Supplement data 1

## Case 1

A 72-year-old-man with diabetes mellitus and systemic hypertension presented with a two-month history of blurred vision in the right eye. The visual acuity was Counting Fingers at 3 feet. The tumor was deeply pigmented, with retinal invasion, orange pigment, and serous retinal detachment. It was located infero-temporally and equatorially and measured 10.9 mm basally, with a thickness of 11.2 mm. (shown in Fig. 1). The patient was advised about the risks and benefits of all the therapeutic options, which included enucleation, iodine plaque brachytherapy and endoresection with adjunctive ruthenium plaque brachytherapy. He declined enucleation, and selected endoresection, confirming acceptance of potential complications of this procedure.

One day before surgery, he had two episodes of generalized tonic-clonic seizure, each lasting about 10 seconds, with both resolving spontaneously without treatment. Intravenous levetiracetam was prescribed by a neurologist (1000 mg loading dose, followed by 500 mg every 12 hours). Systemic evaluation revealed hyponatremia (sodium 122 mmol/L). Electroencephalography and central spinal fluid analysis were normal. The seizures were believed to be caused by hyponatremia caused by hydrochlorothiazide and amiloride, which had been administered for systemic hypertension. The patient did not develop additional episodes of seizure after cessation of these two drugs.

The anesthesiology team visited the patient for preoperative evaluation and preparation. The patient was categorized as NYHA (New York Heart Association Functional Classification) class 2, and ASAPS (American Society of Anesthesia physical status) class 3. According to ASAPS, his estimated mortality risk during general anesthesia was 7.8 - 25.9 %.

General anesthesia was performed as described in Tables 1B and 1C. Tumor endoresection was performed as described in Table 1A. No air was injected into the eye.

Intraoperative monitoring showed a normal level of end-tidal CO2 (ETCO2) (31-34 mm Hg). Nicardipine was used to induce hypotensive anaesthesia at the time of tumor endoresection. The blood pressure was lowered from 160/100 mmHg to 100-120/60-70 mmHg for 30 minutes. There were no intraoperative adverse events other than hyperglycemia, which was normalized with 4 IU of regular insulin. The procedure took 2 hours and 45 minutes. At the end of the operation, breathing was normal after the patient was extubated. No systemic events occurred during the 1-hour period when he was monitored in the PACU. After fully regaining consciousness, the patient was transferred from PACU to the ophthalmic ward.

Four hours and 30 minutes after surgery, while sitting upright and talking to his wife, the patient suddenly developed dyspnea and chest pain. Medical consultations (internal medicine, cardiologist, and cardiothoracic surgery (CVT)) were made. The SpO2 dropped from 100% to 85%, which improved to 94% with an oxygen mask with bag (FiO2 1.0, flow 10 LPM). Twelve-lead electrocardiography revealed a Q wave in lead III without ST-T change. Blood chemistry showed high D-dimer (1,456.0 ng/mIFEU (normal 0-550ng/mIFEU)), with normal Troponin T level. Vital signs monitoring showed blood pressure of 129/69 mm Hg, pulse rate of 90 beats per minute, and respiratory rate of 30 breaths per minute. The initial diagnosis was acute pulmonary embolism, and CT angiography (CTA) was requested. Eight-and-a-half hours after surgery, the patient was admitted to the CT unit. He was sedated with 10 mg of diazepam. His pulse oximetry improved to 97%. During the CTA scan, the patient developed cardiac arrest. Immediate cardiopulmonary resuscitation was initiated. Preliminary CTA scan showed extensive pulmonary air embolism involving right ventricle, central pulmonary arteries, all segmental branches and most of subsegmental branches of pulmonary arteries supplying entire pulmonary segments of both lungs. The patient died after 86 minutes of asystole and cardiopulmonary resuscitation. An intravenous line was inserted in the right arm at the start of the endoresection and removed only when cardiopulmonary resuscitation was abandoned; this was connected to an electric infusion pump to prevent air embolism (Volumat Agilia, Fresenius Kabi AG, Bad Homborg, Germany).

## Case 2

A 41-year-old, healthy female presented with visual field defect in her left eye for several weeks. The visual acuity was 20/20. The tumor was pigmented, with retinal invasion, orange pigment, and subretinal fluid. (shown in Fig. 2A). It was located equatorially in the superior quadrant and measured 7.4 mm in basal diameter with a thickness of 8.0 mm. The patient was advised about the risks and benefits of enucleation, iodine-plaque brachytherapy, and endoresection with ruthenium plaque brachytherapy. She was also informed of the risk of death from pulmonary embolism after endoresection. She declined enucleation, and selected endoresection with full understanding of the potential complications of the procedure.

