Combined pentalogy of Cantrell with ectrodactyly and surgical implant-free repair of a sternal cleft and supraumbilical hernia in an adult cat

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TITLE OF CASE ***Do not include "a case report"***

Combined Pentalogy of Cantrell with ectrodactyly and surgical implant-free repair of a sternal cleft and supraumbilical hernia in an adult cat.

SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

A 20-month-old British shorthair cat was presented for treatment of a ventral thoracic wall defect. Physical examination showed cleft sternum with supraumbilical body wall defect, an immediately palpable heart under the skin between the cleft halves and a unilateral forelimb ectrodactyly. Survey radiographs and sonographic examination revealed ectopia cordis associated with the sternal cleft, a supraumbilical abdominal hernia, ventral diaphragmatic defect, and cardiac abnormalities. Radiography of the dysostotic limb confirmed ectrodactyly. Surgery involved reconstruction of the ventral body wall defects using a transversus abdominis muscle flap supported by an omental flap. Clinical, imaging and intraoperative findings supported the diagnosis of complete PoC. The cat recovered from surgery uneventfully and periodic follow-ups to seventeen months post surgery confirmed a good outcome.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Pentalogy of Cantrell (PoC) is an infrequent but well recognized congenital condition in people, with an incidence of 5.5-7.9 per million live births[1] and approximately 207 reported human cases by 2011.[2] It is defined as the presence of (1) a defect of the inferior sternum; (2) a midline supraumbilical abdominal wall defect; (3) a congenital intracardiac anomaly; (4) a deficit of the anterior diaphragm; and (5) a defect in the diaphragmatic pericardium.[3] Criteria for complete and incomplete PoC have been described.[4] Complete or Class 1 PoC is where all five defects are present, incomplete can be Class 2 where four defects are present or Class 3 where three defects exist. In veterinary medicine, incomplete PoC (Class 3) has been reported in four occasions: an adult cat,[5] two puppies[6-7] and a calf.[8] To our knowledge, a case of complete PoC has not been reported in veterinary medicine to date.

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Congenital skeletal anomalies such as ectrodactyly arise from errors during foetal development and are characterized by abnormal growth of individual bones or parts of bones.[9] Comparable congenital hand anomalies are reported in people[10-11] and in several veterinary species.[12] Ectrodactyly (ektroma = abortion; dactylos = digit) is a congenital digital cleft malformation extending between the metacarpal bones.[12] Ectrodactyly has been described in cats and dogs but is considered rare.[12-15]

The purpose of the case reported here is to describe the clinical and diagnostic imaging findings, surgical approach and outcome in the case of a cat with complete Pentalogy of Cantrell and concomitant unilateral forelimb ectrodactyly.

CASE PRESENTATION ***Presenting features, clinical and environmental history***

A 7kg, 20-month-old neutered male British Shorthair cat was referred with ventral thoracic and abdominal wall defects, initially suspected to be pectus excavatum. He also had left forelimb deformity consistent with ectrodactyly. Other than intermittently visible but readily reducible cranial abdominal hernia and the directly palpable heart under the skin, no significant clinical signs or concerns were reported about the cat's quality of life.

On physical examination the cat was bright, responsive and in generous body score condition (6 out of 9). A large defect was palpable along the caudoventral thoracic wall and cranioventral abdomen. Only the cranial third of the sternum was identifiable. The heart was immediately palpable subcutaneously within this body wall defect; however, the heart rate and rhythm appeared normal despite the displacement. Respiratory rate and effort were normal. The left forepaw had ectrodactyly with absence of normal weight-bearing pads on the underside of the two modified digits present. There was a soft tissue cleft between the two large digits, both of which were rotated medially with minimal webbing between. Lameness was neither seen during examination nor reported in the history (**Video 1**).

INVESTIGATIONS ***If relevant***

Orthogonal radiographic views of the chest, abdomen and deformed limb were taken under general anaesthesia prior to surgery. These revealed a midline defect of the sternum (sternal cleft or bifid sternum) extending from the second sternebra caudally **(Figure 1)**. The cardiac silhouette was displaced ventrally (ectopia cordis) through this defect (**Figure 1**). Although cardiac displacement impeded assessment of the cardiac silhouette this appeared moderately enlarged. The cardiac silhouette was separated from the hepatic silhouette by a large fat opacity in all projections. A small (~1.5cm) defect in the ventral abdominal wall was seen through which some abdominal viscera herniated (**Figure 1**). Radiographic evaluation of the left forelimb showed a parasagittal defect in the paw extending to the carpal bones, which were themselves incompletely formed (**Figure 2**).

