Received: 15 November 2021 | Revised: 26 January 2022 | Accepted: 18 February 2022

DOI: 10.1002/vrc2.333

Vet Record CaseReports

CASE REPORT

Food/farmed animals

Suspected pulmonary oedema development in a pig following general anaesthesia and the associated complications encountered during a subsequent general anaesthetic

Kate Walters[1] | **Jacqueline Brearley**[1] | **Andre Baptista**[2] | **Eleonora Po**[2]

[1]Queen's Veterinary School Hospital, University of Cambridge, Cambridge, UK

[2]Cambridge Farm Vets, University of Cambridge, Cambridge, UK

Correspondence
Kate Walters, Lumbry Park Veterinary Specialists, Alton, UK.
Email: katelwalters49@gmail.com

Abstract

An 85-kg, 6-year-old pig presenting with stranguria was anaesthetised for computed tomography and cystotomy. During this anaesthetic, bradyarrhythmias occurred twice, both responding to medical intervention. A cystotomy tube was placed but the removal of one urethrolith was not possible. Recovery from anaesthesia was uneventful. During hospitalisation, the animal's respiratory rate and effort increased, with crackles on thoracic auscultation. As this responded to antibiotics and a reduction in intravenous fluid therapy, the pig underwent a second anaesthetic for a percutaneous cystolithotomy to remove the urethrolith. On induction of anaesthesia, clear fluid was visible in the oropharynx. This was removed by suction but after intubation large volumes flowed from the respiratory tract via the endotracheal tube. The pig's condition was stabilised during the anaesthetic with intravenous furosemide and intermittent positive-pressure ventilation. Surgery was completed and the animal recovered from anaesthesia. Postoperatively the pig developed severe dyspnoea and cardiopulmonary arrest.

BACKGROUND

The development of pulmonary oedema following sedation and general anaesthesia has been documented in a number of species. In sheep, it is particularly reported after α2-agonist administration.[1,2] Pulmonary oedema has also been reported as a postoperative complication in horses[3] and dogs.[4]

There are no published case reports describing the development of pulmonary oedema in pigs following anaesthesia; however, delayed dyspnoea has been recognised following endotracheal intubation.[5] In this case report, we describe the development of pulmonary oedema in a pig following general anaesthesia. We also describe the associated complications encountered during a subsequent anaesthetic following hospitalisation.

CASE PRESENTATION

A 6-year-old, 85-kg, entire, male, pot-bellied non-commercial pig was presented as an emergency for stranguria. On admission, a venous blood sample was analysed (EPOC Portable blood gas critical care analyser; Woodley Equipment Company, UK), which identified a metabolic alkalosis, hyponatraemia, hypochloraemia, normokalaemia and mild azotaemia (Table 1). Abdominal ultrasound did not show evidence of complete urinary tract obstruction. Cystocentesis was performed by percutaneous transabdominal needle placement (19-gauge, 2-inch hypodermic needle; Terumo AGANI, UK) for urinary analysis and to relieve the pressure in the bladder, and the pig was monitored overnight. The following day, the pig was dribbling urine but still straining unproductively when attempting to urinate. The pig was anaesthetised for abdominal computed tomography (CT). Premedication with xylazine (1 mg/kg; Rompun 2%; Bayer, UK) and ketamine (5 mg/kg; Narketan; Vetoquinol, UK) was administered intramuscularly into the cervical muscles behind the ear, via a 16-gauge, 1.5-inch hypodermic needle and flushed extension line (V-green extension; Vygon, France). This provided profound sedation after 15 minutes and an intravenous (IV) cannula was placed (Jelco 20 gauge; Smiths Medical, UK) in the left lateral auricular vein. Thirty minutes later, during transportation to CT, additional xylazine (1 mg/kg) and ketamine (3.5 mg/kg) were administered IV due to arousal. Anaesthesia was induced 10 minutes later using ketamine (2.4 mg/kg IV). Topical lidocaine (2 ml; Lidocaine 2%; Braun, UK) was applied to the larynx using a rigid urinary catheter (6-Fr 500 mm). Using a laryngoscope and stylet for guidance, the trachea was intubated with a 10-mm cuffed endotracheal tube (ETT) (Kruuse, Denmark).

Anaesthesia was maintained using isoflurane (IsoFlo; Zoetis, UK) in oxygen, delivered via a circle breathing system. Monitoring included pulse oximetry, capnography and manual thoracic auscultation. Intravenous fluid therapy (IVFT) with sodium chloride (NaCl) 0.9% solution (Aqupharm No1; Animalcare, UK) was initiated at 4 ml/kg/h. During CT, the patient was breathing spontaneously (respiratory rate 20 breaths per minute; end tidal carbon dioxide ($P_E'CO_2$) 42–52 mmHg) and heart rate (HR) remained between 84 and 87 beats per minute. CT identified an intraluminal urethrolith just caudal to the ischium, proximal to the bulbourethral gland.

