

## Clinical Reports

# Epidural anaesthesia for transurethral resection of the prostate in a patient with carcinoid syndrome

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*The anaesthetic management of a 63-year-old patient with carcinoid syndrome presenting for transurethral resection of the prostate (TURP) is described. Before surgery antibradykinin, antiserotonin and antihistamine drugs were used in addition to SMS 201-995, a long-acting somatostatin analogue, to prevent the intraoperative release of hormones associated with this syndrome. Several techniques of general anaesthesia have achieved successful patient outcomes. Monitoring included pulse oximetry and radial artery cannulation. After infusion of Ringer's lactate, 750 ml, and 25 per cent albumin, 150 ml, an incremental epidural block with xylocaine two per cent without adrenaline was administered to achieve ideal operating conditions without any change in haemodynamic variables or oxygen haemoglobin saturation. Epidural anaesthesia seems to be a safe alternative to general anaesthesia in patients with carcinoid syndrome presenting for TURP.*

*En association avec l'utilisation périopératoire d'antagonistes des bradykinines, de la sérotonine et de l'histamine, on peut prévenir la libération peropératoire des hormones propres au syndrome carcinoïde en employant le SMS 201-995, un analogue de la somatostatine à longue action. Alors que plusieurs techniques d'anesthésie générale ont été utilisées avec succès, nous avons employé une anesthésie épidurale lors de la résection trans-urétrale de la prostate (RTUP) d'un*

### Key words

ANAESTHESIA: epidural;  
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*homme de 63 ans, porteur d'un carcinoïde. Le monitoring comprenait entre autres, l'usage d'un oxymètre de pouls et d'une canule dans l'artère radiale. Après la perfusion de 750 ml de Lactate Ringer et de 150 ml d'albumine à 25 pour cent, nous avons progressivement injecté de la lidocaïne à deux pour cent avec adrénaline dans le cathéter épidural et obtenu un bloc approprié, sans changement de la saturation artérielle en oxygène ou des variables hémodynamiques. L'anesthésie épidurale constitue donc une alternative valable à l'anesthésie générale pour la RTUP de patients porteurs d'un syndrome carcinoïde.*

Carcinoid syndrome is a rare entity characterized by the classic symptom complex of vasomotor disturbances, intestinal hypermotility, bronchoconstriction and endocardial fibrosis. The pathophysiology is complex. In 1954 the syndrome was thought to be caused solely by serotonin<sup>1</sup> but recently more than 20 hormones have been implicated.<sup>2,3</sup>

The low incidence (8:100,000) results in an anaesthetist being required to provide surgical anaesthesia only rarely during his career for such a patient. The request by Mason and Steane<sup>4</sup> for more case reports of the syndrome resulted in reports of various anaesthetic techniques with successful patient outcomes.<sup>5-8</sup> However, there are no reports of patients being managed with spinal or epidural anaesthesia. Major regional blockade is said to be contraindicated,<sup>4</sup> mainly because of the risk of acute hypotension which could precipitate a carcinoid crisis. The following is a report of a patient undergoing transurethral resection of the prostate under epidural anaesthesia.

### Case report

A 63-year-old Caucasian male with known carcinoid syndrome was admitted to hospital in January 1988 for

evaluation and treatment of abdominal pain. He initially presented in February 1986 with a sigmoid polyp which was seen on barium enema. An exploratory laparotomy was therefore performed. Multiple hepatic metastatic lesions were found and pathologically diagnosed as carcinoid tumour. In retrospect, a two-month history of flushing before admission was his only symptom. The 24-hr urine excretion of 5-hydroxyindolacetic acid was 451 mg (upper limit of normal: 31 mg/24 hours). An echocardiogram at that time was normal. In May 1987, treatment was started with somatostatin for refractory diarrhoea, and four months later right ventricular heart failure was diagnosed.

His major complaints on this admission were of abdominal pain and bloating, fatigue and NYHA class III dyspnoea. Medications included somatostatin, furosemide, codeine and cotazyme. His most recent general anaesthetic was for the laparotomy in January 1986, which had been uneventful apart from postoperative nausea and vomiting. Physical examination revealed a cachectic male with blood pressure 115/70, heart rate 80 bpm, respiratory rate 18 breaths  $\cdot$  min<sup>-1</sup>, and temperature 36.4° C. Telangiectasia were present involving the face and upper thorax. Air entry was diminished in all lung fields on auscultation with the absence of adventitious sounds. Jugular venous pressure was elevated to the angle of the jaw with a prominent V wave when the patient was 45° supine. A right ventricular heave was present. A grade 3/6 pansystolic murmur as well as S<sub>4</sub> were present at the lower left sternal border. Pulsatile hepatomegaly, splenomegaly and ascites were present as was sacral oedema. The haemogram and coagulation screen, electrolytes and renal indices were within normal limits. Albumin and total protein concentrations were decreased at 23 g  $\cdot$  L<sup>-1</sup> and 58 g  $\cdot$  L<sup>-1</sup> respectively. Alkaline phosphatase was elevated at 1205 units  $\cdot$  L<sup>-1</sup>. An ECG showed right atrial enlargement. Bedside pulmonary function tests revealed a mild restrictive defect. The echocardiogram showed moderately dilated right atrium and ventricle with marked tricuspid and pulmonary regurgitation. The left ventricular ejection fraction was normal at 51 per cent.

