Case Report

Anisocoria in liver recipients during the perioperative period: Two case reports

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Summary **Two cases of anisocoria that occurred just after the induction of general anesthesia for living donor liver transplantation are reported. Space-occupying lesions were not observed in brain computed tomography. Mydriasis was temporary in both cases, suggesting that the anisocoria was most likely related to Adie syndrome.**

Keywords: Living-related liver transplant, recipient, anisocoria

1. Introduction

Anisocoria during general anesthesia may indicate a serious neurologic condition. Proper diagnosis of unilateral mydriasis associated with general anesthesia is complicated by decreased responsiveness or unresponsiveness of the patient induced by the anesthetic agents.

Cerebrovascular diseases such as a ruptured aneurysm, cerebral trauma, or a mass lesion should be ruled out. Liver transplant recipients tend to bleed easily due to hepatic dysfunction and coagulation defects and thus have a high risk of brain hemorrhage in the perioperative period (*1*). Many cases also present with an altered state of consciousness due to hyperammonemia.

Treatment with mydriatic medications or eye disorders such as edema or Adie syndrome (*2*) are included in the differential diagnosis (*3*). We report two cases of temporary anisocoria in two liver recipients during the perioperative period.

2. Case reports

2.1. *Case 1*

A 57-year-old female had diabetes for the past 3 years, which was appropriately managed using insulin administration. The patient developed bronchial asthma 9 years ago and has been receiving inhalation treatment. In 1995, the patient developed liver dysfunction and hepatitis C. Interferon was administered for 6 months. The patient developed cirrhosis in 2000, and in 2005 it became difficult to control the ascites. Partial liver transplantation and Hassab's operation were scheduled for decompensated cirrhosis and esophageal varices. The patient's preoperative consciousness level was alert. Anisocoria was not observed in the preoperative examination.

Anesthesia was induced by intravenous administration of 100 μg fentanyl, 10 mg midazolam, and 10 mg vecuronium bromide, while the trachea was intubated *via* the oral route. Anesthesia induction proceeded smoothly. Anesthesia was maintained with air/oxygen/isoflurane; 40% oxygen in air and an end-tidal isoflurane concentration of 1.5 to 3.0 vol%. Fentanyl and vecuronium were added as needed. No significant cyclical fluctuation was observed. After tracheal intubation, pupil diameters of 4 mm on the right and 1 mm on the left were confirmed. The papillary light reflex was slight in both eyes. Considering the possibility of an intracerebral lesion, an urgent head computed tomography (CT) scan was performed under endotracheal intubation, which revealed no abnormal findings. After final evaluation by a neurosurgeon, surgery was continued. There were no changes in the pupil diameters during the surgery and no significant fluctuations in the circulatory dynamics, and thus the patient was returned to the intensive care unit (ICU) postoperatively. The duration of the operation was 15 h and 25 min, and the duration of anesthesia was 18 h and 10 min. A postoperative CT revealed no

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abnormalities and no neurologic abnormalities were observed. After recovery from anesthesia and removal of the endotracheal tube in the ICU, no neurologic abnormalities other than anisocoria were observed. The anisocoria gradually decreased and the pupils became symmetrical within 2 weeks after surgery.

2.2. *Case 2*

A 45-year-old male visited our hospital with a primary complaint of systemic fatigue and was hospitalized with a diagnosis of fulminant hepatic failure. Although his hepatic encephalopathy improved, his total bilirubin remained high. After hospitalization, frequent plasma exchange was required, and an auxiliary partial orthotopic liver transplantation was performed. Anisocoria was not present prior to the induction of anesthesia.

In the operating theater, the patient's level of consciousness was clear. General anesthesia was induced by intravenous administration of 200 μg fentanyl, 200 mg thiopental, 5 mg midazolam, and 10 mg vecuronium bromide, and maintained by air/oxygen/isoflurane. Neither hypoxia, hyperventilation, severe hypotension, nor hypertension were present. After the induction of general anesthesia, anisocoria was observed (pupil diameters of 4 mm on the right and 3 mm on the left). We performed an urgent head CT to check for cerebral lesions, but no organic lesions or neurologic abnormalities were observed. A neurosurgical consultation determined that the operation could continue.

The pupils became symmetrical 11 h after the induction of anesthesia. The duration of the operation was 15 h and 5 min and the duration of anesthesia was 16 h and 50 min. There was nothing specifically notable during surgery. There were no abnormal findings in the postoperative head CT. After recovery from the anesthesia and removal of the endotracheal tube in the ICU, no neurologic abnormalities were observed.

3. Discussion

Anisocoria during general anesthesia has been reported (*4-9*). The causes of anisocoria in these previously reported cases included administration of mydriasis-inducing drugs (peripheral mechanism involving parasympathetic postganglionic fibers) into the ocular or nasal regions (*6-8*) and interventions (*5,9*) in the neck or cranium areas. Kobayashi (*10*) reported a case of anisocoria that occurred in association with a hypertensive episode after anesthetic induction. Adie syndrome was subsequently diagnosed by a positive pilocarpine test.

A relationship between inhalation-induced analgesia and anisocoria has also been reported. Sobel (*11*) described differences in pupil size with an incidence of 0.4% with the use of halothane, 0.8% with cylopropane, and 58% with diethyl ether. For anesthesia with cylopropane and diethyl ether, the elevated levels of catecholamines liberated by these compounds are likely responsible for the pupil dilatation (*12*). The higher incidence of anisocoria with diethyl ether compared to cylopropane is related to the more pronounced parasympathomimetic effect of diethyl ether.

A perfusion disturbance or imbalance in the orbital area may also be related to anisocoria. Rempf (*13*) reported a case in which anisocoria occurred during general anesthesia for renal transplantation. Retinal hypoperfusion detected with cranial and orbital Doppler sonography is a plausible explanation for the anisocoria. Klein (*4*) reported a case of anisocoria with exophthalmus during anesthesia with enflurane. The authors related the symptoms to the position of the head being lowered by 10° and the resulting venous pooling in the orbital area.

In our cases, anisocoria was observed just after the induction of general anesthesia. No space-occupying lesions were observed in the brain CT and the mydriasis was temporary, suggesting that the anisocoria was most likely related to Adie syndrome. The main factors contributing to the manifestation of Adie syndrome may be parasympathetic dominance by anesthetics such as thiopental or isoflurane. Botulism, myasthenia gravis, and dyshidrosis are associated with increased vulnerability of the systemic cholinergic nerves (*14*). Autonomic neuropathies are common in diabetes, and liver diseases and are possibly induced by the autoantibody to autonomic structures. Peripheral somatic neuropathy (93%) and autonomic neuropathy (50%) were common in patients with end stage liver disease (*15*). It is possible that the vecuronium influenced the autonomic tone in our patients (*10*). Adie syndrome should be considered in the differential diagnosis of patients who develop anisocoria in the perioperative setting.

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