Case report of eosinophilia induced by quetiapine

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Summary: An increase in the concentration of eosinophils in blood may lead to endocarditis, myocarditis, and pericarditis. When the absolute eosinophil count increases beyond 1.5 x 10⁹/L, myocardial damage and even death can occur. This case report describes a 47-year-old male with an alcohol-induced psychotic disorder who developed eosinophilia 4 weeks after starting treatment with quetiapine 50-200 mg/d. His maximum recorded absolute eosinophil count was 7.63 x 10⁹/L (normal range <0.5 x 10⁹/L), but the level returned to normal over a 4-week period after stopping quetiapine and no myocardial damage was observed. This patient’s dramatic eosinophilia did not have any associated clinical symptoms; it was only identified as part of a routine blood test a few weeks after starting quetiapine. This is a reminder that all clinicians who treat patients with antipsychotic medications must be vigilant about the occurrence of such rare but life-threatening adverse events.

Keywords: eosinophilia; quetiapine; case report; China

1. Case history

A 47 year-old male migrant worker with a high school education and a 20-year history of heavy alcohol intake was involuntarily admitted to our hospital by his family members on 9 September 2014. The family reported that he had started drinking heavily at the age of 23. He initially drank 100 to 150 ml of high alcohol-content spirits per day, but this subsequently increased to 400 to 500 ml per day. Whenever he briefly stopped drinking, he would feel upset and irritable, cry, and have poor sleep; these symptoms disappeared after he re-started drinking. Starting one year prior to admission he experienced frequent episodes of uncontrolled anger during which he smashed household goods. Then one month prior to admission he developed several new symptoms: he constantly felt nervous and his hands trembled; he exhibited strange behavior such as gesticulating, counting with his fingers, and pointing with his hands; he reported strange experiences, saying things like “I see something on the wall; I can see my dead relatives at home”; and he became suspicious of others, stating that he suspected his wife was having an affair, that people around him were talking about him, and that the eyes of passers-by held special meaning for him.

His medical history was unremarkable. He had no history of allergies, serious infectious diseases, hypertension, diabetes, tumors, or any other illness. He had never been seriously injured, had never had a head injury, and had never had an operation. He did not smoke and had not used other psychoactive drugs. The family reported that formerly his personality was introverted and gentle; there was no history of other psychiatric symptoms or of suicidal ideation or behavior. There was no family history of mental illness or substance abuse.

On admission his blood pressure was 130/80 mmHg, his temperature was 36.1°C, his pulse was 80 beats/min, and his respiratory rate was 19/min. His cardiopulmonary and abdominal exams were normal; his peripheral muscle strength was rated normal at 5+; his muscular tension was slightly elevated; and his tendon reflexes were normal. A resting tremor was evident when he raised both hands. His mental status examination showed clear consciousness and correct orientation, but he had hallucinations and delusions of jealousy and reference. His intelligence, memory, and understanding were normal, but he was irritable, excitable, impulsive, and had a short attention span. He had no insight about his illness.

The admission work-up included the following examinations: (a) a chest X-ray, which was normal; (b) an electrocardiogram, which showed sinus tachycardia (maximum heart rate 136/min) and ST-T changes; (c) an electroencephalogram and cerebral topographic graph, which showed dominance of a low- and medium-amplitude a-wave rhythm, increased slow
waves, and no response to light stimulation; (d) an abdominal ultrasound, which showed liver fibrosis; (e) a transcranial doppler test, which showed reduced blood supply to the right middle cerebral artery; (f) a computerized tomography (CT), which showed multiple small low-density areas in the basal ganglia suggestive of small lacunar lesions; (g) a urine drug test, which found no evidence of morphine, methamphetamine, ketamine, ecstasy, or cannabis use; and (h) routine urinalysis and stool examinations, which were normal. Results of the admission blood work are shown in Tables 1 and 2; routine blood tests indicated a low hemoglobin, and biochemical tests indicated a slightly increased fasting glucose, a low serum potassium level, and grossly elevated liver and myocardial enzymes.

The admission diagnoses were alcohol-induced psychotic disorder, alcohol-induced liver cirrhosis, and hypokalemia. The patient was tapered from alcohol with diazepam (5mg/d), provided psychological counseling and health education about alcohol abuse, and treated with oral potassium, vitamins, and ‘Gan Su’ capsules (a frequently administered Traditional Chinese Medicine to promote the functioning of the liver and the spleen). Quetiapine was given to treat the hallucinations and delusions: 25 mg at noon and 25 mg in the evening on the first day of admission, 50 mg at noon and 50 mg in the evening of the second day, and 100 mg at noon and 100 mg in the evening from the third day forward. Seven days after admission the hallucinations and the delusions had significantly diminished; after 4 weeks of treatment the hallucinations and delusions had disappeared completely and insight was restored.

