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Anesthetic management of a patient with tuberous sclerosis presenting for renal transplantation

E.G. Papaioannou[1], C.V. Staikou[1], A. Lambadariou[1], I.G. Karavokyros[2], and K. Tsinari[1]

[1] Department of Anesthesiology and [2] Renal Transplantation Unit, "Laikon" Regional General Hospital, University of Athens, 17 Aghiou Thoma Street, Athens 115 27, Greece

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Introduction

Tuberous sclerosis (Pringle's disease, Bourneville's disease) is an autosomal dominant disorder with an overall prevalence of about 1 in 29000, 1 in 15000 for those less than 5 years of age, and a birth incidence of 1 in 10000. It is characterized mainly by neurological (epilepsy, mental retardation) and dermatological (angiofibroma) signs [1]. The clinical expression is so variable that relatively mild forms of the disease may be difficult to recognize.

Renal involvement in individuals with tuberous sclerosis includes angiomyolipomas, which are considered pathognomonic when they are multiple and bilateral [2]. Chronic renal failure is rare in tuberous sclerosis, but its precise frequency is not known [3]. End-stage renal insufficiency results from replacement of renal parenchyma by angiomyolipomas and growing cysts or from the removal of the kidneys for intractable hemorrhage [4–7]. Renal transplantation offers prolonged survival and appears to be the treatment of choice in such patients [8–12].

The anesthetic management of patients with tuberous sclerosis has only been reported in a total of eight patients in seven published reports [1,13–18], four of which were in non-English-language journals. None of them referred to a patient undergoing renal transplantation.

Address correspondence to: E.G. Papaioannou, 6, Karvela str., Aghia Paraskevi 153 42, Greece
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We report one case of anesthetic management of a patient with tuberous sclerosis undergoing renal transplantation.

Case report

A 36-year-old woman (160 cm, 56 kg) with tuberous sclerosis, diagnosed 6 years previously, was scheduled for living-donor renal transplantation. The patient had suffered from chronic renal failure for 6 years; the renal parenchyma was replaced by bilateral angiomyolipomas. Four years previously, she underwent unilateral (left) nephrectomy because of massive hematuria and uncontrolled bleeding, but she did not require dialysis. Her blood urea nitrogen was 30 mg·dl^{-1} (21 mmol·l^{-1}) and her serum creatinine was 5.4 mg·dl^{-1} (480 μmol·l^{-1}).

Three times during the past 15 years she had had spontaneous pneumothorax; the last time (10 years previously) she underwent right pleurodesis. After both surgical operations, she was admitted to the intensive care unit (ICU) for routine postoperative management. Her recovery after the nephrectomy was uneventful, and she returned to the ward on the second postoperative day. After the pleurodesis, her stay in the ICU was prolonged to 2 weeks because of a pulmonary infection.

She suffered from petit mal seizures between the ages of 3 and 6 years but had no mental retardation. She was a regular smoker (10 packet-years). She was not under regular medical treatment and had no history of drug allergy. The nephrologists suggested that she should have one session of hemodialysis 12 h before operation. Preoperative physical examination disclosed facial angiofibroma over the cheeks and nose and subungual fibromas and shagreen patch (leathery thickening patch) over the lumbosacral region. Her muscle tone and reflexes in all limbs were normal. Physical examination of the respiratory and cardiovascular system was

unremarkable. The electrocardiographic and echocardiographic results were normal. A chest x-ray showed a widespread honeycomb appearance of the parenchyma of both lungs. Even though the patient's arterial blood gas analysis was satisfactory (pH, 7.43; Pa_{CO_2}, 40.3 mmHg; Pa_{O_2}, 96 mmHg; HCO_3^-, 27.1 mmol·l^{-1}; and Sa_{O_2}, 97.7%), her pulmonary function tests revealed severe obstructive and mild restrictive pulmonary disease [forced vital capacity (FVC), 2.29 l; forced expiratory volume in the first second (FEV_1), 1.71 l; 65% and 56% of the predicted values, respectively]. She was administered salbutamol 0.5 mg and ipratropium 2.5 mg four times and budesonide 200 μg twice daily in aerosol. Cerebral computed tomographic (CT) scan disclosed occipital paraventricular calcification. Pulmonary CT scan revealed multiple cystic lesions bilaterally. Renal CT scan examination (right kidney) suggested multiple cysts and hypodense lesions with negative attenuation value, compatible with angiomyolipomas. The other preoperative investigations (after the hemodialysis session) included hematocrit, 22%; leucocyte count, 6300 · μl^{-1}; platelet count, 224 000 · μl^{-1}; serum glucose, 67 mg·dl^{-1} (4.8 mmol·l^{-1}); blood urea nitrogen, 12 mg·dl^{-1} (8.7 mmol·l^{-1}); serum creatinine, 2.4 mg·dl^{-1} (212 μmol·l^{-1}); sodium, 138 mmol·l^{-1}; potassium, 3.6 mmol·l^{-1}; ionized calcium, 2.25 mmol·l^{-1}; prothrombin time, 11 s [international normalized ratio (INR), 1.1]; activated partial thromboplastin time, 32 s; and fibrinogen, 280 mg·l^{-1}. Informed written consent to general anesthesia for the transplantation was obtained from the patient the day before surgery.

