CLINICAL CASE

Desmopressin-related myocardial infarction in a patient with Wegener’s granulomatosis: A case report and review of the literature

Infarctus du myocarde secondaire à l’injection de desmopressine chez une patiente suivie pour une granulomatose de Wegener : à propos d’un cas et revue de la littérature

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Summary Desmopressin is a synthetic vasopressin analog that increases the plasma levels of coagulation factor VIII, von Willebrand factor, and tissue plasminogen activator. This hemostatic agent, which can be administered either parenterally or intranasally, has been approved for use in the prevention and treatment of hemorrhagic events during surgery in patients with hemophilia A, in cases of prolonged idiopathic bleeding, and for complications associated with platelet antiaggregant therapy. This case report describes cardiac toxicity associated with desmopressin administered according to the recommended indications: a 55-year-old woman diagnosed with Wegener’s granulomatosis (WG) was treated with desmopressin to improve hemostasis and shorten bleeding time before a planned renal biopsy. She developed cardiac arrest within 60 minutes of the desmopressin injection. Cardiopulmonary resuscitation began immediately and was successful, although the patient subsequently died of WG-associated complications. Desmopressin administration thus appears, in some cases, to be associated with a high risk of thrombotic events, possibly by stimulating the rapid release of endothelial factors such as an abnormal multimeric form of von Willebrand factor, which might cause platelet aggregation. Clinicians should be aware of the possible occurrence of this little-known but potentially serious cardiac event associated with desmopressin administration and be prepared to initiate cardiopulmonary resuscitation immediately if needed.

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Résumé La desmopressine (DDAVP) est un analogue synthétique de la vasopressine qui augmente les taux plasmatiques de facteur VIII, du facteur von Willebrand et de l’activateur tissulaire du plasminogène. Cet agent hémostatique, disponible par voie parentérale, est utilisé également dans la prévention et le traitement des accidents hémorragiques chez les patients atteints d’hémophile A, lorsque le temps de saignement est allongé sans étiologie retrouvée et en cas de complications dues aux traitements anti-agrégants. Nous rapportons un cas de toxicité cardiaque après injection de DDAVP. Une femme de 55 ans, suivie pour une granulomatose de Wegener, a été traitée par DDAVP avant la réalisation d’une biopsie rénale afin d’améliorer son temps de saignement. Elle présentait un arrêt cardiaque dans les 60 minutes suivant l’injection de DDAVP. La réanimation cardiorespiratoire était immédiatement commencée et permettait une évolution favorable. La perfusion de DDAVP semble présenter un risque élevé d’événements thrombotiques. Le mécanisme proposé est que le DDAVP stimulerait la libération rapide de facteurs favorisant l’agrégation plaquettaire. Les cliniciens doivent être conscients du risque, peu connu, mais potentiellement grave, d’effet indésirable cardiaque après injection de DDAVP et être prêts à engager une réanimation cardiorespiratoire si nécessaire.

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Introduction

Wegener’s granulomatosis (WG) is a systemic disease of unknown origin that is characterized by vasculitis of the small- and medium-sized blood vessels [1]. During its course, 38% to 100% of patients develop nephropathy [2]. This case report describes a patient with WG and nephropathy who was treated with desmopressin before a planned renal biopsy to improve hemostasis and shorten a prolonged bleeding time [3]. A myocardial infarction occurred 60 minutes after the desmopressin injection. We therefore examined the relation between these events.

Case report

A 55-year-old woman presented with paralysis of the right leg, which had begun 15 days earlier. She had also experienced loss of vision over the previous 72 hours. Clinical examination revealed a tongue ulcer, anterior ischemic optic neuropathy, and sensorimotor neuropathy, while laboratory tests showed an inflammatory syndrome with CRP (375 mg/m²; two injections). These successive treatments failed to halt the disease progression, and the patient died 3 months later from infectious complications involving the gastrointestinal tract.

Discussion

This case report describes a potential case of desmopressin-related myocardial infarction in a patient with WG.