Routine blood tests at the end of the 4th week of treatment showed that the elevated myocardial enzymes at admission had returned to normal limits and that the elevated liver enzymes had improved significantly (Table 2). However, as shown in Table 1, there was an unexpected dramatic increase in the absolute eosinophil count (to 7.63 x 10^9/L) and a corresponding increase in the overall white blood count (to 13.93 x 10^9/L). At this time the patient’s vital signs were normal, he had no physical complaints, there were no signs of infection, and his electrocardiogram showed a sinus rhythm with a heart rate of 78/min. Concerned about the possibility that this was a quetiapine-induced eosinophilia, we reduced the dosage of quetiapine from 200 mg/day to 50 mg/day (administered in the evening) while keeping the other treatments unchanged.

At the end of the 6th week the eosinophil count and white blood count had decreased substantially, but they remained quite high, so the quetiapine was stopped completely. At this time the blood chemistry results assessing liver function, cardiac function, renal function, potassium, and fasting glucose had all returned to normal and a repeat electrocardiogram and encephalogram were also normal. The eosinophil and white blood counts continued to fall over subsequent weeks and returned to normal at the end of the 9th week of admission (3 weeks after stopping quetiapine completely), so the patient was discharged. A repeat blood count at 4 weeks after discharge (that is, 13 weeks after starting quetiapine and 7 weeks after stopping quetiapine) showed normal eosinophil and white blood counts.

2. Discussion

Eosinophils are a type of white blood cell produced by stem cells in the bone marrow that account for 0.5 to 5.0% of all white blood cells in healthy individuals.[1] Eosinophilia, the term for high blood levels of eosinophils, is usually triggered by allergens, infection or inflammation, asthma, parasites, tumors, or myocarditis. However, eosinophilia is also seen in

| Table 1. Routine blood tests during the course of treatmentab |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | white blood cells | neutrophils     | lymphocytes     | eosinophils     | hemoglobin      | platelets       |
| normal range    | 3.50-9.50 x 10^9/L | 1.80-6.30 x 10^9/L | 1.10-3.20 x 10^9/L | 0.02-0.52 x 10^9/L | 130-175g/dL | 100-300 x 10^9/L |
| on admission    | 4.98 x 10^9/L    | 3.53 x 10^9/L    | 1.07 x 10^9/L    | 0.12 x 10^9/L    | 129g/L         | 143 x 10^9/L   |
| 4th week        | 13.93 x 10^9/L   | 3.53 x 10^9/L    | 1.90 x 10^9/L    | 7.63 x 10^9/L    | 127g/L         | 140 x 10^9/L   |
| 5th week        | 12.49 x 10^9/L   | 2.91 x 10^9/L    | 1.91 x 10^9/L    | 7.43 x 10^9/L    | 123g/L         | 152 x 10^9/L   |
| 6th week        | 9.02 x 10^9/L    | 3.06 x 10^9/L    | 1.86 x 10^9/L    | 3.85 x 10^9/L    | 130g/L         | 186 x 10^9/L   |
| 7th week        | 6.02 x 10^9/L    | 2.58 x 10^9/L    | 1.46 x 10^9/L    | 1.65 x 10^9/L    | 136g/L         | 192 x 10^9/L   |
| 8th week        | 7.33 x 10^9/L    | 3.47 x 10^9/L    | 2.82 x 10^9/L    | 0.79 x 10^9/L    | 148g/L         | 184 x 10^9/L   |
| 9th week        | 6.55 x 10^9/L    | 3.80 x 10^9/L    | 2.10 x 10^9/L    | 0.54 x 10^9/L    | 148g/L         | 167 x 10^9/L   |
| 13th week       | 5.73 x 10^9/L    | 3.19 x 10^9/L    | 1.85 x 10^9/L    | 0.35 x 10^9/L    | 149g/L         | 133 x 10^9/L   |

ab quetiapine treatment was 50 mg/d on the first day of admission, 100 mg/d on the second day of admission, 200 mg/d from the third day of admission to the end of the 4th week of admission, reduced to 50 mg/d in the 5th week, and stopped completely at the end of the 6th week.

a figures in bold are outside of the normal range used by the laboratory at Chongqing Mental Health Center
allergic drug reactions, including allergic reactions to clozapine and other antipsychotic medications. In this current case, there was no history of contact with an allergen, no evidence of parasites, and no evidence of cancer that could explain the eosinophilia. On admission the patient had evidence of alcohol-related liver disease and cardiomyopathy – conditions that may be related to eosinophilia – but there was a normal white blood count. After 4 weeks of detoxification, supportive treatment, and the administration of quetiapine to treat alcohol-related hallucinations and delusions, his cardiac enzymes had returned to normal and his liver enzymes had improved, but the eosinophil count had increased dramatically. In the absence of any new signs of infection, we determined that the dramatic eosinophilia was an allergic response to the quetiapine, a conclusion that was supported by the gradual return to a normal white blood count after discontinuing the quetiapine.