Echocardiographic examination was performed by visualising the heart through the caudal sternal cleft. In dorsal recumbency the heart was visible immediately under the skin, sitting adjacent to the liver and a diaphragmatic defect. In sternal recumbency, the heart appeared normally located in the mediastinum. The heart was highly mobile with postural changes, showing both sliding and rotating movements. Both ventricles presented a transverse hyperechoic intracardiac septum (incomplete in the left ventricle) at the distal part of the chamber (**Figure 3**). The mitral and tricuspid valves were within normal limits. There was subvalvular aortic stenosis and the valve appeared bicuspid. Lastly, dextroposition of the aorta was found. No subjective signs of heart failure were detected. Due to financial constraints and the absence of relevant clinical signs, advanced imaging was not performed. Considering the clinical and imaging findings the criteria for provisional diagnosis of an incomplete PoC (Class 2) were met, in addition to the left forelimb ectrodactyly.

DIFFERENTIAL DIAGNOSIS ***If relevant***

n/a

TREATMENT ***If relevant***

Surgery followed diagnostic imaging investigations. Financial constraints on the case meant that costly surgical implants or meshes could not be used, so a method of reconstruction was devised that used only autologous tissues.

The cat was classified in the American Society of Anaesthesiologists Class IV anaesthetic risk category. Premedication comprised of medetomidine (2 mcg/kg IV) and methadone (0.2 mg/kg, IV), and anaesthesia was induced with propofol (3.5 mg/kg IV) and maintained with isoflurane in oxygen. Isotonic crystalloid fluids and intraoperative analgesia with constant rate infusion of ketamine (10 mcg/kg/min IV) and fentanyl (10 mcg/kg/h IV)

were also administered. Intermittent positive pressure ventilation was used throughout anaesthesia. With the patient in dorsal recumbency, the heart was easily obvious beating under the skin of the sternal defect (**Video 2**). A ventral midline skin incision was made extending caudally from the bifurcation of the sternum taking great care to avoid trauma to the heart, which was identified immediately subcutaneous with no other tissue interposed between heart and skin. The hemi-sternebrae along each side of the sternal cleft were deformed in shape creating inward rotation of both "arms" of the cleft. A ventral diaphragmatic defect was identified along with peritoneopericardial diaphragmatic communication, likely obscured on diagnostic imaging by a large amount of fat in the falciform ligament. The pericardium was attached directly to the ventral thoracic wall along each side of the sternal cleft, creating a dome of pericardium covering the dorsal but not the ventral heart (**Figure 4**).

Visual examination of the abdominal cavity revealed an anatomically abnormal liver, distinctly split into a bilobed structure along midline, a bilobed gallbladder and increased distance between the kidneys and the adrenal glands. The rest of the abdomen was grossly unremarkable.

The sternal cleft could be reduced by applying traction, but the reduction in pericardial sac size induced led to visible cardiac constriction. The pericardium was therefore detached from the sternal cleft on each side and left as an incomplete pericardium, analogous to a subtotal pericardiectomy. When drawn together towards midline the deformed "arms" of the sternal cleft also jutted sharply into the caudal pleural space where they pressed into adjacent myocardium creating potential myocardial irritation. Therefore, the decision was made to remove these deformed sternebrae using a rongeurs and reconstruct a caudoventral thoracic body wall using omentum and muscle. The omentum was drawn cranially to cover the thoraco-abdominal defect and sutured in place to provide an inner layer (**Figure 5**). A transversus abdominis muscle flap was placed over the omentum to simultaneous reconstruct the caudal thoracic body wall defect and the ventral diaphragmatic defect. The pectoral muscles on each side were then sutured to the muscle flap to complete thoracic wall reconstruction. The coeliotomy wound was closed in a routine manner in three layers. A 7-inch wound diffusion catheter was placed subcutaneously before closure as part of planned multimodal postoperative analgesia. Residual air was drained from the thoracic cavity via butterfly catheter to restore negative pressure.