Two weeks after his admission in January 1988 intrahepatic arterial chemotherapy with 5-FU and streptozotocin was started via a percutaneously placed catheter. This procedure was uneventful. Subsequently he developed urinary retention and a transurethral resection of the prostate (TURP) was planned.

Premedication was with ampicillin 2 g IV, gentamicin 80 mg IV, ranitidine 150 mg PO, diphenhydramine 25 mg PO, methotrimeprazine 25 mg IV, apromin 200,000 units IV and somatostatin 1.5 ml SC. He was slightly sedated, relaxed and haemodynamically stable upon arrival in the operating room. ECG leads, automatic and

manual blood pressure cuffs and a pulse oximeter were applied. A 16-ga IV catheter was established in the left antecubital fossa and a 20-ga intra-arterial catheter in the right radial artery. Baseline arterial blood gases on air revealed pH 7.45, PCO<sub>2</sub> 38 mmHg, PO<sub>2</sub> 64 mmHg and HCO<sub>3</sub> 26 mmol  $\cdot$  l<sup>-1</sup>. O<sub>2</sub> sat 93 per cent. Oxygen was delivered via nasal prongs. The patient was then positioned in the left lateral decubitus position and an epidural catheter was placed at the L<sub>2-3</sub> interspace. With the patient positioned supine, 750 ml Ringer's lactate and 150 ml 25 per cent albumin was infused IV over 20 min. A test dose of epidurally administered two per cent xylocaine CO<sub>2</sub> was negative and a total of 15 ml of the solution was given in increments of 3 ml over 20 min. A sensory block to T<sub>8</sub> was obtained and the surgery was completed in 45 min. The blood pressure remained stable at 95–110 mmHg systolic throughout the operation. The oxygen saturation was stable at 92–94 per cent. The patient was transferred to the recovery room in good condition and monitored there overnight. He was discharged to the ward the next day.

### Discussion

Mason and Steane in their review of patients with Carcinoid syndrome in 1976 reported 67 per cent to have some complication.<sup>4</sup> This high incidence of complications and the attention drawn to the syndrome resulted in numerous case reports. Miller *et al.* in 1978 reported nine cases of which a major complication occurred in only one.<sup>5</sup> They suggested that anaesthesia for these patients was not as hazardous as previously reported provided the patients were adequately prepared. Their suggested technique was a balanced anaesthetic without volatile inhalational agents. Since then, successful anaesthetic outcomes using volatile agents,<sup>6</sup> butyrophenone-narcotics,<sup>7</sup> and ketamine-diazepam<sup>8</sup> have been reported.

Carcinoid tumours are composed of enterochromaffin cells and usually arise from the small intestine – in particular the ileum and appendix. The tumour most commonly metastasizes to the liver. The ectopic hormones secreted may include: secretin, histamine, prostaglandin (PGE and PGF<sub>2</sub>α), insulin, glucagon, parathormone, vasoactive intestinal peptide (VIP), calcitonin, vasopressin, substance P, neuropeptide K, motilin as well as β-endorphin. These substances may give rise to a variety of signs and symptoms: diarrhoea, abdominal pain, telangiectasia, flushing, cyanosis, pellagra-like lesions, bronchospasm and cardiac fibrosis. The carcinoid flush can vary in its characteristics depending on which hormone is predominantly released from the tumour. Histamine, prostaglandins, substance P and various tachykinins have all been implicated, whereas serotonin and bradykinin are unlikely to be the causative

agents of the carcinoid flush.<sup>9,10</sup> It is important to note that the flush (with associated hypotension) can often be triggered by excitement, anxiety, exercise or ethanol. Flushing can also be induced experimentally by intravenous administration of epinephrine, isoproterenol as well as pentagastrin.<sup>3,11</sup>

