ANAPHYLACTOID OR CARCINOID?

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SUMMARY

A patient with a carcinoid tumour and a history suggestive of carcinoid syndrome, but with no biochemical evidence in support, had a cardiovascular collapse during an anaesthetic with propofol and suxamethonium. Subsequent investigations suggested an anaphylactoid reaction to suxamethonium, but there were features in common with a carcinoid crisis. The necessity for a second anaesthetic soon afterwards posed a dilemma. In the event of a similar reaction during another anaesthetic, a management plan beforehand should include ready availability of appropriate drugs and the use of sympathomimetic drugs that are less likely to exacerbate the situation.

KEY WORDS

Allergy: anaphylactoid reaction. Complications: carcinoid syndrome.

Cardiovascular collapse immediately after induction of anaesthesia may occur from many causes, including pre-existing hypovolaemia, drug overdose, anaphylaxis, arrhythmias, tension pneumothorax and air or pulmonary emboli. The release of vasoactive mediators in patients with the carcinoid syndrome may result in a similar event. In these life-threatening situations, diagnosis depends on making a “best guess” from information about past history combined with clinical signs and evidence from monitoring equipment. Treatment is aimed at cardiovascular and ventilatory support followed by specific therapy (e.g. insertion of a chest drain in a tension pneumothorax).

We describe a patient in whom the cause of an acute hypotensive event was not clarified completely, even with further investigation, and to whom it was necessary to administer a second anaesthetic.

CASE REPORT

A 39-yr-old woman weighing 62 kg presented for diagnostic rigid bronchoscopy. An atypical carcinoid tumour had been resected 6 yr earlier from her left lung. That anaesthetic and two others had been uneventful. During the previous 10 months, whilst working overseas, she had complained of intermittent diarrhoea and flushing, particularly after consumption of alcohol; her systemic arterial pressure had not been measured during these episodes, but she did not complain of feeling faint. All investigations, including ultrasound and computed tomography of her abdomen, had been negative. Repeated measurements of urinary concentrations of 5-hydroxyindoleacetic acid (5HIAA) and serum concentrations of dopamine, noradrenaline and adrenaline did not reveal increased values. Despite the suggestive history, the diagnosis of carcinoid syndrome was presumed to have been excluded by her attending physicians. One month earlier, a left-sided mediastinal mass was seen on a chest x-ray.

The patient was not premedicated and was apprehensive in the anaesthetic room. She had a sinus tachycardia (100 beats min⁻¹). A 21-gauge cannula was inserted in the left antecubital fossa. Anaesthesia was induced with alfentanil 1 mg, propofol to a total of 200 mg and suxamethonium 100 mg. After manual ventilation of the lungs with 100% oxygen, the rigid bronchoscope was inserted and ventilation commenced with a Sanders injector. Within 2 min of insertion of the bronchoscope, pallor and peripheral cyanosis were seen. The ECG showed a sinus tachycardia, but with marked ST depression. Peripheral pulses were not palpable, but a weak carotid pulse was detectable. A diagnosis of drug anaphylaxis was made.

The bronchoscope was removed and replaced with a tracheal tube and the lungs ventilated with 100% oxygen. There was no difficulty in ventilation and no evidence of bronchospasm. The operating table was tilted to put the patient head-down. Hetastarch (Hespan) 500 ml was administered through a 14-gauge peripheral venous cannula together with a bolus of adrenaline 1 mg and calcium chloride 5 mmol. Bradycardia developed and external cardiac compression was begun. An infusion of isoprenaline 0.05 μg kg⁻¹ min⁻¹ was commenced. A systolic arterial pressure of 60 mm Hg registered on the automated, non-invasive sphygmomanometer (Dinamap) when the patient started to regain consciousness and breathe spontaneously. The tracheal tube was removed and oxygen administered by face mask.

The patient complained of chest pain and tingling feet. She had marked facial and upper torso flushing and persistently pale peripheries. Additional colloid was administered for volume replacement and hy-

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The isoprenaline infusion was reduced and then stopped as her arterial pressure increased. There were no pneumothoraces or rib fractures visible on a chest x-ray taken in the anaesthetic room. The patient was transferred to an intensive therapy unit.

She continued to complain of chest pain in association with ST depression until her arterial pressure exceeded 100/60 mm Hg. The flushing remained pronounced. The possibility that the acute event was a carcinoid crisis was confirmed as highly probable on clinical grounds by an endocrinologist. Octreotide (50-μg bolus followed by 100-μg 6-hourly) and ketanserin (10-mg bolus followed by an infusion containing 2 mg h⁻¹) were administered. Her condition improved rapidly.

Twelve hours later, the facial and torso flush were still visible, but the ECG abnormalities had resolved. Serial creatine phosphokinase concentrations did not increase.

Other blood specimens were taken and analysed for IgE, complement concentrations (C3 and C4) and radioallergosorbent assay (RAST) for suxamethonium. Twenty-four-hour urine was analysed for 5HIAA.

Initially, the concentrations of C3 and C4 were decreased, and 24 h after the incident they were normal. The RAST score for suxamethonium was 3 (range 0–4); this is considered to be indicative of sensitivity to suxamethonium. The results of urine 5HIAA measurements in three successive samples were 95, 42 and 43 μmol litre⁻¹, respectively (normal < 40 μmol litre⁻¹).

