CASE REPORT

Neostigmine and pulmonary oedema

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SUMMARY

A 1-year-old child with no pre-existing cardiac or respiratory disease developed frank pulmonary oedema after administration of a neostigmine–glycopyrrolate mixture to reverse neuromuscular blockade during general anaesthesia. Possible cardiac and extra-cardiac factors that could cause pulmonary oedema in this child were ruled out by appropriate investigations. As the pulmonary oedema manifested shortly after administration of the neostigmine–glycopyrrolate mixture, we concluded that neostigmine was the most probable cause. This article briefly reports the occurrence of events and successful management of perioperative pulmonary oedema.

BACKGROUND

Neostigmine, an anticholinesterase, is a drug routinely used in anaesthetic practice to reverse neuromuscular blockade. There are no major adverse drug reactions in most patients. However, a literature survey reveals the occurrence of non-cardiogenic pulmonary oedema (NCPE) following the use of neostigmine to antagonise the neuromuscular blockade as a rare and idiosyncratic complication.¹ Anaphylaxis and cardiovascular collapse have also been reported in another case.² We report one such near-fatal complication after the administration of neostigmine.

CASE PRESENTATION

A 1-year-old child weighing 8 kg was diagnosed to have a palpable, undescended left testis. The patient was posted for diagnostic laparoscopy, open orchidopexy and ritual circumcision (for religious reasons). Preoperative history was unremarkable. Per the parents, the child had not suffered from an upper respiratory illness in the 3-week preceding surgery. On pre-anaesthetic examination, the child was playful, active and alert. Review of systems was normal. Laboratory investigation results were within normal limits.

Surgery was performed under general anaesthesia with controlled ventilation. Injection of midazolam 0.5 mg and glycopyrrolate 0.1 mg intravenously were used as premedication. Anaesthesia was induced with ketamine 20 mg and atracurium 5 mg intravenously. Orotracheal intubation was performed with a size 3.5 mm ID endotracheal tube and mechanically ventilation administered on an intermittent positive pressure ventilation (IPPV) mode. Sevoflurane in 50% O₂ and N₂O mixture with intermittent doses of atracurium was used for maintenance of anaesthesia. Fentanyl 2 µg/kg was administered intraoperatively for analgesia. ECG,

SpO₂, EtCO₂, temperature, FiO₂ and inhalational agent concentration were monitored and found to be normal throughout the surgery. The surgery lasted for 90 min and 150 mL of Ringer's lactate solution was administered intravenously. Urine output was adequate.

At the end of the surgical procedure, neuromuscular blockade was antagonised with glycopyrrolate 0.1 mg and neostigmine 0.5 mg after the child was observed to have spontaneous respiratory efforts. A thorough oral suction was done. Just prior to extubation, pink, frothy secretions were noticed in the endotracheal tube. On auscultation, coarse crepitations were heard bilaterally in all lung areas. The oxygen saturation started dropping gradually and fell to less than 85% eventually.

DIFFERENTIAL DIAGNOSIS

A diagnosis of pulmonary oedema was made.

TREATMENT

Extubation was deferred and the child was paralysed with vecuronium 2 mg stat. Furosemide 10 mg, morphine 1 mg and hydrocortisone 20 mg were administered. The patient was stabilised with the above treatment and was shifted to the paediatric critical care unit after 30 min. Heart rate, blood pressure and SpO₂ were within normal limits. On auscultation, occasional fine crepitations were heard bilaterally, predominantly in the basal regions. Arterial blood gas levels and serum electrolytes in the immediate postoperative period were within normal limits. Echocardiography was normal.

The child was ventilated on an IPPV pressure control mode. Supportive pharmacotherapy was continued.

OUTCOME AND FOLLOW-UP

The patient was ventilated for 24 h and extubated on the first postoperative day, once the child was awake, alert and had regained good muscle power. He was constantly monitored and the postextubation period was uneventful. He was discharged on postoperative day 2.

DISCUSSION

Postoperative pulmonary oedema is a rare but potentially fatal complication. Nearly 50% of the patients who develop perioperative pulmonary oedema will have preoperative evidence of cardiovascular disease.³ Postextubation upper airway obstruction, sepsis, trauma, aspiration pneumonia and fluid overload can all cause NCPE.^{4,5} Various drugs such as narcotics, tocolytics, salicylates, protamine and recombinant interleukins have been

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reported to cause pulmonary oedema as well.⁶ Anaesthetic drugs such as narcotics, ketamine, propofol, neostigmine and naloxone have all been implicated.^{6–9} A case of sudden haemodynamic compromise and severe pulmonary oedema after an uneventful laparoscopic cholecystectomy has also been reported.¹⁰

The present patient was healthy and had no pre-existing cardiorespiratory disease. Postoperative echocardiography revealed no structural cardiac pathology. Therefore, the possibility of cardiogenic pulmonary oedema was ruled out. The child had been fasting for almost 10 h before induction of anaesthesia, thus, aspiration is unlikely to have occurred. He had not received any maintenance intravenous fluids during this period of fasting. Thus, the volume of intravenous fluid administered during surgery for replacement and maintenance was appropriate. This rules out fluid overload as the cause of pulmonary oedema.

There were no signs suggestive of pulmonary oedema intraoperatively and all monitored parameters remained within normal limits. Ketamine-induced or laparoscopy-induced haemodynamic changes leading to pulmonary oedema would have manifested during surgery. Pink frothy secretions were first noticed in the endotracheal tube a few minutes after administration of glycopyrrolate and neostigmine at the end of surgery. At this point of time, the endotracheal tube was still in place and, therefore, upper airway obstruction (which could have caused negative pressure pulmonary oedema) did not cause pulmonary oedema in this patient.

Other causes of NCPE such as renal failure, sepsis, trauma, hyponatraemic encephalopathy were all ruled out. Based on the temporal sequence of the administration of the neostigmine + glycopyrrolate mixture followed by the appearance of frothy secretions as well as the exclusion of all other causes, a diagnosis of neostigmine-induced pulmonary oedema was made.

Raiger *et al*¹ have reported two cases of NCPE following use of neostigmine for neuromuscular blockade reversal. Both patients had no previous cardiovascular illness and underwent non-laparoscopic procedures. Eikermann *et al* studied the effects of neostigmine and sugammadex on upper airway function in rats. They found that neostigmine impairs the upper airway dilator muscle function and reduces upper airway calibre, both of which enhance the risk of upper airway collapse.¹¹ Seed *et al* reported a case of anaphylaxis following neostigmine use. A 64-year-old woman undergoing excision of a breast lump developed generalised rash, bronchospasm, periorbital oedema, bradycardia and hypotension 30 s after reversal with neostigmine. Skin prick tests performed with neostigmine

were positive in this patient.² Thus, idiosyncratic and anaphylactic reactions to neostigmine, albeit rare, have been described hitherto.

Learning points

- ▶ Neostigmine is a widely used drug in anaesthetic practice to reverse neuromuscular blockade with a relatively good safety profile.
- ▶ Very rare occurrences of serious adverse effects such as pulmonary oedema and anaphylaxis have been reported. We report one such complication.
- ▶ It is prudent to be watchful and consider this as a rare causative factor in the differential diagnosis of perioperative pulmonary oedema in the event of its occurrence.

Competing interests None.

Patient consent Obtained.

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