

Letter to the Editor

Anaphylactoid reaction from amifostine

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We read with great interest the report of Lin et al. [1], as they describe a 35-year-old patient experiencing a serious clinical episode shortly after treatment with amifostine. It underlines and continues the debate on the safety of this drug.

Amifostine is often used in radiation- and chemotherapy to protect normal tissues against the harmful side effects. The efficacy of the drug's protective properties has been under debate as in some preclinical studies tumour protection was shown by amifostine [2]. To date, some clinical trials have suggested tumour protection, but in a recently published meta-analysis comprising 1451 patients tumour protection by amifostine was not confirmed [3]. Amifostine has potential serious side-effects, like hypotension, nausea, vomiting, and cutaneous reactions. Lin et al. [1] described a 35-year-old woman who had a pulmonary embolism shortly after amifostine administration. Ten days later, radiation therapy and amifostine treatment were resumed, but 20 min after the amifostine administration she reported chest pressure and shortness of breath. Clinically, hypotension, hypoxia and an erythematous rash were found. A myocardial infarction was diagnosed, based on the ECG and elevated cardiac enzymes.

We would like to make some comments on the report and on the authors' conclusions.

We are not convinced that this patient suffered from an anaphylactoid reaction and we feel that this conclusion has to have a more solid base. Indeed, it might be concluded from the rash, the hypoxia and the hypotension that an anaphylactoid reaction was present. However, a rash does not have to point at an allergic reaction per se. In addition, all other symptoms may also be attributed to the cardiac infarction the patient suffered from. Inclusion of an allergological analysis, e.g. increased tryptase levels hours after the acute reaction or demonstration of IgE antibodies by skin testing and/or RAST, would have made the diagnosis of an anaphylactoid reaction more likely.

The authors state '*To our knowledge, this is the first unambiguous account of an anaphylactoid reaction secondary to amifostine used as a radioprotector*' but in the same report the case report of Vardy et al. [4], published in 2002, is cited. That report clearly described an anaphylactoid reaction from amifostine treatment, although no allergological analysis was reported either. Based on this, the statement of the authors that their report is the first unambiguous account of an anaphylactoid reaction after amifostine is not true.

More interesting is the occurrence of myocardial ischemia in the reported case. Just recently, Buentzel et al. [5] reported the data of a randomised placebo-controlled phase II study on the use of intravenous amifostine during chemoradiotherapy for head-and-neck cancer. In addition to the commonly reported toxicity of amifostine, one patient (male, 54 years of age) in the amifostine arm died of an acute anterior-wall myocardial infarction, three days after the last treatment with amifostine. The autopsy revealed generalised arteriosclerosis, moderate stenotic sclerosis of the anterior coronary artery and a fresh thrombus in the lumen. This death was judged as possibly related to amifostine.

Interestingly, both cases of amifostine related cardiac ischemia represent relatively young patients (35 and 54 years old). To our knowledge no systematic reports have been published reporting the incidence of myocardial ischemia during amifostine treatment. We propose a possible mechanism for myocardial ischemia in these patients could be a low flow state due to amifostine induced hypotension, compromising blood flow in stenotic arteries, subsequently leading to ischemia and infarction.

With this in mind two important questions arise. First: did the authors gather information regarding the coronary anatomy of their patient? This would provide valuable additional information regarding the mechanism for the infarction and the effects of amifostine on the coronary circulation. Second, it is important to know whether this patient, and the patient of Buentzel et al. [5], were prehydrated. Prehydration is the major precaution advised by the manufacturer to prevent deep hypotension after amifostine administration (http://www.medimmune.com/pdf/products/ethyol_pi.pdf).

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