An hour after induction of anaesthesia, the pig was moved to theatre for a tube cystotomy. Pulse oximetry, capnography and electrocardiography (ECG) monitoring were connected. After 15 minutes, sudden-onset second-degree, Mobitz Type II atrioventricular block (AV block) occurred with a HR of 34 beats per minute. Subjectively, there were no T-wave changes on ECG. Atropine (0.02 mg/kg, IV; Hameln Pharma, UK) was given but due to lack of response after 2 minutes, the same dose was repeated. The AV block resolved to normal sinus rhythm and HR increased to 127 beats per minute. Spontaneous ventilation continued throughout this episode.

A venous blood sample indicated marked hyperkalaemia (8.3 mmol/L) and increased azotaemia (Table 1). Within 5 minutes of the first episode, the AV block reoccurred. Further atropine (0.02 mg/kg IV) had no effect and apnoea developed. Manual ventilation was initiated and epinephrine (0.01 mg/kg, IV; Hameln Pharma, UK) was administered. The HR increased from 28 to 174 beats per minute and spontaneous breathing returned. No chest compressions were performed. A calcium gluconate (100 mg/kg; Calciject 40, Norbrook Laboratories, UK, 29.7 mg/ml) infusion was started and given over 30 minutes. With owner's permission to proceed and given the known risk of urethral strictures following urethrotomy, retrieval of the stone via cystotomy was attempted. An arterial cannula was placed in the auricular artery (Jelco 20 gauge) for invasive blood pressure monitoring and a caudal epidural (S3-C1) was performed using lidocaine (2 mg/kg, volume 0.1 ml/kg; Lidocaine 2%; Braun, UK) to reduce isoflurane requirements. Heart rate decreased to

LEARNING POINTS/TAKE HOME MESSAGES

- In cases of respiratory dysfunction, performing thoracic radiography or ultrasonography before proceeding with anaesthesia may provide a clearer understanding of the severity of the condition, and can help with clinical decision-making.
- Invasive blood pressure and arterial blood gas monitoring can provide more accurate information on the severity of disease and can be used to monitor response to treatment. This can help guide ventilation parameters to improve oxygenation in cases of respiratory disease.
- The two main forms of pulmonary oedema are high-pressure oedema and increased permeability oedema. Hydrostatic pressure is the most important pathological factor in both forms.
- For non-cardiogenic cases of pulmonary oedema, furosemide treatment may be less effective and prognosis is usually poorer.
- Initiation of positive-pressure ventilation can be beneficial in severe cases of pulmonary oedema, and the addition of positive end expiratory pressure can improve oxygenation by increasing functional residual capacity.

TABLE 1 Results of blood samples taken from a pig during hospitalisation and two general anaesthetics

	Reference range	Arrival (venous)	Intraoperative (1st anaesthetic arterial)	Preoperative (2nd anaesthetic venous)	Intraoperative (2nd anaesthetic venous)
Sodium (mmol/L)	139–150	137	135	144	136
Potassium (mmol/L)	3.4–4.9	4.4	8.3	4.6	4.5
Calcium (mmol/L)	1.12–1.40	1.18	1.28	1.07	1.42
Chloride (mmol/L)	106–127	97	93	101	92
Haematocrit (%)	35–50	40	29	49	53
Glucose (mmol/L)	3.3–6.4	5.3	10.7	8.1	12.4
Lactate (mmol/L)	0.6–2.90	1.79	0.73	3.93	7.17
BUN (mg/dl)	10–26	36	83	72	76
Urea (mmol/L)	3.6–9.3	13.0	29.6	25.7	27.2
Creatinine (μmol/L)	44–115	256	694	369	573
BUN/Crea (mg/mg)	0.2–400.0	12.6	10.6	17.2	11.7
pH	7.350–7.450	7.558	7.342	7.518	7.167
pCO_2 (mmHg)	35.0–38.0	30.4	68.5	36.5	75.0
pO_2 (mmHg)	85.0–100.0	170.4	531.1	49.7	32.1
HCO_3^- (mmol/L)	15.0–23.0	27.1	37.1	29.7	27.1
BE (mmol/L)	−5.0 to 0.0	4.8	11.4	6.8	−1.4
cSO_2 (%)	90.0–100.0	99.7	100.0	88.6	44.5

Note: The pig presented with stranguria and developed pulmonary oedema during hospitalisation. Samples were analysed by an EPOC portable blood gas critical care analyser (Woodley Equipment Company, UK).

90–100 beats per minute within 15 minutes of epinephrine administration and remained there for 30 minutes before gradually returning to 80–90 beats per minute. Invasive mean arterial blood pressure (MAP) remained between 60 and 70 mmHg. As it was not possible to remove the urethrolith, a tube cystotomy was completed and the pig was recovered from anaesthesia. The trachea was extubated 20 minutes after cessation of isoflurane and the pig was returned to its pen to continue active warming under heat lamps 15 minutes later.

