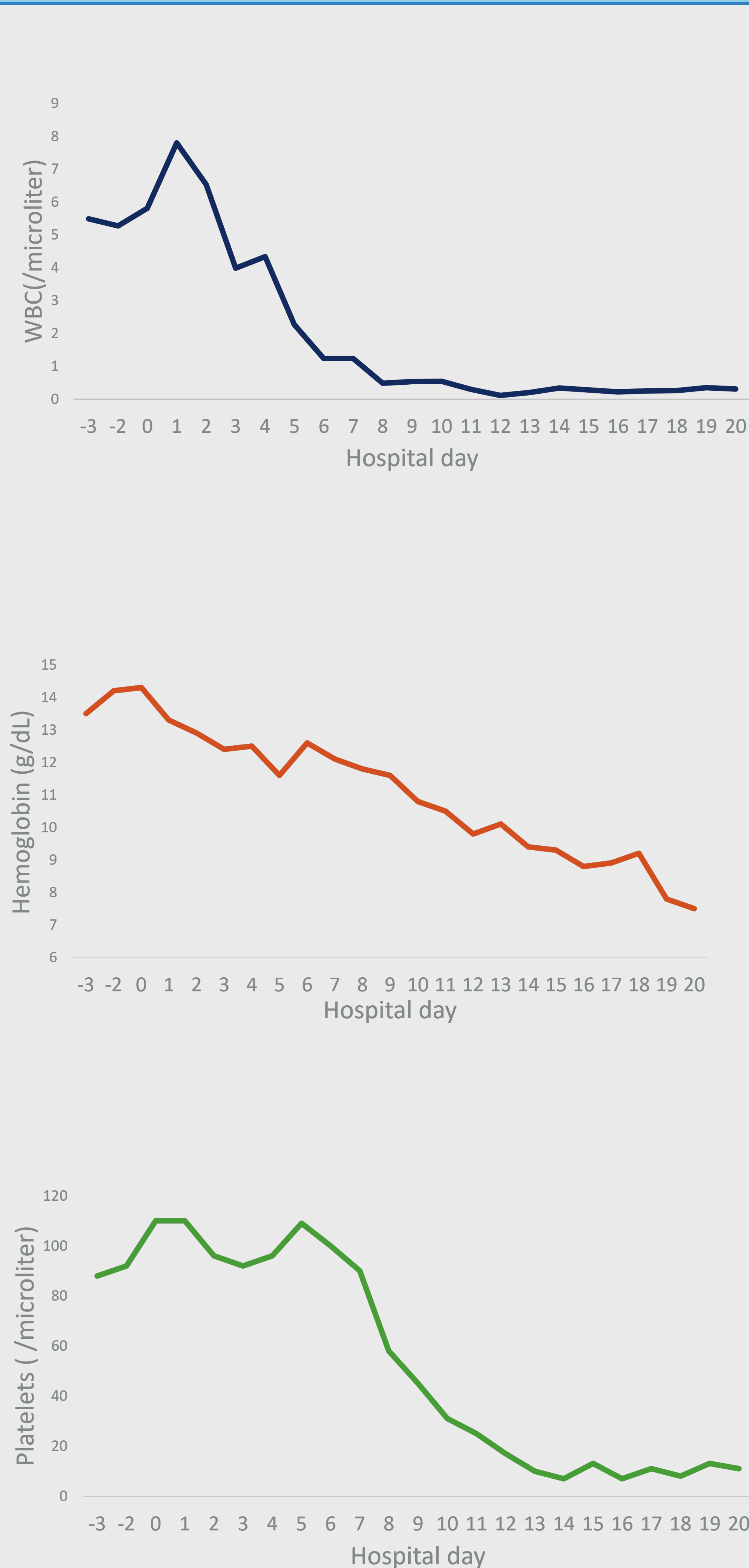
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## Background

- Aplastic anemia is a rare but life-threatening hematopoietic stem-cell disorder with an incidence of 2-3 cases per million people per year and characterized by pancytopenia of the peripheral blood and hypocellular bone marrow.
- Antipsychotics have been associated with aplastic anemia. However, much of the literature on hematologic side effects is centered around clozapine and agranulocytosis
- The differential for pancytopenia includes viral/bacteria infections, myelodysplastic syndromes, autoimmune radiation, chemotherapy, medication, and toxins.
- Pathogenesis includes hematopoietic stem/progenitor cell deficiency, abnormal bone marrow microenvironment, immune dysfunction, and genetic susceptibility.
- Here, we present a case of long-acting injectable (LAI) paliperidone-associated aplastic anemia, which has not previously been reported in the literature.

## Case Report

- Patient is a 62-year-old-male with a past psychiatric history of schizophrenia and alcohol use disorder and past medical history of alcoholic cirrhosis, obstructive sleep apnea, hypertension, chronic kidney disease stage II, benign prostatic hyperplasia, and compressive myelopathy with neurogenic bladder admitted to inpatient psychiatry due to worsening AH (background commentary), paranoid delusions (surveillance, threat, persecution), thought insertion, and thought disorganization (tangential, derailment) in setting of medication non-compliance. Improved back to baseline with initiation and uptitration of risperidone and discharged.
- Readmitted to medicine within 48 hours for a urinary tract infection, stercoral colitis, and decompensated psychosis in the setting of medication noncompliance. He was treated with IV antibiotics, restarted on risperidone per the recommendation of the CL team, and discharged after 4 days.
- Readmitted within 48 hours due to failure to thrive and decompensated psychosis. Due to concern for medication noncompliance, the CL team recommended stopping risperidone and starting paliperidone LAI.



## Case Continued

- Paliperidone LAI was administered on HD1 (156 mg) and HD8 (117 mg).
- CL team was reconsulted on HD9 due to concern for antipsychotic-related pancytopenia.
- Bone marrow biopsy on HD19 was consistent with aplastic anemia.
- Filgrastim, cyclosporine, and eltrombopag were started.
- Patient became bacteremic with MRSA and *E. faecalis*. He was treated with metronidazole, ceftriaxone, and vancomycin.
- He developed acute hypoxic respiratory failure due to septic emboli vs respiratory infection and died on HD23.

## Discussion

- Antipsychotics have been associated with several hematologic disorders, including agranulocytosis and thrombocytopenia. Aplastic anemia has only been reported in 3 cases, with chlorpromazine, clozapine, and perphenazine being the associated agents.
- Risperidone undergoes metabolism by cytochrome P450 2D6 in the liver to paliperidone.
- When this patient was started on risperidone, there was a slight decrease in his white blood cell count, but it was still within normal range. However, the initiation of paliperidone correlated with the beginning of pancytopenia.
- The cytopenic effects from risperidone were likely masked due to difficulty converting risperidone to paliperidone in the setting of liver dysfunction due to alcoholic cirrhosis.
- In patients with liver dysfunction, it may be worth doing an oral paliperidone trial prior to initiation of LAI and checking daily CBCs, even though the manufacturer states that a trial with oral risperidone is appropriate and no changes need to be made for hepatic impairment.
- Additionally, given the poor substrate with many inpatients, it may be worth delaying LAI initiation until closer to discharge once overall health has improved.
- Typically, management of adverse effects from antipsychotics starts with removing the offending agent. Unfortunately, in the case of LAIs, this is not an option.

## References

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2. Nooijen, P. M. M., Carvalho, F. & Flanagan, R. J. Haematological toxicity of clozapine and some other drugs used in psychiatry. *Human Psychopharmacology* vol. 26 Preprint at <https://doi.org/10.1002/hup.1181> (2011).
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