Neutropenia Following Electroconvulsive Therapy: A Case Report

Electroconvulsive therapy (ECT) has been a long-established and effective treatment modality of psychiatric diseases since the 1930s. Common posttreatment adverse effects, including headache, gastrointestinal distress, and musculoskeletal problems, have been well-discussed [1]. But our patient developed the extremely rare condition of neutropenia following ECT.

Case Report

A 39-year-old woman Taiwanese patient was admitted to the psychiatric ward for scheduled ECT for treatment-resistant bipolar II disorder with recurrent suicidal behavior. The patient had been hospitalized many times for bipolar II disorder since her early 20s. But she had never previously received ECT treatment. She had been on vortioxetine, trazodone, triazolam, flurazepam, quetiapine, ziprasidone, lorazepam, and clonazepam for at least one year and reported good adherence. She had no past medical history of neutropenia, seizures, or brain trauma. She reported no family history of psychiatric disease.

On admission, the patient's white blood cell (WBC) count was 4580/μL and her absolute neutrophil count (ANC) was 2600/μL. General laboratory surveys, electrocardiogram, brain computed tomography and chest X-ray were found no contraindications to ECT. Throughout her admission, she continued taking the psychiatric medications listed above. On day two of admission, ECT was initiated at a charge of 1.10 times the seizure threshold. During ECT delivery, she was sedated with 200 mg of intravenous thiamylal, and we induced generalized seizures lasting 20–40 seconds. ECT was executed another three times in the following seven days based on standard ECT protocol. The patient experienced nausea, vomiting, dizziness, and episodic retrograde amnesia after each of these four times but recovered after supportive care.

But on day 10, after the fifth ECT therapy was delivered, the patient developed neutropenic fever, with a high fever up to 40°C, WBC of 670/μL and ANC of 410/μL. She also presented herself with hemodynamic changes of hypotension and tachycardia, dizziness, nausea, mild dyspnea, and general arthralgia. C-reactive protein was 0.70 mg/dl and procalcitonin level was 1.68 Mg/dL. No infection source was found despite having comprehensive surveys. She had received piperacillin-tazobactam for 12 days. Granulocyte colony-stimulating factor (G-CSF) filgrastim 300 μg was given once. The numbers of WBC and ANC were recovered the following day, on day 11, to 15,650/μL and 13,930/μL, respectively, and gradually returned to her baseline on day 15. The finding of her peripheral blood smear on day 21 was unremarkable. She received the remaining seven ECT treatments starting from day 23, and no subsequent neutropenia, fever, or hemodynamic instability occurred. On day 38, her mood was no longer depressed, and her hemogram was normal. Therefore, she was discharged after completing a course of 12 ECTs.

Comment

The diagnostic approach to neutropenia includes surveying for Duffy-null-associated neutrophil count (DNAC), infections, cytotoxic or immunosuppressive medications, hematological malignancy, and autoimmune conditions. This patient is a Taiwanese woman, and DNAC is atypical in this population. Considering her high procalcitonin level of 1.68 ng/mL, viral infections were less likely. Sepsis-induced neutropenia related to certain bacterial pathogens, including salmonellosis, shigellosis, and tuberculosis, are possible. But they are unlikely causes of neutropenia in our case because there were no corresponding clinical symptoms and she had negative finding in blood cultures. In addition, her HIV screening was negative. She also had no history of blood dyscrasias, hematological malignancy, or autoimmune diseases.

As for medications, anesthetics are known to play a rôle in blood dyscrasias. Reversible leukopenia after prolonged thiopental infusion in patients with refractory intracranial hypertension has been described. However, almost all the patients in these studies received a loading bolus of thiopental followed by continuous infusion and achieved coma-inducing barbiturate plasma concentration [2, 3]. In contrast, our patient only received a 200 mg bolus of thiamylal per an ECT. She had also been taking quetiapine and ziprasidone. These two regimens are also associated with leukopenia, but this mostly presented between 20 and 90 days after drug initiation [4-7], while our patient had been taking these medications for over one year and had not previously developed leukopenia. Having excluded other common causes of neutropenia, there is a high suspicion of ECT leading to neutropenia in this patient. Fortunately, our case continued the remaining seven ECTs without recurrence of neutropenia, perhaps because she had already received G-CSF, which still has a protective effect.

The association between ECT and neutropenia is understudied. To the best of our knowledge, only one previous study with three patients was reported chronic and persistent ECT-associated neutropenia. All of the patients experienced low neutrophil counts ranging from 1100 to 1500 /μL during the ECT courses and the neutrophil counts began to rise only after the discontinuation of ECT. All three patients were female,

just as our patient and two of the three patients had previous histories of drug-induced neutropenia [8].

Mechanisms underlying ECT-associated neutropenia may involve the release of inflammatory mediators and increased stress on the pituitary-adrenal axis. A review article on molecular biomarkers of ECT in patients with major depressive disorder suggested an acute inflammatory response following ECT, with increased plasma levels of interleukin 1 and 6. These cytokines exerted an immediate action on the up-regulation of the hypothalamic-pituitary-adrenal axis, leading to the excretion of adrenocorticotropic hormones and the consequent elevation of cortisol and epinephrine [9]. This mechanism coincides with a "marginated phenomenon" hypothesis proposed by a preliminary study. In this study, the percentage of polymorphs was dropped soon after ECT and then began to rise to the pre-ECT baseline level after 2 h. The reduced percentage of polymorphs can be explained by a stress-induced low-dose epinephrine release, leading to vasodilation with an exodus of the marginated population [10].

In summary, post-ECT neutropenia is a serious adverse effect that warrants more attention from clinicians. Although neutropenia following ECT has rarely been reported, and more research is required to establish a causal relationship, our findings and past case reports support that it is a complication clinicians need to be aware of, especially considering the serious consequences of this clinical condition. We suggest hematological surveys in patients following ECT to detect neutropenia, and survey and treatment of infection should patients subsequently develop a neutropenic fever (This case report was approved by the institutional review board for publication at Taipei Veterans General Hospital [protocol number = 2022-10-002CC and date of approval = October 18, 2022], with the requirement of obtaining a written informed consent from the patient).

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Conflicts of Interest

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