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RESEARCH ARTICLE

HEMATOLOGICAL TOXICITY OF PSYCHOTROPIC MEDICATIONS: A CASE REPORT

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Abstract

Hematological toxicity can be clinically important during psychotropic treatment. We present the case of a 40-year-old Guinean man with schizoaffective disorder who developed neutropenia and leukopenia after starting chlorpromazine (300 mg/day), and a second neutropenic episode under carbamazepine (800 mg/day). He had never been treated with antipsychotics before. Then a first hematological abnormality appeared ten days after initiating chlorpromazine, and the second episode occurred three weeks after introducing carbamazepine. In these situations, cessation of the suspected drug led to rapid normalization of hematological values.These events were reported to the pharmacovigila nce center, and these medications were formally contraindicated for our patient. Chlorpromazine and mood stabilizers like carbamazepine are known causes of leukopenia and agranulocytosis, in this case , ethnic neutropenia was initially considered but the clear temporal association between drug exposure and hematological abnormalities supported a diagnosis of drug-induced neutropenia.This case illustrates the importance of systematic blood count monitoring when initiating psychotropic drugs known to cause hematologic adverse effects.

Introduction:-

Several psychotropic medications can cause hematological adverse effects, especiallydue to bone marrow suppression or immune-mediated mechanisms. Clozapine is the best-known example of these hematological effectshowever ,there is other antipsychotics, particularly phenothiazines, may also cause neutropenia or agranulocytosis (1).Data from the AMSP European pharmacovigilance system(Arzneimittelsicherheit in der Psychiatrie) program revealed various cytopenia among more than 120,000 psychiatric inpatients for showing the need for routine blood monitoring (1).Carbamazepine is generally used as a mood stabilizer,ithas also been associated with several blood adverse effectslike leukopenia, anemia, thrombocytopenia, and agranulocytosis (2,3).
The objective of this report is to illustrate the clinical and therapeutic challenges encountered in managing hematological effects induced by chlorpromazine and carbamazepine, and to document the importance of biological monitoring to ensure optimal patient care.

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Case Report:-

A 40-year-old Guinean man with schizoaffective disorder was admitted in our hospital due a symptomatic reactivation of his mental disorder. He had never treated with antipsychotics before. On admission, the initial psychiatric evaluation revealed a manic syndrome accompanied by delusional features and insomnia. His only medical history was chronic tobacco use.We started for him a treatment combining risperidone (2 mg with gradual dose escalation), chlorpromazine (300 mg/day), and sodium valproate (500 mg/day) and then baseline blood tests demonstrated mild leukopenia and neutropenia which were confirmed on repeat testing. Chlorpromazine was therefore stopped and replaced with lorazepam (5 mg/day) then four days later, the complete hematological evaluation normalized.sodium valproate was replaced with carbamazepine, titrated up to 800 mg/day, because of limited clinical improvement, while quetiapine (300 mg/day) and risperidone (8 mg/day) werecontinued, and three weeks later, hematological evaluation revealed a new neutropenic episode, which led to immediate discontinuation of carbamazepine ,reduction of Quetiapine to 150 mg/day, and the rest of treatment was continued. After one week, the patient's blood values had returned to normal.The clinical evolution of the patient's leukopenia and neutrophil counts in response to successive psychotropic treatments is summarized in Figure 1.These hematological reactions were reported to the pharmacovigilance center, and chlorpromazine and carbamazepine were officially contraindicated for our patient , then due to the limited clinical improvement,we started a low-dose of olanzapine (5 mg/day) with a strict hematological monitoring.