During hospitalisation, urine output was maintained between 1 and 2 ml/kg/h, measured via the tube cystotomy. However, despite dribbling urine, the pig was still unable to void a normal stream. Appetite had remained normal, but vomiting had occurred twice during hospitalisation. To counteract losses due to vomiting and ensure maintenance fluid balance, IVFT with NaCl 0.9% solution was continued at 4 ml/kg/h. Two days later, respiratory rate and effort increased (40 breaths per minute), with some crackles on thoracic auscultation.

Antibiotic treatment (amoxicillin and clavulanic acid 9.2 mg/kg; Combiclav; Norbrook Laboratories, UK) and a reduction in IVFT to 2 ml/kg/h produced some clinical improvement and respiratory rate reduced to 26 breaths per minute.

Three days after the first procedure, the pig underwent a second general anaesthetic for attempted percutaneous cystolithotomy (PCCL). Venous blood results taken the morning of surgery indicated that the hyperkalaemia had resolved to 4.6 mmol/L, with mildly decreased calcium (1.07 mmol/L) and a haematocrit (HCT) of 49% (Table 1).

Butorphanol (0.1 mg/kg IV; Torbugesic; Zoetis, UK) was administered as premedication and anaesthesia was induced with ketamine (2.4 mg/kg IV). During laryngoscopy for tracheal intubation, clear fluid was seen at the back of the oropharynx, which was suctioned before topical laryngeal lidocaine application as before. The trachea was intubated using a 12-mm cuffed ETT guided by a stylet. When the head was lowered after tracheal intubation, large volumes of clear fluid poured out of the ETT from the respiratory tract. The trachea was suctioned via the ETT and the head was lowered to provide drainage. Furosemide (1 mg/kg) was given intravenously and the trachea was suctioned as required. Intermittent positive-pressure ventilation (IPPV) was initiated using a Hallowell ventilator (Hallowell EMC; MA, USA) with a tidal volume of 10–12 ml/kg as haemoglobin oxygen saturation was <90%. This stabilised to levels >95% after IPPV initiation. Isoflurane delivered in oxygen via a circle breathing system was commenced for maintenance of anaesthesia. Capnography, pulse oximetry and electrocardiography were used for monitoring and Hartmann's IVFT (2 ml/kg/h; Aqupharm No11; Animalcare, UK) was administered. Despite regularly changing the heat and moisture exchanger, the capnograph sample line repeatedly blocked with fluid accumulation and the $P_E'CO_2$ reading fluctuated between 15 and 58 mmHg; this was suspected to be inaccurate. Intraoperative venous blood results suggested that the $PvCO_2$ was 75 mmHg (Table 1). Respiratory rate and tidal volume were altered to try to reduce this, although confirmation of this was difficult due to the unreliability of the capnograph. Calcium gluconate (50 mg/kg) was given via infusion over 30 minutes to address the mild hypocalcaemia and minimise the risk of hyperkalaemia-induced arrhythmias. Arterial catheterisation was attempted but was unsuccessful, so non-invasive blood pressure was measured using high-definition oscillometry (PetMap Graphic II; Ramsey Medical and CardioCommand, USA) with a 5.5-cm cuff on the forelimb. Tachycardia was present (HR 150–170 beats per minute), with no change after additional analgesia with ketamine and butorphanol, or to a crystalloid bolus (10 ml/kg; Aqupharm No11; Animalcare, UK). Ventricular tachycardia developed 15 minutes after starting surgery, which returned to sinus tachycardia following lidocaine (2 mg/kg IV). Non-invasive MAP readings were between 58 and 104 mmHg.

Endoscopic retrieval of the stone from the abdominal bladder was unsuccessful due to the anatomical shape of the porcine trigone and the internal urethral orifice, which did not allow entrance of the endoscope into the internal urethra. Successful removal of the stone was finally achieved by urethrotomy. The procedure lasted 4 hours.

Following cessation of IPPV, fluid began to accumulate in the ETT again. Additional furosemide (1 mg/kg IV) was administered, and the table was tilted to bring the head below the body to allow the fluid to drain out of the ETT in addition to being suctioned. Once the fluid flow had lessened, the table was returned to horizontal to prevent the abdominal contents pressing on the diaphragm and hindering ventilation. The trachea was extubated as late as possible (35 minutes after cessation of isoflurane) to ensure that the swallowing reflex was strong. Haemoglobin oxygen saturation was 96% on room air before the pig was moved into its pen to continue active warming 25 minutes later (rectal temperature 35.0°C). No signs of laryngeal obstruction in this initial recovery period were observed following extubation. Shortly after, the pig was quiet, alert and responsive, and was moving around the pen, urinating spontaneously.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for accumulation of fluid in the oropharynx:

- Pulmonary oedema
- Regurgitation
- Vomiting
- Hypersalivation

Due to the clear, nonviscous appearance, continued production and collection within the ETT, pulmonary oedema is the most likely diagnosis.

