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Cardiogenic shock and multiorgan dysfunction secondary to clozapine☆

Shock cardiogénico y disfunción multiorgánica secundaria a clozapina

Clozapine was the first antipsychotic drug to be defined as atypical due to its particular properties and is currently known for its use in refractory psychosis. It produces minimum extra pyramidal effects but is not, however, exempt from several side effects such agranulocytosis and myocarditis.

We present the case of a 62-year-old woman, an ex-smoker, obese and with a psychiatric history of schizoaffective disorder. She was hospitalized due to psychotic imbalance. She began new treatment there with clozapine, taking a dose of 900 mg/day from week three. Her stay in hospital was complicated by a right distal tibioperoneal fracture which was surgically resolved.

She was admitted to the Intensive Care Unit due to respiratory failure, hypoxemia and a fever of 39 °C, with no response to pipercillin-tazobactam and ciprofloxacin initiated whilst there. Chest x-ray showed signs of heart failure without clear pneumonic infiltration. A transthoracic echocardiography was requested (TTE), with biventricular dysfunction being highlighted as the only pathology.

After 24 h stay in the ICU the patient's condition worsened which led to obligatory endotracheal intubation and a situation of cardiogenic shock. The TTE showed progressive impairment of the ejection fraction of left ventricle at 10%, together with generalised hypokinesia.

Surveillance of the different aetiologies leading to the development of cardiogenic shock was performed, including pulmonary thromboembolism, ischaemic cardiopathy, valvulopathies, sepsis-associated myocardial depression... they were all ruled out, with focus placed on myocarditis as the principal trigger factor.

Myocarditis is an acute inflammatory process the aetiology of which is linked to an infectious process (the most common viral cause) and/or an immune response (drugs, toxic agents). Clinical presentation is highly variable, from mild forms, even asymptomatic to more serious forms which involve heart failure, cardiogenic shock and death. Diagnosis is based on analytical tests (CK, troponine) and on imaging (electrocardiograms, TTE) although none is specific. During recent years magnetic resonance has become a non invasive technique of choice (84% sensitivity and 74% specificity), although the gold standard still continues to be heart biopsy.

The patient began with cardiogenic shock symptoms 3 weeks after initiating treatment with clozapine. Since other aetiological causes, such as viral and toxic were ruled out, the most plausible diagnostic impression was pharmacological.

Myocarditis from clozapine was described by Killian in 1999.[1] Genetic, environmental and/or clinical factors (new treatment, fast establishment of complete dose of medication or concomitant use with other drugs) may mean that the levels reached in the blood would be different. In approximately 80% of cases symptomatology appears during the first month of treatment.[2] Early suspicion and detention is vital for a fast management by associated morbimortality. The clinical characteristics were started between the second and third week of treatment and these include fever, dyspnoea, eosinophilia, increased LDH, CPK and troponin, together with non specific changes in the ECG, none of which were pathognomonic of the symptoms.

At present, benefits from the use of clozapine in patients with resistant schizophrenia are unquestionable but side effects must be known to optimise usage and to make it safe. Clozapine necessarily requires standardised haematological controls to avoid agranulocitosis, but there are other side effects such as myocarditis which could also have fatal

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consequences but which do not require any special control today.

Myocarditis does not present with patognomonic symptoms, as it is quite nonspecific, the use of biomarkers and of TTE as screening is under dispute.[3–5] Several authors agree in controlling with TTE in patients with cardiopathies and with risk factors such as diabetes, a tobacco habit or advanced age.

As a result of this clinical case we believe there is s need to carry out TTE prior to treatment initiation with clozapine for a safer drug usage. In Australia, given the high recorded rate (1/100 inhab.),[6] this is routinely performed prior to the initiation of the drug and after 6 and 12 months.[7] Other authors[5,8,9] conclude that there are no specific recommendations or consensus when monitoring for myocarditis and cardiopathies.

We may therefore conclude that the use of TTE is disputed because the real incidence of myocarditis in the Spanish population is unknown, and its use is recommended when there is high clinical or analytical suspicion in patients with cardiovascular risk factors or previous heart diseases.

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