Melanotan II: a possible cause of renal infarction: review of the literature and case report

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Abstract

Renal infarction is an uncommon condition resulting from an acute disruption of renal blood flow and it is potentially life-threatening disease. The cause and outcome of renal infarction is not well established and is frequently misdiagnosed or diagnosed late. Melanotan II is a non-selective melanocortin-receptor agonist and its effect on humans is an increasing of skin pigmentation, producing of spontaneous penile erection and sexual stimulation. Melanotan II inducing rhabdomyolysis and renal failure have been described previously. We present a review of Melanotan II and the possible effects of this drug on the kidneys by including a case of a renal infarction most likely attributed to Melanotan II. In the mechanism of renal injury with Melanotan II, thrombotic pharmacological influence and possible direct toxic effect on renal parenchyma must be considered.

Keywords Renal infarction · Melanotan II · Kidney injury · Barbie drug

Introduction

The most common etiological and pathogenic causes of renal infarction include hypercoagulative states, cardioembolic disease, renal artery injury and idiopathic causes [1–4]. Here, we present a review of Melanotan II and the possible effects of this drug on the kidneys by including a case of a renal infarction most likely attributed to Melanotan II. Melanotan II also called “Barbie drug” [5] is mostly purchased illegally via Internet and its effect on humans is an increasing of skin pigmentation, producing of spontaneous penile erection and sexual stimulation [6]. Melanotan II is a non-selective melanocortin-receptor agonist and by this mechanism an alpha-melanocyte stimulating hormone [7].

Case report

A previously healthy 45-year-old Caucasian male was admitted to the emergency room with right-sided abdominal pain, vomiting and increased frequency of voiding with no fever after a vacation in Southern Europe. Past medical history included gastroesophageal reflux which was symptom controlled with 20 mg Esomeprazole and a perforated appendectomy in childhood. He admitted to moderate alcohol consumption which increased during vacations. The condition is initially interpreted as renal colic with an ultrasound of the abdomen being reported as normal. The patient was discharged home with a single dose of Diclofenac (Non-Steroidal Anti-Inflammatory Drug); however, he returned the next day with increasing pain and a new fever (38.5 °C). A computer tomography (CT) scan was performed which revealed a right sided renal infarction affecting approximately 50% of the kidney with marked decrease contrast enhancement and a minimal surrounding edema (Fig. 1). The renal arteries were considered to have a normal appearance and there was no evidence of renal stones or hydronephrosis. The pancreas, spleen, liver, adrenals and left kidney were of a normal appearance. Cholelithiasis without signs of cholecystitis was also noted. The patient is subsequently admitted to the

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Fig. 1 CT-scan of the right sided renal infarction

department of nephrology for further investigation. It was noted that the patient had an intense tanning of his skin and an additional investigation revealed that he had administered a total of 27 mg of Melanotan II subcutaneously within the last 6 months for the purpose of increasing his suntan. The patient self administered Melanotan II 10 mg per injection twice within a period of 6 months and 7 mg 3 weeks before the admission to the hospital. He obtained the medication via a web shop. A sample of the drug was provided by the patient for additional investigation at a forensic center and the presence of Melanotan II was confirmed and no other pharmacologic substances were revealed in the specimen. The patient underwent investigations of the cardiovascular system including a CT-scan of the aorta, echocardiography to rule out arrhythmias and a heart ultrasound. No sources for embolus were found. Although previously normotensive, his blood pressure was recorded at 165/95 mmHg. Abnormal hematological investigations included C-reactive protein 152 mg/L, serum creatinine 102 $\mu\text{mol/L}$, blood glucose 6 mmol/L, aspartate aminotransferase (AST) 1.96 $\mu\text{kat/L}$, alanine aminotransferase (ALT) 1.23 $\mu\text{kat/L}$. Coagulative studies (international normalized ratio and activate partial thromboplastin time) and further coagulation analyses after a complementary contact with coagulation expertize revealed no abnormalities. Urinalysis by dipstick showed hemoglobin 1+. No signs for dehydration or rhabdomyolysis were found in this patient. Repeat AST and ALT were taken 2 weeks later and were reported to be within normal range. After 2 months an Iohexol-clearance-measurement was performed and showed a slightly reduced renal function (81 mL/min per 1.73 m²). The patient's hypertension persisted and an Angiotensin-converting-enzyme (ACE)-inhibitor was introduced in the treatment. During the investigations the patient was treated with low molecular

heparin, which was then stopped when all investigations were completed.

Discussion

The literature of pharmacologically induced renal infarctions is sparse [8]. Melanotan II inducing rhabdomyolysis and renal failure has been described previously where the systemic toxicity of Melanotan II with sympathomimetic excess causing renal dysfunction [6]. In the mechanism of renal injury, thrombotic pharmacological influences must be considered [8]. Melanotan II has five melanocortin receptor subtypes (MC-R) which reveal different biological functions based on localization [9]. In the skin and adrenal cortex, MC1-R and MC2-R are melanocytic and adrenocortical receptors [10–13]. Melanotan II stimulate the melanocytes in the skin (by stimulation of MC1-R) to increase the production of eumelanin which result in sunless tanning of the skin [5, 14, 15]. MC3-R is mostly expressed in the brain and digestive tract [13, 16], MC4-R is located in the nervous system [12, 13] and MC5-R is found in endo and exocrine glands [10, 11, 13]. The reported adverse effects relate to the location of the receptors are thus wide ranging including nausea, abdominal pain, anxiety, flushing, dizziness, headaches, appetite suppression, stomach pain, cramping, severe constipation, spontaneous penile erections, muscle pain and induction of cancer in the skin. The effects of Melanotan II can result in an overstimulation of the sympathetic nervous system [6]. We believe that this vasoconstriction could possibly explain the mechanism of the renal infarction in our case report. Additional pharmacological considerations as a potential drug in the mechanism of renal injury include the proton pump inhibitor Esomeprazole [17] and Diclofenac, however, this was administered after the onset of the symptoms, but may have affected the renal function in the later phase of this case [18–20]. Complementary contact has been taken with the Swedish Poisons Information Centre and since January 1, 2008 until May 20, 2019, in total 215 cases (93% in adults) of given information to Melanotan II side effects were registered. No case of Melanotan II induced renal infarction has been reported to the Swedish Poisons Information Centre. To our knowledge, this case is the first that described the possible direct toxic effects of Melanotan II on renal parenchyma.

A limitation of this case report was that no examination of blood concentration of Melanotan II or its metabolites was performed at admission. It is known that this drug can be detected by liquid chromatography and mass spectrometry. However, there exists no routine for this in our country.

In conclusion, Melanotan II inducing rhabdomyolysis and renal failure has been described previously. In the mechanism of renal injury with Melanotan II, thrombotic

pharmacological influence and possible direct toxic effect on renal parenchyma must be considered.

Compliance with ethical standards

Conflict of interest The authors have declared that no conflict of interest exists.

Human and animal rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent Informed consent was obtained from all individual participants included in the study.

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