OUTCOME AND FOLLOW-UP

Two hours after returning to its pen, the pig developed severe dyspnoea and cardiopulmonary arrest. The pig received cardiopulmonary resuscitation with thoracic compressions, and the trachea was intubated to allow manual ventilation. Upon tracheal intubation, a large volume of clear liquid poured out of the endotracheal tube, which was actively suctioned, suggesting the worsening progression of pulmonary oedema. The interventions were

not successful; the pig died. As the owners declined postmortem examination, no further investigations into the cause of the pulmonary oedema were possible.

DISCUSSION

Pulmonary oedema has been reported in pigs relating to viral diseases (Porcine circovirus-associated disease[6]), toxic challenges (fumonisin B1, bracken[7–9]), exposure to chlorine gas[10] and after intense exercise.[11] Delayed dyspnoea has been reported in pigs[5]; however, there are no case reports of pulmonary oedema development in pigs following anaesthesia. Due to the lack of postmortem examination, the underlying cause of the presumed pulmonary oedema can only be hypothesised. An important consideration is that the oedema was limited to the lungs with no signs of free fluid in the abdomen or peripheral oedema. In hindsight, although quality may have been poor due to the size of the animal, thoracic radiography or ultrasonography should have been performed before or during the second anaesthetic. Although an improvement in respiratory rate and pattern was observed after a reduction in fluid therapy and antibiotic administration, upon induction, it was evident complete resolution had not occurred. Imaging may have better characterised the severity of the disease and helped to guide clinical decision-making. In addition, clinical knowledge of pulmonary oedema would have justified delaying or avoiding the second surgical intervention.

Pulmonary oedema can be multifactorial in nature, complicating treatment options.[12] The two main forms of pulmonary oedema are high-pressure oedema caused by increased pulmonary capillary hydrostatic pressure and increased permeability oedema caused by damage of the microvascular barrier allowing leakage of fluid.[12]

High-pressure oedema is most commonly associated with left-sided heart failure.[12] This can be secondary to structural changes, ischaemic damage or congenital defects. Congenital cardiac malformations[13] and acquired diseases, such as hypertrophic cardiomyopathy,[14] have been documented in pigs; however, in this case there was no audible murmur to suggest these conditions. Bradyarrhythmia was observed during the first anaesthetic, and in humans, acute left-sided heart failure is a well-reported sequela following acute myocardial infarction.[15] Although a diagnostic ECG was not conducted, no gross abnormal ECG changes were visible after these episodes. This means ischaemic damage to the heart is an unlikely cause, but it cannot be totally excluded.

Fluid overload or fluid retention will also increase hydrostatic pressure within the pulmonary circulation, which can lead to pulmonary oedema.[12] Similarly, if oncotic pressure that opposes the hydrostatic pressure is reduced, such as in hypoalbuminaemia, the net movement of fluid out of the vasculature will be greater. Fluid therapy is considered a risk factor for animals with cardiac disease[12] and has been linked to pulmonary oedema development during feline anaesthesia.[16] In this case, a reduction in respiratory rate and effort was noted following a reduction in IVFT rate, but not complete resolution. Therefore, fluid therapy is likely to have contributed to, but is unlikely to be the sole cause, of pulmonary oedema due to the ongoing presentation. Hypoalbuminaemia was not present in this case.

On admission, urea and creatinine were mildly elevated, with potassium in the normal range. Changes were suspected to be post-renal and as the patient was dribbling urine, only a partial obstruction was expected. In hindsight, bloods should have been rechecked before the anaesthetic. Following the bradyarrhythmia during the first anaesthetic, blood results indicated a marked increase in potassium, urea and creatinine. At the time, this was related to the urethrolith; however, upon reflection this could have indicated a renal component. Acute kidney injury (AKI) is associated with a number of pulmonary conditions, of which pulmonary oedema and acute respiratory distress syndrome (ARDS) are the most common in humans.[17] Oedema as a result of AKI, usually manifests as generalised oedema, associated with hypoalbuminaemia,[17,18] altered capillary permeability, volume overload[17] and inflammatory cell infiltration.[19] Although urine output was maintained during hospitalisation, AKI could have occurred and could explain the less-than-expected improvement in the azotaemia following the tube cystotomy. Fluid retention secondary to renal damage could therefore have contributed to the pulmonary oedema.