A variety of pharmacological agents has been used in an attempt to prevent the release of biologically active substances from the tumour. We used methotrimeprazine preoperatively; this is a phenothiazine derivative with antiserotonin and analgesic properties. This drug has also been used intravenously in the treatment of hypertensive episodes that sometimes may occur during surgery in patients with carcinoid syndrome.<sup>5</sup> He was also given aprotinin which inhibits the activation of kallikrein and is therefore especially useful to control symptoms associated with increased bradykinin production. Diphenhydramine (H<sub>1</sub> antagonist) and ranitidine (H<sub>2</sub> antagonist) were also given to ameliorate the adverse action of histamine on end-organs, although histamine is more commonly released from gastric carcinoids.<sup>12</sup> We also used SMS 201-995, a long-acting somatostatin analogue as part of our preoperative drug regimen. This agent has been used successfully both as a prophylactic agent as well as in the treatment of an acute carcinoid crisis during anaesthesia.<sup>13-16</sup> Somatostatin is a tetradecapeptide originally isolated from the ovine hypothalamus, but which has since been found in a variety of human tissues. It has a wide spectrum of biological actions.<sup>17,18</sup> It inhibits neuroendocrine secretion in the pancreas and gastrointestinal tract – in particular the secretion of gastrin, CCK, vasoactive peptide (VIP), motilin and glucagon. In addition, it inhibits the secretion of acid and pepsinogen from the stomach. Somatostatin also has an inhibitory effect on gastrointestinal motility. The exact cellular mechanism of action of somatostatin on target organs is not fully understood, but is thought to be related to interference of cAMP production by inhibition of the enzyme adenylate cyclase.<sup>17</sup> The use of SMS 201-995 in the treatment of carcinoid syndrome is now commonplace,<sup>19</sup> and improvements in symptoms such as wheezing, diarrhoea, abdominal pain and flushing have been noted, as well as an inhibitory effect on tumour growth in some patients. We omitted the administration of a corticosteroid preoperatively, since these have been found to be useful only in the treatment of carcinoid tumours arising from the embryonic foregut, e.g., bronchus.<sup>3,11</sup>

Our patient was clearly affected by three of the four classical carcinoid syndrome manifestations with the absence of bronchospasm, although some symptoms (flushing, abdominal discomfort, diarrhoea) had responded favourably to treatment with SMS 201-995. As there were no contraindications to its use we elected epidural

anaesthesia. Epidural anaesthesia modifies the endocrine metabolic response to lower abdominal surgery resulting in lower serum catecholamine levels during surgery.<sup>20,21</sup> Epidural anaesthesia was chosen over spinal anaesthesia to avoid a rapid sympathectomy; this allowed a titrable level of block with slower onset, thus avoiding sudden dilatation of the splanchnic vasculature which might have produced hypotension. Furthermore, major neural blockade is preferred to general anaesthesia for TURP in our institution for reasons outlined elsewhere.<sup>22</sup> General tracheal anaesthesia may be associated with a stress response with tachycardia and hypertension especially at the time of tracheal intubation and extubation.<sup>23,24</sup> In addition, many intravenous anaesthetics and muscle relaxants have side-effects involving the autonomic nervous system as well as releasing histamine. A combination of albumin and crystalloid was given as a preload. Hypoalbuminaemia, as was present in our patient, is often secondary to impaired hepatic function due to fluid engorgement and tumour metastasis and metabolic diversion of tryptophan into production of 5-hydroxyindoleacetic acid. A central venous pressure line was not inserted. It was felt that it would be difficult to interpret as a result of the decreased right ventricular function and tricuspid and pulmonic regurgitation although in retrospect, it might have been of value in view of the possibility of absorption of irrigation fluids from the operative site. A pulmonary artery catheter was not used because of potential difficulty in insertion and as it may have been technically difficult to float because cardiac output values would not be valid because of severe tricuspid and pulmonary regurgitation.

The treatment of hypotension in a carcinoid crisis consists of rapid intravenous infusion of fluids. Methoxamine is considered the vasopressor of choice as it is a peripheral alpha-receptor agonist.<sup>11</sup> However, it is likely that small intravenous boluses (50 µg) might be useful adjuvants in the treatment of a carcinoid crisis with marked flushing and hypotension.<sup>5</sup>

In summary, we have described epidural anaesthesia as a successful anaesthetic technique for a patient with symptomatic carcinoid syndrome. It provided excellent surgical anaesthesia and stable haemodynamic variables and a sensory blockade that persisted for three hours after surgery. We do not agree that regional anaesthesia is contraindicated or offers no benefit as had been suggested earlier.<sup>4</sup> Instead, regional anaesthesia should be considered a reasonable alternative technique for a patient with carcinoid syndrome who presents for elective lower abdominal or lower extremity surgery. However, specific prophylactic agents including SMS 201-995 should be used preoperatively, and a careful history and physical examination should be undertaken to ascertain that a

response to treatment had occurred. The need for vigilant intra- and postoperative monitoring of these patients is emphasized.

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