Reports suggest that eosinophilia induced by antipsychotic medication usually occurs between 7 and 42 days after starting the medicine, with the average time of onset being 21 days after starting the medication. In the current case, eosinophilia occurred on the 30th day after starting quetiapine, so it is consistent with the literature. Clozapine is the most commonly reported eosinophilia-inducing antipsychotic medication, but it has also been reported in patients using other atypical antipsychotic medications such as risperidone and olanzapine. Eosinophilia induced by antipsychotic medication is presumed to be an allergic response of the immune system; blockage of H1 neurotransmitter receptors results in an increase in histamine and, thus, an increase of eosinophils in the peripheral blood. Among commonly used antipsychotic medications, clozapine has the strongest blocking effect on H1 receptors; this may explain the relatively higher incidence of eosinophilia among patients receiving clozapine than among patients using other types of antipsychotic medications. Like clozapine, quetiapine is also a receptor antagonist with a similar, though weaker, blocking effect on histamine H1 receptors, so it is not surprising that it could also induce eosinophilia. Interestingly, Zipris and colleagues reported that in some cases where it is essential to continue treatment with antipsychotic medications, clozapine can be replaced by quetiapine when the former induces eosinophilia.

Eosinophilia, particularly when it persists, is not a benign condition. Chronic eosinophilia with absolute eosinophilia counts above 1.5 x 10^9/L (i.e., hypereosinophilic syndrome) can lead to endocarditis, myocarditis, myocardial damage, and even death. In this case the dramatic increase in eosinophils with quetiapine treatment was not associated with any physical symptoms; it was only recognized after the results of a routine blood test indicated the very high level of eosinophils. This afforded us the opportunity of stopping the antipsychotic medication and, thus, preventing the organ damage that often accompanies chronic eosinophilia. Moreover, unlike patients with chronic psychotic conditions, this patient had a time-limited substance-induced psychosis, so we did not have the problem of trying to change the antipsychotic

### Table 2. Liver function tests, myocardial enzymes, renal function tests, potassium level, and blood glucose on admission and after 4 weeks and 6 weeks of admission

| Test                          | Normal Range | on Admission | End of 4th Week | End of 6th Week |
|-------------------------------|--------------|--------------|-----------------|-----------------|
| **Liver enzymes**             |              |              |                 |                 |
| gamma glutamyl transferase (GGT) | 10-60 U/L   | 734.3 U/L    | 92.9 U/L       | 53.1 U/L        |
| alanine aminotransferase (ALT) | 9-50 U/L    | 63.3 U/L     | 35 U/L         | 33 U/L          |
| albumin (ALB)                 | 40-55 g/L    | 41 g/L       | 40 g/L         | 40.6 g/L        |
| direct bilirubin (DBIL)       | 0-6.8 µmol/L | 8.1 µmol/L   | 2.8 µmol/L     | 4.2 µmol/L      |
| **Myocardial enzymes**        |              |              |                 |                 |
| aspartate aminotransferase (AST) | 15-40 U/L  | 149.6 U/L    | 38.9 U/L       | 40 U/L          |
| creatine kinase (CK)          | 38-174 U/L  | 405.0 U/L    | 36 U/L         | 52 U/L          |
| creatine kinase MB (CK-MB)    | <24 U/L     | 24 U/L       | 12 U/L         | 8 U/L           |
| α-hydroxybutyrate dehydrogenase (α-HBDH) | 72-182 U/L | 233 U/L      | 116 U/L        | 122 U/L         |
| **Renal function tests**      |              |              |                 |                 |
| urea                          | 2.9-8.2 mmol/L | 2.93 mmol/L | 4.37 mmol/L    | 3.41 mmol/L     |
| creatinine                    | 44-97 µmol/L | 51 µmol/L    | 63 µmol/L      | 61 µmol/L       |
| **Potassium**                 |              |              |                 |                 |
| 3.5-5.3 mmol/L               | 3.47 mmol/L  | 4.28 mmol/L  | 4.45 mmol/L    |                 |
| **Fasting glucose**           |              |              |                 |                 |
| 3.89-6.11 mmol/L             | 6.31 mmol/L  | 4.29 mmol/L  | 4.81 mmol/L    |                 |

* Figures in bold are outside of the normal range.
treatment to another medication that did not induce eosinophilia.

Eosinophilia is a relatively rare allergic reaction to antipsychothic medication that can have serious physical effects if it is not recognized and managed early. All clinicians who prescribe antipsychotic medications need to routinely conduct blood count tests to screen for this condition, particularly when starting a new antipsychotic medication.

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Informed consent
The patient described in this report provided written informed consent to publish this case report.

Authors’ contributions
LC collected the data and wrote the first draft. PT collected and summarized relevant references. XT revised the manuscript. All authors approved the final manuscript.

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