When all results were available and assessed it was decided to proceed to definitive surgery (completion pneumonectomy). In view of the potential for a carcinoid reaction, octreotide 100 μg was given the night before operation and again on the morning of operation. Premedication comprised temazepam 40 mg. Anaesthesia was induced with etomidate 16 mg, fentanyl 200 μg and atracurium 45 mg and was maintained with fentanyl, atracurium and enflurane in nitrous oxide and oxygen. A mediastinal mass, that did not involve lung, was excised at left thoracotomy. Anaesthesia was uneventful and the patient was returned to the high dependency unit with a fentanyl infusion administered via a patient controlled analgesia system. Histology of the lesion confirmed an atypical carcinoid tumour similar to the initial lesion.

DISCUSSION

It was our first impression that cardiovascular collapse was caused either by the hypotensive effects of propofol or by an acute drug reaction, most likely to suxamethonium. Despite not having suxamethonium for any previous anaesthetics, the patient was found to have antibodies to this drug; and has been issued with a warning card to this effect. However, the specificity of the RAST assay for suxamethonium is not clear. The quaternary ammonium group present in all neuromuscular blocking agents appears to be the binding site for IgE-mediated allergy. Cross reactivity with other drugs bearing this group would be expected [1]; this patient had received alcuronium, pancuronium and vecuronium during previous anaesthetics. Other workers feel that the assay is specific to suxamethonium, not the quaternary ammonium group [2].

If the collapse on induction of anaesthesia was caused by hypotension or an anaphylactic reaction to suxamethonium, treatment with volume loading, oxygen and adrenaline represented appropriate therapy [3, 4]. Adrenaline has alpha and beta effects and, in addition to increasing peripheral vascular resistance, inhibits further release of histamine [3, 5] and so aids in the termination of an anaphylactoid reaction. The use of adrenaline did not result in an improvement in arterial pressure or tissue perfusion.

Carcinoid syndrome, in a patient with a bronchial tumour is unusual in the absence of hepatic metastases [6], even though bronchial lesions drain directly into the systemic circulation. The syndrome is related to tumour mass, so that only a large volume of tumour, such as that found with metastases, produces enough vasoactive material to result in symptoms [7]. Bronchial carcinoid tumours form approximately 1 % of bronchial tumours.

The past history and inconclusive results of urinary 5HIAA measurements in our patient suggested that carcinoid syndrome could not be excluded definitely as the cause of collapse. Temporally, it coincided with the rigid bronchoscope being sited in the left main bronchus, close to what proved to be tumour mass. It is conceivable that the distortion and manipulation by this instrument could compress the tumour. The first measured concentration of urinary 5HIAA after bronchoscopy was increased, but this is of unknown significance in a patient who has recently had an acute hypotensive episode. 5HIAA is specific for serotonin secreting tumours, but many other vasoactive substances can be released [8] which are not detected by screening for 5HIAA alone. Octreotide causes a decrease in urinary 5HIAA excretion [9] and so may have masked an increase in 5HIAA after the acute episode. A large increase in 5HIAA concentration would not be expected, as this is a metabolite of serotonin which produces hypertension.

Premedication for definitive surgery included octreotide, a long acting somatostatin analogue that blocks vasoactive mediator release [10] and appears to be the drug of choice [9–12]. Neuromuscular blockers and opioids may cause release of histamine and, secondarily, release of substances from carcinoid tumours. Fentanyl, etomidate and atracurium were chosen for induction of anaesthesia and muscle relaxation because this combination has a low propensity for histamine release [12]. In the event of hypotension, octreotide was available for immediate administration. Ketanserin [13], cyproheptadine [14] and aprotinin [15] were also available; these drugs block end-organ effects of substances released from carcinoid tumours. During the initial event the only one of these available in the operating theatre was aprotinin. This drug is reputedly unhelpful in acute carcinoid crises [11].

The potential for sudden collapse unresponsive to these drugs was a dilemma. The idea of using
adrenaline, as at the occasion of acute collapse, was considered, but had to be rejected. In carcinoid crisis, adrenaline causes release of vasoactive substances which may perpetuate the crisis [10, 13].

As there was no bronchospasm and cardiac output during acute anaphylaxis has been shown to increase [15], a directly acting alpha agonist was felt most appropriate, and methoxamine was prepared.

During episodes of acute cardiovascular collapse in which bronchospasm is not apparent, a vasoconstrictor may be more appropriate than adrenaline as first choice. Methoxamine has been shown to produce a greater systemic arterial pressure, improved organ blood flow and a greater likelihood of successful resuscitation, during cardiac arrest in dogs, compared with low or high dose adrenaline [16].

The cause of our patient's collapse remains unclear. The rapid response to treatment with octreotide would tend to suggest that a carcinoid crisis was the primary pathology. The presence of antibodies to suxamethonium is confusing. This experience suggests that, even in the presence of asymptomatic or chemically excluded carcinoid syndrome, specific therapy should be available in patients with a possible carcinoid tumour.

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REFERENCES