Due to the limited number of licensed drugs for food-producing animals, xylazine was used in this case to provide good sedation and muscle relaxation, despite its associated bradycardia and diuretic effect. Xylazine has been linked to bradycardia and arrhythmias in a variety of species,[20,21] and therefore is likely to have contributed to the bradyarrhythmia in the first anaesthetic, especially in the presence of the hyperkalaemia that was subsequently identified. In addition, pulmonary oedema secondary to $\alpha 2$-agonists have been reported in cats and sheep.[22,23] In sheep, dose-dependent respiratory depression has been described, with animals becoming hypoxaemic and cyanotic (PaO_2 30–50 mmHg), but without concurrent hypercapnia.[1] These changes have been attributed to pulmonary hypertension, increased transpulmonary pressures and increased shunt fraction, related to alterations to pulmonary parenchyma from pulmonary oedema.[2] In rats and sheep, xylazine administration was associated with thinning of the alveolar endothelium,[24,25] and its effect may derive from cytokine-induced granulocyte activation.[26] Thus, $\alpha 2$-adrenoreceptor agonists contribute to both hydrostatic and increased permeability oedema formation.

In the management of the bradyarrhythmia in this case, calcium gluconate was administered to stabilise the myocardium, and anticholinergics and epinephrine were used to treat bradyarrhythmia. The use of epinephrine to treat the life-threatening bradyarrhythmia will also have helped to address the hyperkalaemia by driving potassium intracellularly.[27] In small animal medicine, atipamezole and insulin-dextrose infusions might also have been initiated in animals with hyperkalaemia[28]; however, licensing in food-producing animals has to be considered. Alkalising fluids and sodium bicarbonate can be used for cases where acidaemia is also present.[28,29] Resolution of the underlying cause of hyperkalaemia was the primary aim, hence the tube cystotomy was performed to bypass the obstruction in this case. One important consideration is that albeit 90 minutes after xylazine, atropine was administered without antagonising the xylazine with atipamezole. This may have exacerbated pulmonary hypertension, which could have contributed to the development of pulmonary oedema. Xylazine was avoided for the second anaesthetic.

Increased permeability oedema causing acute lung injury or ARDS has multiple potential causes. These can be the pulmonary manifestations of acute systemic inflammatory disorders, such as systemic inflammatory response syndrome (SIRS)[30] and AKI.[7] Alternatively, they can be the local inflammatory mechanisms secondary to inhaled allergens or the aspiration of regurgitated or vomited material.[31]

During hospitalisation, the pig vomited twice and therefore aspiration could have occurred and initiated an inflammatory exudative response in the lung.[31] Excessive activation of pro- and anti-inflammatory mediators can result in an exacerbated systemic immune response and the development of ARDS[31] and SIRS. These two conditions often present simultaneously, because the unregulated inflammatory response damages, and may even destroy, type I and type II alveolar epithelial cells.[30] Damage to the alveolar–capillary membrane increases its permeability and is associated with recruitment of neutrophils into the airspace. The resulting acute inflammatory exudate inactivates surfactant, leading to collapse and consolidation with progressive loss of functioning lung.[32] In addition, the inflammatory process inhibits the hypoxic pulmonary vasoconstriction mechanism, which is present in normal lung to prevent ventilation–perfusion mismatch. Under inhalational general anaesthesia, this mechanism is also inhibited.[33,34] The lack of this mechanism means that patients with ARDS are considerably more hypoxaemic than those with heart failure with similar radiographic appearances.[32] ARDS is the most severe form of increased permeability oedema, and clinical experience suggests that survival in veterinary species is low.[12] In this case, aspiration pneumonia may have indeed complicated matters and contributed to the development of pulmonary oedema.

The pig was tachycardic (150–170 breaths per minute) and hypothermic (35.0°C) during the second anaesthetic, which satisfies two of the four criteria for SIRS diagnosis in humans.[35] Porcine septic shock is associated with an increase in mean pulmonary artery pressure and pulmonary vascular resistance,[36] and pigs are sensitive to sepsis-induced capillary leak. Therefore, pulmonary oedema is a very common sequela of sepsis in pigs.[36] Although, the pig was normotensive on oscillometric blood pressure, which is unusual in SIRS, it may still be a contributing factor in this case.

Difficulties with arterial catheterisation and the lack of arterial blood gas analysis and invasive blood pressure monitoring makes definitive conclusions about the aetiology of the tachycardia difficult. Lack of response to analgesics, elevated haematocrit and increasing lactate on venous blood samples could indicate relative hypovolaemia, poor perfusion and anaerobic cellular respiration. Decreased oxygen diffusion across the alveolar–capillary membrane due to the pulmonary oedema would result in reduced PaO_2 despite a high FIO_2. Although haemoglobin oxygen saturation was >95% after IPPV initiation, the decreased oxygen content of the blood, coupled with hypovolaemia and poor perfusion, would decrease oxygen delivery to tissues and may have contributed to the tachycardia.[37]

Fluid therapy was conservative due to the pulmonary oedema and colloids were avoided. Although they would increase the colloid oncotic pressure within the vasculature and contribute to volume expansion, severe disruption to the endothelium can occur in critically ill patients,[38] risking colloids leaking into the pulmonary parenchyma.

