Chlorpromazine-Induced Anemia in Schizophrenia Patient: A Case-Report

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Abstract. Introduction: Chlorpromazine is a typical class of antipsychotics used in Indonesia for psychotic diseases. At the Ghrasia mental hospital in Yogyakarta, chlorpromazine is given to patients with manic-type schizophrenia. The side effects of chlorpromazine include extrapyramidal, agranulocytosis, leukocytosis, and hemolytic anemia. Anemia is one of the rare side effects of chlorpromazine. **Case**: We report a case of a 57-year-old male who was referred to Ghrasia Hospital for a second hospitalization on 19 December 2019. At the first hospitalization, the patient was diagnosed with undifferentiated schizophrenia. The patient prescribes risperidone, clozapine, and trihexyphenidyl for therapy. The patient was diagnosed with manic-type schizoaffective disorder in the second hospitalization. Currently, prescribed therapies are risperidone, chlorpromazine, trihexyphenidyl, and diazepam. The patient then developed anemia the day after with Hb of 11.5g/dL (14–18g/dL). The next day patient was recommended for a hematocrit examination. The result was hematocrit of 37% (38,8–50%). The physicians then stopped the administration of chlorpromazine on day two. The patient was treated with tablets containing iron fumarate 300 mg, magnesium sulfate 0.4 mg, copper sulfate 0.4 mg, vitamin C 100 mg, folic acid 2 mg, vitamin B12 15 mcg, and intrinsic factor 25 mg. Chlorpromazine was readministered on 30 December 2019 (day 12th) with an initial dose of 100 mg and a subsequent 25 mg. The physicians prescribe an iron-containing multivitamin tablet. From the analysis results using the Naranjo algorithm, a score of 7 was obtained, which means that chlorpromazine was probable to cause anemia. **Conclusion**: In this case, chlorpromazine probably caused anemia. The patient was still given chlorpromazine ten days later, so monitoring the complete blood count was necessary.

Keywords: Chlorpromazine · Drug-induced anemia · Typical antipsychotic · Side effect

1 Introduction

Chlorpromazine is a typical antipsychotic. Despite being a first-class antipsychotic, chlorpromazine is still the treatment of choice for schizophrenia. Until now, chlorpromazine is still a gold therapy, especially to bridge the use of typical and atypical

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antipsychotics [1, 2]. The mechanism of chlorpromazine in psychosis is known because of the ability of chlorpromazine to affect brain cells, thought to act on dopamine receptors. However, chlorpromazine is not cell-specific, so it causes many side effects. Side effects include dry mouth, blurred vision, urinary retention, restlessness, tremor, facial stiffness, stumbling gait, and repetitive movements of the face and body that are difficult to reverse [3].

One of the side effects that have been reported is anemia. Anemia caused by chlorpromazine is rare. Several incidents have been reported to have occurred in the 70s and 80s [4–6]. Some antipsychotics do have a hematological effect. The effect of antipsychotics on the blood system is estimated through 2 effective mechanisms, non-immune and immune. Some occurrences of hematological effects caused by antipsychotics can be resolved by discontinuation of antipsychotics. Identifying the cause of the hematological abnormality needs to be adequately done to ascertain whether the anomaly is due to antipsychotics or other reasons [7, 8].

2 Case

We present a case of a 57year old male patient that was administered for a second hospitalization. The patient was hospitalized for the first time in February 2019 with a diagnosis of undifferentiated schizophrenia. The therapy given was risperidone, clozapine, and trihexyphenidyl. The patient was hospitalized for 23 days and was declared to be improving. The patient was brought back to the hospital on 19 December 2019 because he started talking to himself and disturbing others, such as stealing and throwing stones. The doctor's diagnosis for this patient was schizoaffective disorder. The doctor prescribed risperidone, chlorpromazine, trihexyphenidyl, and diazepam therapy. The hemoglobin of this patient was 13 g/dL. One day after drug administration, laboratory results found the patient's hemoglobin was 11.5 g/dL with a hematocrit of 37%. The doctor then stopped the chlorpromazine. After chlorpromazine was discontinued, the patient had no explanation for anemia. But no laboratory result was seen in the medical record to support the finding. The patient was given a tablet containing iron fumarate 300 mg, magnesium sulfate 0.4 mg, copper sulfate 0.4 mg, vitamin C 100 mg, folic acid 2 mg, vitamin B12 15 mcg, and intrinsic factor 25 mg. On 23 December 2019, the patient became unstable, did not sleep at night, and was pacing. The patient rested well the next day but did not want to take medicine. On 28 December, the patient wanted to retake the drug. After taking medication, the patient becomes more controlled and can communicate well. Finally, the patient was allowed to go home on 30 December. The doctor prescribed chlorpromazine again using the initial dose of 100mg/day; then, the maintenance dose was 25 mg/day. The patient becomes an outpatient. Physicians recommend monitoring Hb levels and kidney function.