Desmopressin is a synthetic vasopressin analog that increases plasma levels of coagulation factor VIII, von Willebrand factor, and tissue plasminogen activator. This hemostatic agent, which can be administered either parenterally or intranasally, has been approved for use in the prevention and treatment of hemorrhagic events during surgery in patients with hemophilia A and factor VIII coagulant levels greater than 5% in von Willebrand’s disease (Type I), in cases of prolonged idiopathic bleeding, and in the event of complications due to platelet antiaggregant treatment. It is also indicated for the treatment of central diabetes insipidus and in the evaluation of glomerular filtration rates. Desmopressin can also be administered to patients with bleeding disorders before a kidney needle biopsy. The optimal means of evaluating and dealing with hemorrhagic risk...
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are extremely controversial issues. In vitro bleeding time, in particular, is often measured before kidney biopsies, despite the lack of any reported correlation between this test and bleeding complications [4–6]. Certain authors recommend the routine administration of desmopressin or estrogens in cases of severe renal failure, without any bleeding test [7]. However, because hemostatic disorders in patients with renal failure are multifactorial in origin, the role of the various agents that are likely to be effective in treating them needs to be more clearly determined in the specific context of renal biopsies.

The literature includes several similar instances of coronary thrombotic events associated with desmopressin (Table 1). In most of these reports, desmopressin was administered to patients with hemophilia A or von Willebrand’s disease [9–12]. However, a myocardial infarction has also been reported in a 59-year-old woman who received, as in our case, desmopressin via injection (0.4 μg/kg) before a renal biopsy because of a prolonged bleeding time [13]. In that case, the woman, who was simultaneously being treated by chemotherapy for breast cancer, presented with deterioration of renal function and thrombocytopenia. Chemotherapy was temporarily suspended and a renal biopsy scheduled. Thirty minutes after the desmopressin infusion, the patient experienced an acute inferior myocardial infarction, rapidly complicated by nodal bradycardia. She recovered from this event, and the subsequent renal biopsy showed features consistent with hemolytic uremic syndrome. Another case has been reported in a 47-year-old man with risk factors for coronary artery disease. He received desmopressin 0.3 μg/kg before giving blood (his 89th donation with desmopressin). He had a myocardial infarction 30 minutes after injection [14].

Desmopressin can also cause non-coronary arterial thrombotic events, as two case reports have described [15,16]. A 27-year-old woman who had been receiving oral desmopressin 200 μg once daily for 3 months for nocturnal enuresis came to the emergency department for severe abdominal pain and was found to have had a massive abdominal thrombosis (celiac trunk, hepatic artery, lineal artery, left gastric artery and superior mesenteric artery). Laboratory results showed a dramatic elevation of factor VIII activity, vWF Ag, and vWF-Rico activity [15]. The second case involved an elderly man with evidence of atherosclerosis and uremic bleeding diathesis who developed two strokes immediately after an infusion of desmopressin [16].

In our case, the initial presentation with WG implies a potential risk of developing cardiac symptoms [17]. The duration of time between parenteral administration of desmopressin and cardiac ischemia seems consistent with the drug’s reported kinetics: its maximal effect on coagulation factor VIII levels and on von Willebrand factor is known to be reached within 2 hours. Thus, as indicated by the official French assessment procedure for adverse drug reactions, the role of desmopressin as a triggering factor of myocardial infarction is a plausible hypothesis in this case [18].

Levi et al. conducted a meta-analysis of pharmacological strategies to decrease excessive blood loss during cardiac surgery. Five of the seven trials in which desmopressin was administered and the incidence of myocardial infarction was recorded showed a trend towards a higher incidence of perioperative myocardial infarction in the desmopressin-treated patients. Desmopressin treatment in this meta-analysis was associated with an almost 2.4-fold increased risk of perioperative myocardial infarction compared with placebo (2.39; 95% confidence interval: 1.02—5.60) [19]. The authors concluded that the risk of myocardial infarction must be considered before ordering desmopressin infusions.

In view of its established pharmacological properties, the underlying mechanism might be that desmopressin stimulates the rapid release of endothelial factors including both normal and abnormally large multimeric forms of von Willebrand factor, which could cause platelet aggregation [20]. Moreover, vascular susceptibility, including the vasculitis in our patient and the thrombotic microangiopathy in the woman with breast cancer described above [13], might be a precipitating factor.

Table 1  Myocardial infarction associated with desmopressin (DDAVP) administration, as reported in the literature.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Medical history</th>
<th>Time between DDAVP infusion and myocardial infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>McLeod, Lancet 1990 [14]</td>
<td>47</td>
<td>Male</td>
<td>Cardiovascular risk</td>
<td>30 min</td>
</tr>
</tbody>
</table>

Conclusion

Because desmopressin administration seems to be associated with an infrequent but nevertheless significant risk of...
thrombotic events, it is important for doctors to understand that this drug should be used with the utmost caution and under close surveillance in both young and older patients, especially those with preexisting thrombotic risk factors or acute vasculopathies such as WG.

**Disclosure of interest**

The authors declare that they have no conflicts of interest concerning this article.

**References**