Direct injury to the alveolar membranes following inappropriate ventilation (ventilator-induced lung injury[39]) or low alveolar pressure (laryngeal obstruction[3,40]) have been reported in veterinary species. The pig was not mechanically ventilated in the first anaesthetic and is therefore an unlikely cause. However, pigs are susceptible to laryngeal obstruction.[41] Delayed dyspnoea after endotracheal intubation has been reported in pigs,[5] with laryngeal oedema identified on postmortem examination. Laryngeal obstruction was not observed in this pig following extubation in the first anaesthetic, and increases in respiratory rate and effort were slow and progressive over 2 days. However, signs in sedated animals can be subtle and although not perceived, complete or partial obstruction cannot be ruled out. If it had occurred after premedication for the second anaesthetic, it could explain the large volumes of fluid that were subsequently identified at induction, which previously clinically presented as only mild changes. This would be particularly exacerbated, if underlying pulmonary changes for other reasons (aspiration, inflammation, pulmonary hypertension, fluid overload, sepsis) were already present.

Management of pulmonary oedema should be targeted to the underlying cause; however, the multifactorial nature of pulmonary oedema development makes this very challenging.[12] A reduction in pulmonary capillary pressures can be beneficial to both pathophysiological forms, and the use of diuretics and vasodilators has been described.[12] Furosemide is one of the first-line treatments for high-pressure oedema.[12] In addition to diuresis, furosemide also acts as a pulmonary venodilator and bronchodilator and causes an increase in colloid oncotic pressure secondary to haemoconcentration.[42–44] Response to furosemide treatment is more profound with cardiogenic pulmonary oedema, although it can be beneficial in non-cardiogenic cases.[12] The pig had shown an initial response to the furosemide administration; however, higher doses could have been used. In small animal veterinary medicine, furosemide has been used more aggressively in animals with severe cardiogenic pulmonary oedema, with doses of 6 mg/kg and dosing by infusion reported.[45] Nitric oxide donors, such as nitroprusside and nitroglycerin, have also been used to cause arteriodilation and venodilation in cases of high-pressure oedema.[12] In humans, bronchodilators have been associated with worse outcomes[46]; however, clenbuterol has successfully been used as an adjunctive therapy in the management of pulmonary oedema in a horse.[4]

In humans, stabilisation of patients with ARDS includes positive-pressure ventilation.[47] This would explain the improvement in SpO_2 and reduced fluid production after IPPV initiation, as well as the deterioration following cessation of ventilation in this case. The addition of positive end expiratory pressure (PEEP) is associated with better oxygenation,[48] as it prevents alveolar collapse, thereby increasing functional residual capacity and recruiting previously unventilated alveoli.[49] Unfortunately, the ventilator available in this case was not able to provide this function and therefore progressive alveoli collapse could also have exacerbated the decrease in surface area for diffusion. Despite the pig maintaining haemoglobin oxygen saturation on room air

during recovery, oxygen supplementation should have been considered to increase arterial oxygen content and tissue oxygen delivery, especially as the oxygen demand increased as the pig started moving around.

In conclusion, this case report describes pulmonary oedema in a pig following general anaesthesia. The definitive cause of the oedema could not be ascertained, and is likely multifactorial. Its progression may have been exacerbated by the potentially concomitant renal dysfunction, fluid overload, aspiration pneumonia and possible sepsis. The occurrence of laryngeal obstruction must also be considered as a contributing factor. The lack of arterial catheterisation limited the information available from invasive monitoring, which may have highlighted the need for alternative management of ventilation and blood pressure. In cases of respiratory dysfunction, preanaesthetic thoracic imaging may help to classify the severity of the changes and guide clinical decision-making.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a review article with no original research data. Permission for publication was gained in the form of written owner's consent.

FUNDING INFORMATION

The authors received no specific funding for this work.

ORCID

Kate Walters https://orcid.org/0000-0003-3029-0187
Eleonora Po https://orcid.org/0000-0002-9777-6707

