Exacerbation of a chronic pancreatitis in a multiple sclerosis patient treated with mitoxantrone

U. Kallweit[a, b], M. Harzheim[a], D. Pöhlau[a]

[a] Multiple Sclerosis Centre, Department of Neurology, Kamillus-Klinik, Asbach (D)
[b] Department of Neurology, Universitätsspital Zürich

Summary

Kallweit U, Harzheim M, Pöhlau D. Exacerbation of a chronic pancreatitis in a multiple sclerosis patient treated with mitoxantrone. Schweiz Arch Neurol Psychiatr. 2007;158:334–5.

Acute exacerbation of a chronic pancreatitis occurred twice in a multiple sclerosis patient due to mitoxantrone treatment. Mitoxantrone should not be given in patients suffering from chronic pancreatitis because of the potential induction and fatal outcome of an acute pancreatitis.

Keywords: multiple sclerosis; mitoxantrone; chronic pancreatitis; escalating therapy

Background

Mitoxantrone (Mx), an immunosuppressive agent from the antracenedione family that was initially used as an antineoplastic agent, has been shown to be an effective treatment in relapsing-remitting (RR), progressive relapsing (PR) and secondary progressive (SP) multiple sclerosis (MS) patients [1]. Mitoxantrone has anti-inflammatory activity and reduces relapse rate, progression of disability and the occurrence of gadolinium-enhancing T_1 lesions as well as new lesions on T_2-weighted cranial MRI [2].

The most common short-term side effects include nausea, vomiting, amenorrhoea, alopecia and increased susceptibility to infection. Other, especially long-term side effects can be serious and/or potentially life threatening, such as infertility, cardiac toxicity and myelosuppression. In post-marketing data collection a therapy-related acute leukaemia (TRAL) has been reported in MS patients and cancer patients treated with mitoxantrone [3]. The risk of leukaemia following treatment with mitoxantrone is increased for patients who have been treated with other types of anthracycline chemotherapies before. No reports on side effects of mitoxantrone treatment referring to chronic or acute pancreatitis in MS patients are reported in the literature.

Correspondence:
Dieter Pöhlau, MD
Multiple Sclerosis Centre
Department of Neurology
Kamillus-Klinik
Hospitalstrasse 6
D-53567 Asbach
e-mail: DieterPoehlau@aol.com

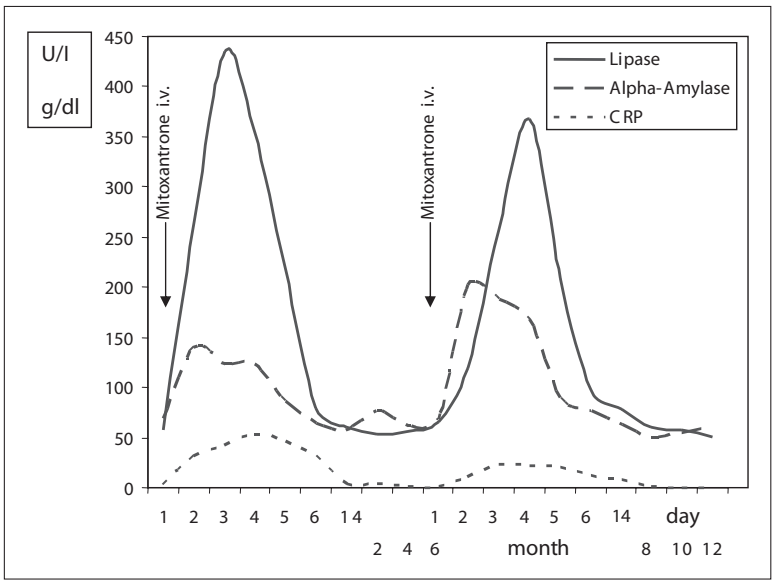
Case report

To our best knowledge we present the first case of an acute pancreatitis in a secondary progressive MS patient treated with mitoxantrone.

A 48-year-old female with a 20-year history of multiple sclerosis, relapsing-remitting in the beginning and secondary progressive course for the past 11 years with three relapses in the last two years, presented with a further deterioration of the disease. General weakness, inability to walk more than 100 metres without unilateral assistance and bladder incontinence occurred subacutely within three weeks. Tetraparesis of 3/5 and severe spasticity in the legs were observed. The expanded disability status scale (EDSS) was six when admitted to our hospital and had deteriorated with one point within the last 12 months. The brain MRI at admission to the hospital revealed multiple disseminated supra- and infratentorial white-matter lesions in T_2-weighted images, but no gadolinium-enhancing lesions in T_1-weighted images. She was also suffering from chronic biliary pancreatitis for 12 years. At this time she did not receive any immunomodulatory treatment. Due to her deterioration we decided to administer mitoxantrone. The patient received the recommended dose of 9 mg/m^2 intravenously. Prior to the immunosuppressive treatment clinical and laboratory findings including serum levels of amylase, lipase and bilirubin were normal (see fig. 1).

One day after administration of mitoxantrone the patient complained of diffuse abdominal pain. Clinical, laboratory and sonographic findings led

Figure 1 Course of lipase, α-amylase and C-reactive protein under intravenous mitoxantrone treatment.



to the diagnosis of acute pancreatitis. Blood tests showed increased alpha-amylase up to 140 U/l, lipase up to 435 U/l and C-reactive protein (54 g/dl). After conservative treatment clinical and laboratory findings were normalised.

Initially we interpreted this complication as a coincidence with the administration of mitoxantrone. In the further course the clinical condition of the patient deteriorated due to multiple sclerosis. Six months later we discussed the risk of a second induction of pancreatitis if mitoxantrone would be given again but the patient gave her informed consent to continue mitoxantrone treatment.

Clinical, laboratory and sonographic examinations prior to treatment showed normal results and the patient received 9 mg/m^2 mitoxantrone intravenously again. About 12 hours after the infusion she reported severe abdominal pain. Laboratory findings again indicated acute pancreatitis (see fig. 1). Conservative treatment led to a fast and complete remission of the acute pancreatitis. Further mitoxantrone treatment was stopped. Six months later amylase and lipase were normal and there were no clinical signs of pancreatitis.

Discussion and conclusion

Acute exacerbation of chronic pancreatitis is a severe and potentially fatal complication. Mitoxantrone causes topoisomerase II inhibition which impairs DNA repair and exerts cytocidal effects and intercalates into DNA and RNA which possibly leads to a direct damage. Clearance of mitoxantrone is through biliary excretion, thus drug levels may increase in patients with biliary dysfunction [4]. In the literature there are only few reports on mitoxantrone treatment and pancreatitis. Civalleri et al. [5] report in a small study about chemoembolisation treatment of hepatocellular carcinoma with mitoxantrone. In this study 3% of the patients developed acute pancreatitis.

In our case the pathogenesis of the repetitive acute exacerbation due to mitoxantrone treatment remains unclear. The patient had no previous history of spontaneous occurrence of acute exacerbation of her chronic biliary pancreatitis and no other cause than the application of mitoxantrone was found.

There are no reports on pancreatitis due to mitoxantrone treatment in MS patients. This case report once more indicates that mitoxantrone treatment requires careful monitoring. Mitoxantrone should not be given in MS patients suffering from chronic pancreatitis because of the potential induction and fatal outcome of an acute pancreatitis.

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