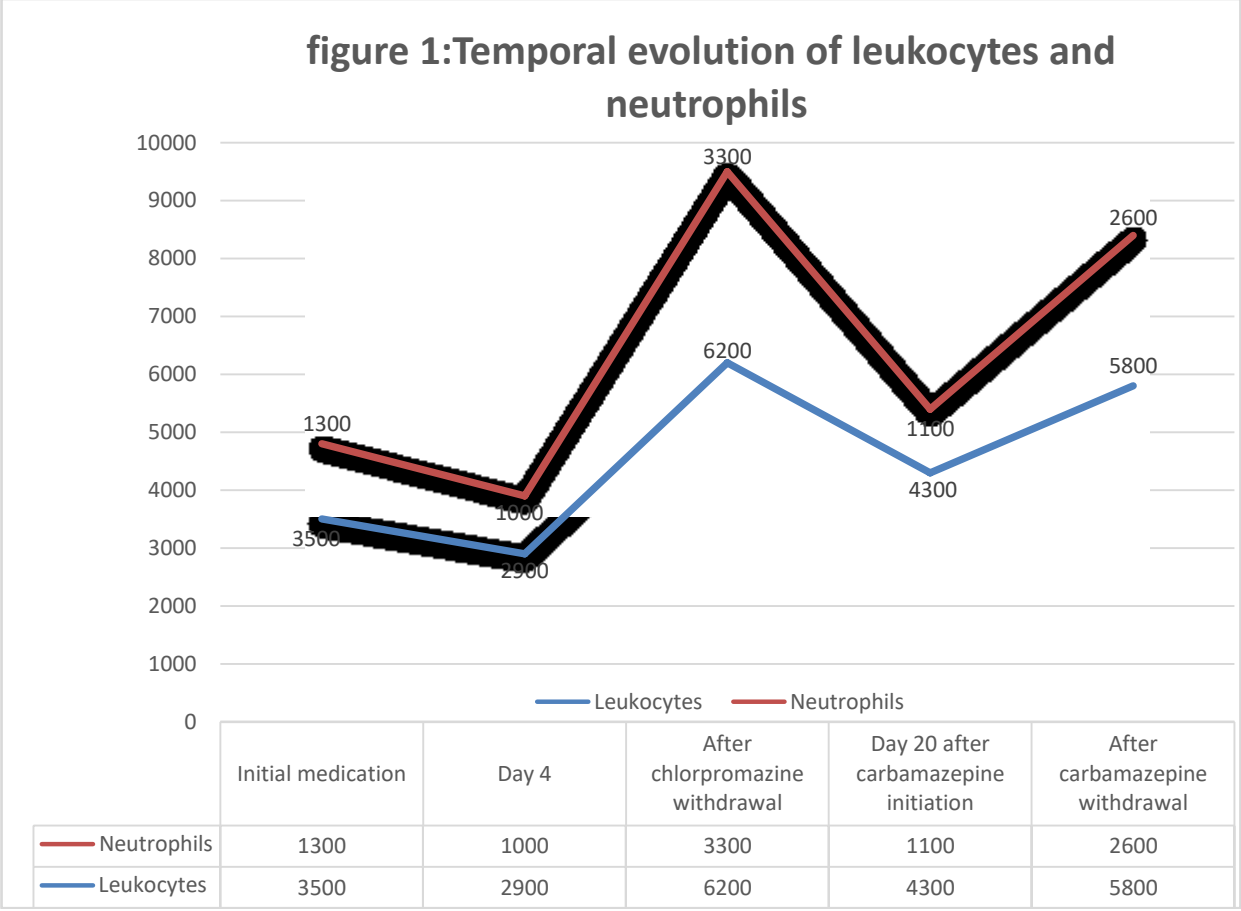

Table 1. Chronology of administered psychotropic medications and related treatment modifications.

Medication	Dose	Reason for change or discontinuation
Chlorpromazine	300 mg/day	Stopped due to neutropenia

Valproate	500 mg/day	Replaced due to limited effect
Risperidone	2→8 mg/day	Continued
Lorazepam	5 mg/day	Substituted for chlorpromazine
Carbamazepine	Up to 800 mg/day	Stopped due to neutropenia
Quetiapine	300→150 mg/day	Dose reduced after neutropenia
Olanzapine	5 mg/day	Started due to limited response and stopped risperidone

Discussion:-

Agranulocytosis is a rare but potentially serious complication, with an incidence of roughly 6–8 cases per million individuals every year, and medications account for most cases (2).In this case, the initial leukopenia could have been related to benign ethnic neutropenia, which is more frequent in people of African origin (3), but the clear normalization of blood values after discontinuation of the suspected drugs confirmed this hypothesis (3).Chlorpromazine-induced neutropenia is consistent with the historical association between phenothiazines and bone marrow suppression. Leukopenia occurs in approximately 0.8% of patients, and agranulocytosis has been reported in 0.05%, especially in the first three months of treatment (3).Other phenothiazinesuch as thioridazine, perphenazine, prochlorperazine, and trifluoperazine have also been associated with cases of agranulocytosis, similarly, rare cases of this hematological adverse effects have been reported with butyrophenones, including haloperidol(4).