REFERENCES

1. Doherty TJ, Pascoe PJ, McDonell WN, Monteith G. Cardiopulmonary effects of xylazine and yohimbine in laterally recumbent sheep. Can J Vet Res. 1986;50(4):517–21.
2. Celly CS, McDonell WN, Young SS, Black WD. The comparative hypoxaemic effect of four alpha 2 adrenoceptor agonists (xylazine, romifidine, detomidine and medetomidine) in sheep. J Vet Pharmacol Ther. 1997;20(6):464–71.
3. Senior M. Post-anaesthetic pulmonary oedema in horses: a review. Vet Anaesth Analg. 2005;32:193–200
4. Melis S, Schauvliege S, Bosmans T, Gasthuys F, Polis I. Pulmonary edema as a postoperative complication in two obese patients (a horse and a dog). Vlaams Diergen Tijds. 2014;83:60–5.
5. Murison PJ. Delayed dyspnoea in pigs possibly associated with endotracheal intubation. Vet Anaesth Analg. 2001;28(4):226.
6. Cino-Ozuna AG, Henry S, Hesse R, Nietfeld JC, Bai J, Scott HM, et al. Characterization of a new disease syndrome associated with porcine circovirus type 2 in previously vaccinated herds. J Clin Microbiol. 2011;49(5):2012–6.
7. Osweiler GD, Ross PF, Wilson TM, Nelson PE, Witte ST, Carson TL, et al. Characterization of an epizootic of pulmonary edema in swine associated with fumonisin in corn screenings. J Vet Diagn Invest. 1992;4(1):53–9.
8. Colvin BM, Harrison LR. Fumonisin-induced pulmonary edema and hydrothorax in swine. Mycopathologia. 1992;117:79–82.
9. Harwood DG, Palmer NM, Wessels ME, Woodger NG. Suspected bracken poisoning in pigs. Vet Rec. 2007;160(26):914–5.
10. Gunnarsson M, Walther SM, Seidal T, Bloom GD, Lennquist S. Exposure to chlorine gas: effects on pulmonary function and morphology in anaesthetised and mechanically ventilated pigs. J Appl Toxicol. 1998;18(4):249–55.
11. Schaffartzik W, Arcos J, Tsukimoto K, Mathieu-Costello O, Wagner PD. Pulmonary interstitial edema in the pig after heavy exercise. J Appl Physiol. 1993;75(6):2535–40.
12. Adamantos S, Hughes D. Pulmonary edema. In: Silverstein DC, Hopper K, editors. Small animal critical care medicine. Canada: Saunders Elsevier; 2009. p. 86–97.
13. Hsu FS, Du SJ. Congential heart disease in swine. Vet Pathol. 1982;19:676–86.
14. Liu SK, Chiu YT, Shyu JJ. Hypertrophic cardiomyopathy in pigs: quantitative pathologic features in 55 cases. Cardiovasc Pathol. 1994;3(4):261–8.
15. Weir RA, McMurray JJ, Velazquez EJ. Epidemiology of heart failure and left ventricular systolic dysfunction after acute myocardial infarction: prevalence, clinical characteristics, and prognostic importance. Am J Cardiol. 2006;97(10A):13F–25F.
16. Brodbelt DC, Pfeiffer DU, Young LE, Wood JLN. Risk factors for anaesthetic-related death in cats: results from the confidential enquiry into perioperative small animal fatalities (CEPSAF). Br J Anaesth. 2007;99(5):617–23.
17. Presberg KW, Effros RM. Pulmonary edema and other disorders in acute renal failure. In: Critical care nephrology. Dordrecht: Springer; 1998. p. 1037–44.
18. Bobkova I, Chebotareva N, Kozlovskaya L, Shilov E. Edema in renal diseases – current view on pathogenesis. Nephrology. 2016;2(1):e47–55.
19. Klein CL, Hoke TS, Fang WF, Altmann CJ, Douglas IS, Faubel S, et al. Interleukin-6 mediates lung injury following ischemic acute kidney injury or bilateral nephrectomy. Kidney Int. 2008;74:901–9.
20. Schumann R. Xylazine is known to cause arrhythmias in several species. Lab Anim Sci. 1992;42(5):434.
21. Gómez de Segura IA, Tendillo FJ, Mascías A, Santos M, Castillo-Olivares JL, Steffey EP. Actions of xylazine in young swine. Am J Vet Res. 1997;58(1):99–102.
22. Kästner SB. A2-agonists in sheep: a review. Vet Anaesth Analg. 2006;33(2):79–96.
23. Raekallio MR, Virtanen M, Happonen I, Vainio OM. Adverse reactions of α_2-adrenoceptor agonists in cats reported in 2003–2013 in Finland. Vet Anaesth Analg. 2017;44(4):803–10.
24. Amouzadeh HR, Qualls CW, Wyckoff JH, Dzata GK, Sangiah S, Mauromoustakos A, et al. Biochemical and morphological alterations in xylazine-induced pulmonary edema. Toxicol Pathol. 1993;21(6):562–71.
25. Celly CS, Atwal OS, McDonell WN, Black WD. Histopathologic alterations induced in the lungs of sheep by use of alpha2-adrenergic receptor agonists. Am J Vet Res. 1999;60(2):154–61.
26. Stephens KE, Ishizaka A, Larrick JW, Raffin TA. Tumor necrosis factor causes increased pulmonary permeability and edema. Am Rev Resp Dis. 1988;137:1364–70.
27. Moratinos J, Reverte M. Effects of catecholamines on plasma potassium: the role of alpha- and beta-adrenoceptors. Fundam Clin Pharmacol. 1993;7(3–4):143–53.
28. Rioja Garcia E. Urogenital disease. In: Seymour C, de Vries M, Duke-Novakovski T, editors. BSAVA manual of small animal anaesthesia and analgesia. UK: Blackwell; 2016. p. 356–65.
29. Constable PD. Clinical assessment of acid-base status. Strong ion difference theory. Vet Clin North Am Food Anim Pract. 1999;15(3):447–71.
30. Simon RH, Paine R 3rd. Participation of pulmonary alveolar epithelial cells in lung inflammation. J Lab Clin Med. 1995;126:108–118.
31. Raghavendran K, Nemzek J, Napolitano LM, Knight PR. Aspiration-induced lung injury. Crit Care Med. 2011;39(4):818–26.
32. Griffiths M, Proudfoot A. ARDS, up close and personal. Thorax. 2016;71:1073–5.
33. Wang JY, Russell GN, Page RD, Jackson M, Pennefather SH. Comparison of the effects of sevoflurane and isoflurane on arterial oxygenation during one lung ventilation. Br J Anaesth. 1998;81:850–3.
34. Marshall C, Lindgren L, Marshall BE. Effects of halothane, enflurane, and isoflurane on hypoxic pulmonary vasoconstriction in rat lungs in vitro. Anesthesiology. 1984;60:304–8.
35. Comstedt P, Storgaard M, Lassen AT. The systemic inflammatory response syndrome (SIRS) in acutely hospitalised medical patients: a cohort study. Scand J Trauma Resusc Emerg Med. 2009;17:67.
36. Goldfarb RD, Dellinger P, Parrillo J. Porcine models of severe sepsis; emphasis on porcine peritonitis. Shock. 2005;24:75.
37. Kato H, Menon AS, Slutsky AS. Mechanisms mediating the heart rate response to hypoxemia. Circulation. 1988;77(2):407–14.