OUTCOME AND FOLLOW-UP

The cat recovered from anaesthesia in a warmed and oxygen-enriched incubator. Open mouth breathing and mild tachypnoea were seen during early recovery, but these resolved after a further 2-hour oxygen supplementation. The cat was hospitalized for two

days for multimodal analgesia and monitoring before discharge. During hospitalization, the cat received ketamine in a constant rate infusion (5 mg/kg/h IV) for the first 24 hours, instillation of bupivacaine 0.5% (0.5mg/kg) through the wound diffusion catheter every 6 hours and methadone (0.2 mg/kg IV) according to pain scoring[16] for 48 hours. Meloxicam was also initiated following surgery (0.2 mg/kg subcutaneously) followed by 5-day oral administration (0.05 mg/kg) once daily.

Limited funds did not allow physical re-examination of our patient postoperatively. On telephone consultations with the owner up to seven months after surgery, the cat was reported to have recovered completely and returned uneventfully to a normal routine. Seventeen months postoperatively, the cat was reported to develop acute kidney injury of unspecified aetiology and was humanely euthanized after short hospitalization at the primary veterinary practice. No other concerns were raised by the owner up to that stage.

DISCUSSION *Include a very brief review of similar published cases*

This case study reports a cat with PoC and concurrent left forelimb ectrodactyly, as well as the successful surgical correction of the PoC-associated body wall defects. The additional pericardial defect found intraoperatively supported the diagnosis of a complete (Class 1) PoC. To the authors' knowledge this is the first reported case of complete PoC in veterinary medicine literature which also receives reconstructive treatment with autologous tissue.

PoC is a congenital syndrome seen sporadically in people[1] and extremely rarely in veterinary medicine.[5-8] If all five anomalies that define the complete form of PoC are not present, then incomplete PoC exists, with the class determined by the number of abnormalities present.[4] The combination and severity of the defects found are sometimes incompatible with life with neonates delivered stillborn, while others require early surgical correction. Overall, the associated mortality rate is high (up to 73%).[2] The syndrome affects males more often (ratio 1.35-2:1)[2, 17-18]; it is impossible though to determine sex predilection in veterinary patients due to lack of sufficient case numbers across affected species.

Occasionally, individual components of PoC are reported in cats,[19-22] but as a syndrome PoC has only been reported once to date, in an incomplete form, in an adult female.[5]

Further to the defined pentad of signs, in up to 28% of cases other congenital deformities are also seen with PoC in humans[4, 18, 23] and these involve mainly thoracic and abdominal organs but also craniofacial and limb anomalies.[18] In veterinary medicine, a dog with incomplete PoC had concurrent patent ductus arteriosus[6] and a calf was reported with concurrent Taussig-Bing syndrome.[8] The abnormalities we saw in various abdominal organs in our case i.e. split liver and bilobed gallbladder, could potentially be explained by

an underlying failure of normal coelomic midline development. In people, PoC-related anomalies are thought to result from a failure of normal development in early embryonic life. Specifically, they relate to failure of normal development of the transverse septum of the diaphragm and ventromedial migration of the paired mesodermal folds of the upper abdomen.[3] In cats, PoC anomalies are thought to occur between days 19 and 28 of gestation from a series of errors in the conformational fusion process.[24]

Although rare in cats, ectrodactyly is usually unilateral and affects only the thoracic limb.[12-15] Clinical signs of deformity and lameness may progress with age, even if the malformation has been present since birth.[12] A combination of PoC with ectrodactyly, as seen in our case, has been reported in people[25] but not, to date, in cats. Although our cat had an unusual forelimb gait there was no impact on mobility or quality of life. However, due to the young age at presentation the possibility of developing associated orthopaedic signs in the future could not be ruled out. Causes of ectrodactyly can be hereditary[13] via an autosomal dominant defect with variable expression but no apparent breed or sex predilection (primarily abnormal developmental process) or environmental[12] (interference with a primarily normal developmental process). A trigger that would cause genetic errors during organogenesis and organ differentiation, apart from the PoC-related defects, could explain the concurrent limb deformity and abdominal organs malformation seen in our case.

The cat previously reported with incomplete PoC in the veterinary literature had successful surgical correction of its body wall defects using metallic mesh combined with porcine small intestinal submucosa.[5] The authors reported good outcome three months postoperatively. The use of similar surgical implants to reconstruct the body wall defects was precluded in our case due to financial constraints, although it would have carried the hypothetical advantage of creating a more rigid body wall to provide greater cardiac protection. There is, however, another case report in the veterinary literature that describes a pregnant cat with sternal cleft, peritoneopericardial hernia and a large abdominal wall hernia that could also be consistent with incomplete PoC, although the authors did not identify it as such.[26] Surgical treatment in the latter case used autologous tissues with a good outcome, suggesting that autologous tissue repair could be adequate for our patient.