Carbamazepinehas been linked to hematological abnormalities, the combined incidence of thrombocytopenia, agranulocytosis, and aplastic anemia ranges from 1% to 2% (3,5). A pharmaco-epidemiological study from McLean Hospital involving 977 patients reported leukopenia in 2.1% of treated individuals, with most cases occurring in the early weeks of treatment. And recovery is usually rapid approximately 6 days after the drug is stopped (3).These observations raise questions about the underlying mechanisms, in the literature the hematological toxicity of carbamazepine may result from inhibition of colony-stimulating factors in the bone marrow ;an effect potentially reduced by lithium and from its direct toxic action on bone marrow progenitorscells , similar to other psychotropic (4,5).A study evaluated the risk of blood dyscrasias with psychotropic medication clozapine (0.18%) and carbamazepine (0.14%) were the most commonly associated with white blood cell abnormalities (5) ,similarly mirtazapine may cause bone marrow suppression via immune-mediated mechanismsleading to cytopenia (4).
Although carbamazepine is the second most common psychotropic agent associated with drug-induced agranulocytosis, unlike clozapine, no strict hematological monitoring guidelines have been established for its use (5).

Some literature suggests that carbamazepine should be discontinued if leukocyte count drops below 3000/mm^3, the absolute neutrophil count falls below 1500/mm^3, or platelet levels decrease to under 100,000/mm(5) and patients with low leukocyte or neutrophil counts before starting treatment are reported to be at increased risk of carbamazepine-induced leukopenia or neutropenia (6).A review from Sedky and Lippmann reported hematological toxicities across multiple psychotropic classes, including neutropenia, leukopenia, and agranulocytosis (4); phenothiazines may cause leukopenia and agranulocytosis(4) also, atypical agents especially clozapine remains the most frequently associated with severe neutropenia, while olanzapine, quetiapine, and risperidone have also been implicated. Mood stabilizers cause different hematological effects ; lithium tends to produce leukocytosis, whereas carbamazepine is implicated for inducing leukopenia, agranulocytosis, or thrombocytopenia. Valproate is mainly associated with thrombocytopenia, with leukopenia representinga less common (4).Within antidepressants agents, including sertraline, have rarely been associated to agranulocytosis. Tricyclics have also been related with this risk, also trazodone has been reported to cause leukopenia or anemia in some cases (4).

To prevent serious complications, patients should be informed about early signs of blood dyscrasias. These include fever, sore throat, skin rash, and unexplained bruising. (5)Early detection is important.Although hematological side effects remain rare, their severity necessitates justifies rigorous clinical vigilance. For this reason, several authors have proposedpatient education and routine hematological monitoring prescribing psychotropic medications with known blood-related adverse effects. The most intensive monitoring should be reserved for high-risk individuals, especially during the first three months (5,6).Inconclusion,careful clinical and hematologic monitoring is crucial to detect and manage adverse effect of psychotropic medication.

Key Points:
-Carbamazepine and chlorpromazine may cause hematologic toxicity.
-Blood monitoring is essential during the first 3 months of treatment by carbamazepine.
-Clinical vigilance and patient education are vital for early detection of adverse effects.

Conclusion:-

The treatment approach of patients treated with antipsychotics or mood stabilizers must include individualized strategies and systematic hematological monitoring to identify the adverse effects and prevent a severe complication. Every clinician should be vigilant, especially during the first weeks of treatment with agents known for their potential of hematologictoxicity.This case highlights the importance of early and rigorous monitoring blood when using hematologically risky psychotropics like carbamazepine and phenothiazines.

Conflicts of Interest:-
The authors declare no conflicts of interest.

Authors' Contributions:-
All authors approved the final version.

Patient Consent:-
informed consent was obtained from the patient for publication.

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