38. McDermid RC, Raghunathan K, Romanovsky A, Shaw AD, Bagshaw SM. Controversies in fluid therapy: type, dose and toxicity. World J Crit Care Med. 2014;3(1):24–33.
39. Parker JC, Townsley MI, Rippe BE, Taylor AE, Thigpen JA. Increased microvascular permeability in dog lungs due to high peak airway pressures. J Appl Physiol. 1984;57(6):1809–16.
40. Algren JT, Price RD, Buchino JJ, Stremel RW. Pulmonary edema associated with upper airway obstruction in dogs. Pediatr Emerg Care. 1993;9(6):332–7.
41. Mirra A, Arnold M, Casoni D, Gámez Maidanskaia E, Garcia Casalta LG, Levionnois O. Fatal upper airway obstruction in a pig after general anaesthesia. Vet Anaesth Analg. 2022;49:145–6.
42. Luz da PL, Shubin H, Weil MH, Jacobson E, Stein L. Pulmonary edema related to changes in colloid osmotic and pulmonary arterial wedge pressure in patients with acute myocardial infarction. Circulation. 1975;51:350–7.
43. Schuster CJ, Weil MH, Besso J, Carpio M, Henning RJ. Blood volume following diuresis induced by furosemide. Am J Med. 1984;76(4):585–92.
44. Ali J, Chernicki W, Wood LD. Effect of furosemide in canine low-pressure pulmonary edema. J Clin Invest. 1979;64(5):1494–504.
45. Filipejová Z, Agudelo Ramírez CF, Crha M. Comparison of continuous versus intermittent furosemide administration in dogs with acute heart failure. Acta Vet Brno. 2016;85:239–45.
46. Matthay MA, Brower RG, Carson S, Douglas IS, Eisner M, Hite D, et al. Randomized, placebo-controlled clinical trial of an aerosolized beta-2 agonist for treatment of acute lung injury. Am J Respir Crit Care Med. 2011;184(5):561–8.
47. Hashimoto S, Sanui M, Egi M, Ohshimo S, Shiotsuka J, Seo R, et al. The clinical practice guideline for the management of ARDS in Japan. J Intensive Care. 2017;5:50.
48. Villar J. The use of P.E.E.P. in the treatment of A.R.D.S. In: Matalon S, Sznajder JL, editors. Acute respiratory distress syndrome. NATO ASI series (Advanced Science Institutes Series). Vol 297. Boston, MA; Springer; 1998. p. 265–74.
49. Falke KJ, Pontoppidan H, Kumar A, Leith DE, Geffin B, Laver MB. Ventilation with end-expiratory pressure in acute lung disease. J Clin Invest. 1972;51:2315–23.

How to cite this article: Walters K, Brearley J, Baptista A, Po E. Suspected pulmonary oedema development in a pig following general anaesthesia and the associated complications encountered during a subsequent general anaesthetic. Vet Rec Case Rep. 2022;e333. https://doi.org/10.1002/vrc2.333