3 Discussion

Several cases of side effects of anemia on the use of chlorpromazine have been reported. The first reports came from Cooperberg & Eidlow in 1956. Subsequent case reports appeared in 1977. The 1956 case was the case of a patient with anxiety neurosis treated with chlorpromazine 150 mg/day. The patient had jaundice and anemia. The hemoglobin was 14,3 g% on admission and dropped to 10,9 g% within ten days. Anemia that occurs was thought to be because chlorpromazine has a structure containing benzene with a combination of nitrogen, NH, or NH2 ring, which is hematotoxicity. In 1977, two cases of a report on anemia caused by chlorpromazine were due to drug-induced oxidants. In the first case, the hemoglobin was 11 g/dL on admission and dropped to 8,8 g/dL on day eight. In the second case report, the hemoglobin was 11,9 g/dL and fell to 9,5 mg/dL after the 17th day of treatment. The mechanism of hemolysis in the two cases reported was not related to the immune system. Red cell pyknocytosis and Heinz bodies observed in case 2 suggest a direct 'toxic' effect, possibly oxidative, on red blood cells. In 1971, Pisciotta and Milwaukee reviewed the possible mechanism to explain chlorpromazine causes anemia. According to both, chlorpromazine is a drug that causes disturbances in the hematological system. Chlorpromazine affects proliferating cells directly and retards growth and development in several experimental models. Most case reports regarding the effect of chlorpromazine on hematology are cases of agranulocytosis [4–6].

In our case, the patient was anemic one day after giving Chlorpromazine 25 mg/day (Hb 13 g/dL fell to 11,5 g/dL). This condition requires looking at other factors that cause anemia; moreover, our data from medical records is only Hb and hematocrit data. This patient's risk factors for anemia in this patient are age over 55 years and chronic psychiatric conditions [9, 10]. The doctor then recommends monitoring after chlorpromazine is prescribed again because this patient has become an outpatient.

Therefore, causality analysis is essential. We performed the analysis using the Naranjo algorithm and the Liverpool algorithm. Based on the analysis, Naranjo scored 7, meaning chlorpromazine could probably cause anemia. This score is because the doctor had stopped prescribing chlorpromazine and the patient's condition improved. Liverpool algorithm was used and also concluded that chlorpromazine probably caused anemia. The analysis results can be seen in Table 1 and Fig. 1.

4 Conclusion

Chlorpromazine probably caused anemia in this case and treated with a tablet containing iron fumarate 300 mg, magnesium sulfate 0.4 mg, copper sulfate 0.4 mg, vitamin C 100 mg, folic acid 2 mg, vitamin B12 15 mcg, intrinsic factor 25 mg.

Table 1. Causality assessment using Naranjo [11].

No	Question	Yes	No	Don't know	Score
1	Are there previous conclusive reports on this reaction?	1	0	0	1
2	Did the adverse event appear after the suspected drug was administered?	2	−1	0	2
3	Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	1	0	0	1
4	Did the adverse reaction reappear when the drug was readministered?	2	−1	0	0
5	Are there alternative causes (other than the drug) that could have caused the reaction on their own?	−1	2	0	2
6	Did the reaction reappear when a placebo was given?	−1	1	0	0
7	Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	1	0	0	0
8	Was the reaction more severe when the dose was increased,or less severe when thedose was decreased?	1	0	0	0
9	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	1	0	0	1
10	Was the adverse event confirmed by any objective evidence?	1	0	0	0
	Total				**7**

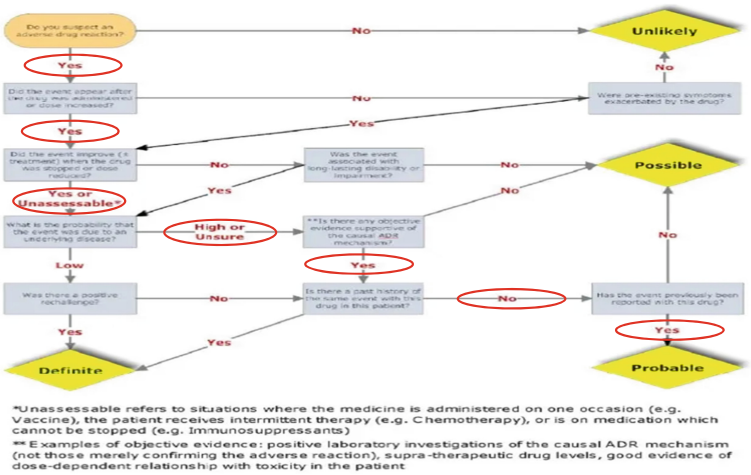

Fig. 1. Causality assessment using liverpool algorithm [12].

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