Simple direct apposition of sternal cleft crura is an option where the diagnosis is made at a sufficiently young age. During the first few months of life, the sternal cleft can be easily closed due to the elasticity and relative expandability of young cartilage compared to the adult bony chest wall.[27] Caudal sternal clefts in a 4-month and a 5-month old puppies with incomplete PoC and as an isolated defect in a 2-month-old kitten were closed using direct primary approximation of the sternal halves using crimped monofilament nylon lines,

stainless steel monofilament wire and absorbable monofilament sutures, respectively.[6-7, 20] A limiting factor may be where direct primary closure causes reduced abdominal and/or thoracic domain with significantly increased intra-compartmental pressure, as this is poorly tolerated in the presence of severe cardiac malformations in people with PoC.[18] In our patient, the sternal cleft could be significantly reduced but deformity of the "arms" meant that this caused potentially clinically significant ventral thoracic wall abnormality and myocardial compression. Therefore, the deformed hemivertebrae (sternebrae 4 caudally) were removed and an alternative method used to reconstruct the body wall defect.

PoC has been described only in the last decade in small animal medicine[5-7]; this could suggest previous underreporting of recognized cases or failure to recognize this rare syndrome among veterinary patients. It may also be that severely affected animals die or are euthanized without veterinary intervention. Ectrodactyly, likewise, may not always be reported if there is no significant impingement on mobility.

Our cat was a purebred British shorthair, meaning a more limited genetic pool, so the possibility of a breed related abnormality could be considered. Unfortunately, no information was available about the siblings although the parents were described as "normal". The patient recovered from surgery uneventfully and on periodic communication with the owner the cat resumed a normal routine thereafter. Unfortunately, the cat was euthanized 17 months later due to acute kidney failure of unspecified aetiology. Although it cannot be confirmed, and no abnormalities were identified during diagnostic evaluations prior to surgery, an underlying structural anomaly of renal function cannot be ruled out.

This case report has several limitations, some of which were unfortunately related to the tight financial constraints. Other limitations include the absence of advanced imaging pre-operatively and the lack of post-operative imaging documenting resolution of the abdominal wall defects and ectopia cordis. A computed tomography scan prior to surgery would have given a more complete image of the anomalies present and potentially could have detected additional abnormalities. Ideally, direct physical follow-up examination would have been performed but this information had to be obtained from the owner and referring veterinarian.

This is the first case reporting a complete form of PoC in veterinary medicine successfully repaired with autologous tissue. This case shows that surgical treatment of adult feline patients with a good outcome is feasible without primary closure of the sternal cleft and also without necessarily using surgical implants. The use of autologous over non-autologous tissue has a cost advantage as well as precludes implant-related complications such as long-term risk of infection and implant migration. It is the hope of the study authors

that this report will add to the current knowledge and help increase clinical awareness of this uncommon condition.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- First report of complete Pentalogy of Cantrell in veterinary medicine and increase awareness of this rare condition.
- Consider autologous tissue to repair congenital body wall defects.
- Use of a transversus abdominis muscle flap to close a caudo-ventral thoracic wall defect.

CONFLICT OF INTEREST STATEMENT ***Required. A statement should be included even if there are no conflicts of interest to declare (e.g., "The author(s) declare(s) they have no conflicts of interest.")***

The authors declare no conflict of interest related to this report.

ETHICS STATEMENT ***Required. A statement explicitly describing the ethical background to this study and any institutional or national ethical committee approval must be included within the manuscript.***

All the investigations and treatments were performed as necessary for the patient's best interest. Owner's written permission to use images/videos and clinical record for publication and/or educational purposes.

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OWNER'S PERSPECTIVE ***Optional***

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IMAGE QUIZ ***Optional (but highly encouraged) – please provide 1 or 2 sentences to describe one of the images in your article. The "Image quiz" will be published with your article if accepted. Don't forget to indicate which image the quiz relates to***

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MULTIPLE CHOICE QUESTION ***provide one multiple choice question based on the description above (may be "what's the likely diagnosis?")***

POSSIBLE ANSWERS TO MULTIPLE CHOICE QUESTION ***Max 6***

CORRECT ANSWER ***With a brief explanation (the answer will also be linked to the published case)***

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