The anesthesiology team visited the patient for preoperative evaluation and preparation. The patient was categorized as NYHA class 1, and ASAPS class 1. According to ASAPS, her estimated mortality risk during general anesthesia was 0-0.3 %.

General anesthesia was performed as described in Table 1B and 1C. Tumor endoresection was completed as described in Table 1A. No air infusion was used during the procedure.

Because of the previous fatality, the anesthesia was administered with extreme caution and special monitoring, which included intraoperative transthoracic echocardiography and insertion of a 7 Fr, double-lumen, central venous catheter in the right internal jugular vein to detect and aspirate air embolism, if it occurred. The central venous line was primed with saline irrigation before catheter insertion and all extension lines were clamped and capped at all time to prevent air entry into venous system. This central venous line was not connected to any infusion system. It was removed several days later.

Intraoperative monitoring showed a normal level of ETCO2 (30-33 mmHg). The blood pressure was lowered from 120/70 mm Hg to 90-110/55-65 mm Hg during the endoresection. There were no adverse events during the operation, which lasted 2 hours and 20 minutes. Preoperative and intraoperative transthoracic echocardiography during all time of tumor endoresection, 3 hours before the collapse, did not show air embolism. The patient showed normal breathing after extubation and no systemic adverse events occurred during monitoring in the PACU. One-and-a-half hours after the monitoring in PACU, when fully recovered with full consciousness, the patient was transferred, without oxygen support, from PACU to the intensive care unit as a precaution, in case pulmonary embolism developed.

Five hours and 30 minutes after surgery, while lying supine, the patient suddenly developed chest tightness and difficulty breathing. Vital signs included a blood pressure of 90/61 mm Hg, pulse rate of 80 beats per minute, and a respiratory rate of 30 breaths per minute. The SpO2 dropped from 100% to 90%, which was not improved with an oxygen mask with bag (FiO2 1.0, flow 10 LPM). One hour later, her SpO2 decreased to 50-70%. Endotracheal intubation was performed, with the patient awake. The ETCO2 was abnormally low (5 mm Hg), suggesting low pulmonary blood flow and high dead-space ventilation. Transthoracic echocardiography revealed right ventricular enlargement, D-shaped left ventricle, and biventricular air embolism, especially in left ventricle. Transesophageal echocardiography revealed a patent foramen ovale (PFO). During full support and mechanical ventilation with 100% oxygen, blood gas analysis showed a PaCO2 of 58.9 mm Hg, PaO2 of 57.2 mmHg, and SaO2 of 82.5%. The diagnosis was massive air embolism with acute cor pulmonale.

Two hours later, the blood pressure decreased slightly from baseline. The pulse rate was 130 beats per minute and the SpO2 gradually decreased to 50-60%. A chest X-ray revealed pulmonary edema in her left lung, resulted from previous intravenous fluid loading (1,000 ml) and Durant’s maneuver (left lateral decubitus position). The patient was sedated and paralyzed. ECMO (extracorporeal membrane oxygenation) was initiated in V-A (veno-arterial) mode. The ECMO setting was 3.0 L/min of ECMO flow and sweep gas with FiO2 equal to 1. ECMO flow was increased until the pulse pressure was at suitable level, to prevent the Harlequin syndrome.

Twelve hours after ECMO initiation, the vital signs were stable. Transthoracic echocardiography showed decreasing air in left ventricle, but signs of right ventricular strain persisted. Nitric oxide (NO) was administered for pulmonary vasodilation. After NO administration, the pulse pressure and ETCO2 increased to normal, indicating increased cardiac output and pulmonary blood flow. The next day, the radioactive plaque was removed from the eye as scheduled, in the ICU, using surgical loupes (2.5X magnification) without complication. This was achieved with topical anesthesia, as the patient was still heavily sedated. No scleral defect or choroidal exposure was noted at the surgical site. Sedation and paralysis were withdrawn on the next day. Weaning of ECMO and mechanical ventilation were done simultaneously, and stopped on the third post-operative day. An intravenous line, fitted with an electric infusion pump, was inserted at the start of the endoresection and removed before the patient was discharged from the hospital.

Close in-patient monitoring was continued for another 7 days, without incident, before discharge from hospital. At the latest follow-up examination, six months after the operation, the patient showed no systemic morbidity. The visual acuity in the operated eye was 20/30. The retina was well attached without tumor recurrence. (shown in Fig. 2B). The patient made a full recovery.