Case Report

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Clozapine-Induced Acute Interstitial Nephritis: A Case Report

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ABSTRACT

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Introduction

Clozapine is nowadays the most effective treatment for refractory schizophrenia. It has proven to be superior in terms of efficacy compared with 1st generation antipsychotic and other 2nd generation antipsychotic [1]. Moreover, it does not cause extrapyramidal side effects nor tardive dyskinesia and its impact on prolactin level is negligible [2]. This atypical antipsychotic is also used to treat other conditions such as schizoaffective disorder. However, clozapine is underprescribed, due to potentially life-threatening side effects such as neutropenia, agranulocytosis, myocarditis and myocardiopathy and other additional problems including weight gain, orthostatic hypotension, constipation and sialorrhea [3].

Among uncommon adverse reaction, acute interstitial nephritis (AIN) should also be taken into account. Very few cases have been described and the underlying mechanism is still unclear [4-6]. It could be related to a nonspecific inflammatory response, which is often observed in the early weeks of treatment with clozapine. This drug indeed exerts some immunomodulatory effects that have clinical implications [7]. We report a case of a patient who experienced acute renal failure twice. Both episodes followed initiation of treatment with clozapine.

Case Presentation

A 54-year-old woman with a known history of schizoaffective disorder was admitted to our hospital in November 2020. She was diagnosed with schizoaffective disorder in 1988, at the age of 22. She had been treated with different antipsychotics during the past 30 years (quetiapine, haloperidol, chlorpromazine, levomepromazine, clotiapine, lurasidone) and she has a history of repeated and prolonged hospitalizations. The patient is also affected by hypothyroidism treated with levothyroxine, type 2 diabetes in insulin therapy and gallstones. Furthermore it is reported in her clinical history an episode of acute renal failure in December 2017, probably due to carbolithium, and an episode of acute pancreatitis in October 2019. In November 2020 a new hospitalization was necessary because of the relapse of the psychotic symptoms with agitation and suspiciousness in spite of the antipsychotic therapy with lurasidone and clotiapine. In consideration of the antipsychotic resistance, the therapy was switched to clozapine on 17th November, commenced at 25 mg/day up to 50 mg/day. On 19th November there was the onset of fever, partially responsive to paracetamol. In the following days the progressive increase of fever up to 39.5°C and the onset of desaturation occurred: oxygen therapy and an empirical antibiotic therapy were necessary. Eventually, all the causes of an infective disorder were excluded.

On 23rd November we observed a PLT reduction (96.000/uL), so clozapine was suspended. From 5th December we observed a progressive increase of the creatinine value, from 2,95 mg/dl up to 3,90 mg/dl. Her previous creatinine value was 0,85 mg/dl on 19th November 2020. The main causes of acute renal failure were

excluded. The abdomen CT showed kidneys of normal size and morphology, without parenchymal bulks, stones or distension of the urinary tract, with a minimal edema of the perirenal fat on the left . The patient was evaluated by a nephrologist, who suggested to move her in the Unit of Nephrology to find the cause of the renal failure and to treat it. The cause was not established, but the renal function values gradually normalized. On 22nd December the patient was re-admitted to the Unit of Psychiatry. The patient's clinical and psychiatric conditions gradually improved, so she was dismissed on 28th January.

On 2nd February a new episode of psychomotor agitation and relapse of psychotic symptoms occurred and the hospitalization was necessary. The patient was suspicious and contentious and she had persecutory delusions. On 11th February, considering the patient's psychopatological conditions, clozapine was reintroduced. Again fever occurred after a single tablet of clozapine, followed by renal failure (06/02: creatinine value 1,19 mg/dl; 13/02 creatinine value 2,14 mg/dl, progressively increased up to 3,65 mg/dl in few days).

Evaluated by the nephrologist, a steroid therapy was prescribed and, on 16th February, the patient was moved again to the Unit of Nephrology. The diagnosis of iatrogenic interstitial nephritis caused by Clozapine was confirmed as diagnosis by exclusion and, after the stabilization of the renal function, the patient was re-transferred to the Unit of Psychiatry. The therapy was switched to brexpiprazole: the renal function progressively improved up to 1,15 mg/dl and the patient's clinical conditions slowly improved, until the dismissing on 14th April. The case was followed up for 6 months and we observed a gradual recovery of the renal function: actually the creatinine value is 0,99 mg/dl.

Discussion

To the best of our knowledge, this is the first case of clozapine-induced nephrotoxicity ever described in Italy. Acute interstitial nephritis is an immune-mediated condition featuring tubulo-interstitial inflammation and oedema. It can be infective, autoimmune or even idiopathic but more commonly it is induced by various drugs, such as NSAIDs and antibiotics like aminoglycosides and vancomycin [8-9]. The diagnosis of drug-induced acute interstitial nephritis is based on its clinical and laboratory manifestations, characteristic morphologic features of the kidney on biopsy, and the identification of a causative agent. In practice, satisfying all three criteria is fraught with limitations, particularly in patients exposed to several potentially incriminated drugs [10]. In this regard, a possible limitation of our study is the lack of renal biopsy.

Our results are in agreement with previous evidence, reporting the importance of renal function monitoring prior to clozapine initiation and during titration. Moreover, it is fundamental when clozapine is prescribed together with other potentially nephrotoxic medications. Further, is it of great interest to remember that early recognition of this phenomenon, also involving nephrologists, leads to prompt intervention and adequate treatment.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Consent

Written informed consent was obtained from the patient for publication of this paper.

References

1. Leucht S, Komossa K, Rummel-Kluge C, Corves C, Hunger H, et al. (2009) A meta-analysis of head-to-head comparisons of second-generation antipsychotics in the treatment of schizophrenia. Am J Psychiatry 166(2): 152-163.
2. Miller D (2000) Review and management of clozapine side effects. The Journal of clinical psychiatry 61(8): 14-7.
3. Iqbal MM, Rahman A, Husain Z, Mahmud SZ, Ryan WG, et al. (2003) Clozapine: a clinical review of adverse effects and management. Ann Clin Psychiatry 15(1): 33-48.
4. Lally J, Al Kalbani H, Krivoy A, Murphy KC, Gaughran F, et al. (2018) Hepatitis, Interstitial Nephritis, and Pancreatitis in Association With Clozapine Treatment: A Systematic Review of Case Series and Reports. J Clin Psychopharmacol 38(5): 520-527.
5. Elias TJ, Bannister KM, Clarkson AR, Faull D, Faull RJ (1999) Clozapine-induced acute interstitial nephritis. Lancet 354(9185): 1180-1181.
6. Chan SY, Cheung CY, Chan PT, Chau KF (2015) Clozapine-induced acute interstitial nephritis. Hong Kong Med J 21(4): 372-374.
7. Røge R, Møller BK, Andersen CR, Correll CU, Nielsen J (2012) Immunomodulatory effects of clozapine and their clinical implications: what have we learned so far? Schizophr Res. 140(1-3): 204-213.
8. Praga M, González E (2010) Acute interstitial nephritis. Kidney Int 77(11): 956-961.
9. Perazella MA, Markowitz GS (2010) Drug-induced acute interstitial nephritis. Nat Rev Nephrol 6(8): 461-470.
10. Raghavan R, Shawar S (2017) Mechanisms of Drug-Induced Interstitial Nephritis. Adv Chronic Kidney Dis 24(2): 64-71.

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