As premedication, our patient received diazepam 5 mg orally the evening before going to bed and 1 h before the operation. Twenty minutes before entering the operating room, she was administered ranitidine 50 mg and ondansetrone 4 mg i.v. Anesthesia was induced with midazolam 2 mg, fentanyl 100 μg, and thiopental 250 mg i.v., and tracheal intubation was facilitated by succinylcholine 55 mg. Ventilation was controlled artificially (tidal volume, 400 ml; frequency, 12 breaths min^{-1}; and I/E ratio, 1:2) with 50% oxygen in air so that the peak inspiratory pressure remained below 15 cmH_2O and the end-tidal carbon dioxide concentration was 35 to 40 mmHg. The patient was managed without positive end-expiratory pressure (PEEP) in order to minimize the risk of pulmonary barotrauma. Anesthesia was maintained by isoflurane administration in concentrations titrated according to the patient's hemodynamic stability, without exceeding 1 minimum alveolar concentration (MAC). To maintain analgesia, fentanyl (8 μg·kg^{-1}·h^{-1}) was administered in divided bolus doses. According to the train-of-four (TOF) response, atracurium was administered by continuous intravenous infusion at 7 μg·kg^{-1}·min^{-1}. The patient was placed in the supine position. The left dorsalis pedis artery and the right internal jugular vein were cannulated. A nasogastric tube and a Foley catheter were also inserted. Intraoperative monitoring included precordial stethoscope, two-lead electrocardiography, intra-arterial pressure, central venous pressure (CVP), pulse oximetry, end-tidal carbon dioxide concentration, and urine output. Solutions of dopamine and nitroglycerine in dextrose 5%, in doses of 5 to 10 μg·kg^{-1}·min^{-1} and 0.5 to 1.5 μg·kg^{-1}·min^{-1}, respectively, were used to maintain the mean arterial pressure (MAP) between 75 and 110 mmHg throughout the procedure. CVP was maintained at 6 to 13 mmHg. Five minutes before graft reperfusion, the patient received methylprednisolone 500 mg and furosemide 40 mg i.v. The measured blood loss of approximately 380 ml and intraoperative fluid needs were replaced by 3 l of crystalloid (normal saline) and 2 units of blood. The operation lasted 170 min, and 20 min later the tracheal tube was removed and the patient was transferred to the renal transplantation unit. The urinary output from the time of graft reperfusion was 1100 ml (550 ml·h^{-1}). No untoward events related to anesthesia or surgery occurred. For postoperative pain relief, the patient received morphine in continuous i.v. infusion at a rate of 1 mg·h^{-1} and paracetamol 600 mg intramuscularly four times daily. Her medication for the respiratory system (except for budesonide) was resumed immediately after the operation. The patient stayed in the hospital for 10 days after transplantation. She did not suffer from rejection episodes, and her postoperative course was in general uncomplicated. Currently, 20 months after renal transplantation, the general condition of the patient is excellent. The blood urea nitrogen and serum creatinine concentrations are 16 mg·dl^{-1} (11.7 mmol·l^{-1}) and 1.8 mg·dl^{-1} (161 μmol·l^{-1}), respectively, and the results of urinanalysis are normal. Maintenance therapy includes cyclosporine 175 mg, azathioprine 100 mg, and prednisone 8 mg daily.

Discussion

According to the current literature, the anesthetic experience of patients with tuberous sclerosis undergoing renal transplantation has never been reported. We tailored our patient's management to the prevention of seizures, pneumothorax due to barotrauma, hypovolemia caused by probable massive hemorrhage, and maintenance of a satisfactory level of graft perfusion by obtaining cardiovascular stability.

Our patient had had no epileptic seizures since the age of 6 years and was not receiving any antiepileptic drugs. Our preventive strategy included diazepam 5 mg as premedication and avoidance of propofol, etomidate, and enflurane as hypnotic agents [1]. Antiemetics for prevention of regurgitation and succinylcholine

$1\,mg \cdot kg^{-1}$ for rapid sequence intubation were used to minimize the risk of aspiration due to uremia-induced delayed gastric emptying, since our patient had end-stage renal failure but a low-normal posthemodialysis serum potassium concentration.

Physical examination of the cardiovascular system, as well as electrocardiography and echocardiography, did not reveal any pathological signs. However, we focused on maintaining a slightly low MAP and elevated CVP (using temporarily vasoactive agents) in order to achieve optimal graft perfusion and avoid the risk of massive hemorrhage from the remaining right kidney as a result of high arterial pressure.

Lung involvement due to tuberous sclerosis was present in our patient, although it is considered rare (<1%) [1]. In order to minimize the risk of a new incident of pneumothorax due to barotraumas, we adjusted the ventilatory settings (low tidal volume, about $7\,ml \cdot kg^{-1}$) in such way that the peak inspiratory pressure was kept low (below $15\,cmH_2O$). We also avoided PEEP and nitrous oxide and preferred air, because in patients with pulmonary cysts, nitrous oxide may expand the air space and cause rupture.

A relatively high (50%) concentration of inspired oxygen was used to achieve optimal tissue oxygenation of the graft. Finally, we tried to ensure that the patient would have adequate intra- and postoperative analgesia to obtain arterial pressure stability and a stress-free postoperative period.

The anesthetic management of a 36-year-old female patient with tuberous sclerosis undergoing renal transplantation from a living donor has been presented. Patients with tuberous sclerosis are good candidates for renal transplantation, with a similar prognosis as other recipients with the same demographic characteristics [8,10–12]. Some authors recommend binephrectomy after starting dialysis before or at the time of transplantation, given the risk of cancer and hemorrhage because of angiomyolipomas [3,8,19]. Perioperative anesthetic management of these patients should be tailored according to the systems affected by tuberous sclerosis, although more experience is needed [1].

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