Anaphylaxis with midazolam in pediatric hematology-oncology unit: a case report

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Dear Editor,

Four courses of chemotherapy were given to a 17-year-old male patient (body weight 73 kg) who was being followed up with a diagnosis of acute myeloid leukemia in our Pediatric Hematology-Oncology Clinic and bone marrow aspiration and lumbar puncture were performed before each course. Throughout these treatments, sedation was provided with midazolam seven times and bone marrow aspiration and lumbar puncture were performed. The patient had no known history of drug allergy or food allergy. The patient was taken into the intervention room before the fifth course of therapy for ordinary bone marrow aspiration and lumbar puncture. Before the procedure, 5 mg midazolam was administered by the intravenous route for the objective of sedation. In the first minute after the drug was administered, vomiting, dyspnea, and chest pain developed and hypotension (80/40 mm Hg) occurred. A diffuse urticarial rash appeared on the body and edema developed in the face and upper part of the neck. It was thought that an anaphylaxis-like reaction against midazolam had occurred; 0.5 mg adrenaline and 40 mg methylprednisolone were administered intravenously and 100% oxygen was given by mask. Adrenaline and methylprednisolone were administered again because hypotension continued, and 500 mL normal saline was loaded with rapid infusion. After fifteen minutes, the patient's vital values became normal, the interventional procedures were postponed and he was taken to his room.

Midazolam is a short-acting benzodiazepine that can be used for the objective of sedation in different clinical areas (1). It is mostly preferred for minor interventional procedures because it has a short half-life and an antidote (flumazenil). Midazolam can be used by physicians

other than anesthesiologists. Mild sedation with midazolam can be performed even under outpatient conditions before bone marrow aspiration and/or lumbar puncture in pediatric hematology/oncology patients (2). Midazolam may cause severe adverse effects including respiratory depression, laryngospasm and cardiac arrhythmia (3).

Anaphylaxis is a rapidly developing systemic hypersensitivity response and may be life-threatening. Drug-related anaphylaxis may develop with release of granules from mast cells or basophils secondary to immunoglobulin (Ig)E-mediated or non-IgE-mediated processes (4). Anaphylaxis with midazolam is very rare and has been reported in a few case reports. In these reports, anaphylaxis or anaphylaxis-like reaction was observed in adult patients and in operating rooms (1, 3, 5). However, anaphylaxis developed in our pediatric Hematology-Oncology ward in our patient and the symptoms rapidly improved with treatment. The diagnosis of drug-related anaphylaxis is generally made with clinical symptoms and signs (4). In addition, increased triptase levels, which can be measured in two hours after the emergence of the signs and symptoms supports the diagnosis, but we could not get the triptase level studied in our patient in this period (1). Nevertheless, development of signs and symptoms which were specific for anaphylaxis (dyspnea, edema, hypotension, urticaria and vomiting) immediately after midazolam was administered, was compatible with midazolam anaphylaxis. Another interesting characteristic of our patient was the fact that he was the first case of midazolam anaphylaxis reported in the childhood age group. Advanced age is known to be a risk factor in drug-related anaphylaxis and this may explain the rarity of midazolam anaphylaxis in children (4).

Midazolam is a commonly used sedative in Pediatric Hematology-Oncology Clinics. It should be kept in mind that midazolam may lead to anaphylaxis as well as many adverse effects and the necessary drugs and equipment to intervene in anaphylaxis should be available for procedures performed outside operating rooms.

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