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Case Report

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Haematomyelia and myelomalacia following an inadvertent thoracic intraspinal injection in a cat

Guillaume F Dutil[1], Daniela Schweizer[2], Anna Oevermann[3], Veronika M Stein[1] and Arianna Maiolini[1]

Abstract

Case summary A 4-month-old cat was presented with acute paraplegia after the referring veterinarian performed a subcutaneous injection (cefovecin and dexamethasone) in the caudodorsal thoracic area, during which the cat suddenly became uncooperative. A complete neurological examination performed 1 day after the injection revealed paraplegia without deep pain perception and reduced segmental spinal reflexes in the pelvic limbs. Findings were consistent with either an L4–S3 myelopathy or a T3–L3 myelopathy with subsequent spinal shock. MRI showed swelling of the spinal cord from T1 to L1 with heterogeneous T2-weighted intramedullary hyperintensity and no contrast enhancement. A centrally located intraspinal signal void was visible in T2*-weighted images. These changes were compatible with a suspected traumatic intraspinal injection. Despite intensive supportive care over 4 days, neurological status did not improve and the cat was euthanased. Gross pathology findings revealed severe intramedullary haemorrhage and myelomalacia in the T10–L1 spinal cord segments. Histopathology of the spinal cord after haematoxylin and eosin staining revealed a severe intramedullary space-occupying haemorrhage with focal malacia. A trajectory-like, optically empty cavity containing some eosinophilic droplets at the edges was detected. Although no further evidence of trauma was noted in the surrounding structures, the spinal cord changes were compatible with a perforating trauma.

Relevance and novel information To our knowledge, this is the first report of thoracic intraspinal injection causing myelomalacia defined by an ante-mortem MRI and confirmed post mortem by histopathology. The traumatic myelopathy appeared to be most compatible with an intraspinal injection causing vascular rupture.

Keywords: MRI; intramedullary; haemorrhage; spinal cord injury; paraplegia; perforating trauma

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Introduction

Parenteral injections are routinely performed in small animal veterinary medicine.[1] Although these procedures are usually safe, there have been reports of accidental damage to the nervous system, such as lesions of the sciatic nerve[2] and of the caudal brainstem,[3] caused by inappropriate routes of administration. This case report describes a detrimental spinal cord injury (SCI) in a cat following an intended subcutaneous (SC) injection in the thoracolumbar paravertebral area.

Case description

A 4-month-old intact male Ragdoll cat living indoors with its breeder was presented to the veterinarian for suspected upper airway infection. The cat was up to date with vaccinations and regularly treated with topical parasiticides. It received an injection of cefovecin (Convenia;

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Table 1 Haematology and serum biochemistry results

	Result	Reference interval
Haematology		
Haematocrit (%)	29	27–47
Erythrocytes ($\times 10^{12}$/l)	6.46	5.29–11.2
Haemoglobin (g/l)	100	82–153
Thrombocytes ($\times 10^{9}$/l)	350	180–430
Leukocytes ($\times 10^{9}$/l)	24.8*	6.5–15.4
Biochemistry		
Sodium (mmol/l)	144	144–159
Potassium (mmol/l)	4.5	3.11–4.93
Chloride (mmol/l)	110	110–126
Calcium (mmol/l)	2.54	2.22–2.92
Total protein (g/l)	95.4*	55–76
Albumin (g/l)	28.9*	30.3–40.5
Immunoglobulin (g/l)	66.5*	24.7–35.5
Urea (mmol/l)	5.37*	6.46–12.2
Creatinine (μmol/l)	32*	52–138
Magnesium (mmol/l)	0.81	0.63–1.27

*Abnormal result

Zoetis) and dexamethasone (Dexadreson; MSD) using a syringe with a 23G × 1″ (0.6 × 25 mm) needle, during which it suddenly became uncooperative. About 50% of the compound (0.3 ml) was injected before the cat became acutely paraplegic. Owing to the immediate onset of severe neurological signs, the first-opinion veterinarian referred the case for further evaluation of possible neurological damage associated with the injection procedure.

At the time of referral, 22 h after the injection, general physical examination revealed an intermittent minimal serous ocular discharge, no sneezing or nasal discharge and mild lymphadenomegaly of the mandibular and superficial cervical lymph nodes with a normal body temperature. Neurological examination revealed a mild obtundation, paraplegia with absent deep pain perception and postural reactions, mildly reduced muscle tone and moderately reduced segmental spinal reflexes in both pelvic limbs. Thoracic limbs did not show any abnormalities and cranial nerve evaluation was normal. Perineal reflex was absent and the urinary bladder was large and turgid. No discomfort was evocable during palpation along the vertebral column. Based on these findings, the neuroanatomical localisation was consistent with either an L4–S3 myelopathy or a T3–L3 myelopathy with subsequent spinal shock. Main differential diagnoses included traumatic intraspinal injection, vertebral trauma, vascular insult or inflammatory disease.

Serial blood pressure measurements were within normal limits. Haematology and serum biochemistry (Table 1) revealed a moderate leukocytosis (24.8×10^{9} cells/l) and a moderate increase of total proteins (95.4 g/l) associated with mildly decreased albumin (28.9 g/l) and a severe increase of immunoglobulins (66.5 g/l). An ELISA for feline leukaemia virus and feline immunodeficiency virus (Test SNAP Combo Plus FIV/FeLV; IDEXX) was negative.

MRI of the thoracolumbar area was performed under general anaesthesia with a 1-Tesla unit (Panorama High Field Open 1.0 Tesla; Philips Medical Systems) 24 h after injection. The patient was premedicated with butorphanol (0.2 mg/kg IV [Torbugesic; Zoetis]) and medeto-midine (0.005 mg/kg IV [Domitor; Provet]), while anaesthesia was induced with propofol (until effect [Propofol 1%; Fresenius Kabi]) for endotracheal intubation and maintained with 2% isoflurane (Forene; AbbVie) in oxygen (60%) and air. MRI revealed a swelling of the spinal cord with attenuation of the cerebrospinal fluid (CSF) signal in the heavily T2-weighted (T2W) fast-spin echo T2 sequence from T1 to L1. The swelling was most severe at the level of the thoracolumbar junction. The spinal cord showed heterogeneous T2W intramedullary hyperintensity (Figure 1a–c) and focal hypointense signal at the level of T10 to L1. In T2*-weighted images, there was an intramedullary signal void extending from T10 to T13 (Figure 1 b′,c′). In T1-weighted (T1W) images, the lesion had slightly heterogeneous signal intensity and did not show any contrast enhancement after intravenous (IV) injection of gadodiamide (0.15 mmol/kg [Omniscan; GE Healthcare]). No notable changes were detected in any intervertebral discs or in the paraspinal muscles (Figure 1a–c).

Although an injection trajectory could not be identified on imaging, the haemorrhagic and oedematous pattern was compatible with the suspected traumatic intraspinal injection. An acute non-compressive nucleus pulposus extrusion (ANNPE) or another traumatic impact of the spinal cord were considered as differential diagnoses. Owing to these findings, an ascending–descending haemorrhagic myelomalacia was suspected.

Analysis of CSF collected from the cerebellomedullary cistern revealed a very mild neutrophilic (71%) pleocytosis (10 leukocytes/μl; reference <8 leukocytes/μl) and a negative Pandy test.

Medical therapy included IV fluid administration (2 ml/kg/h IV [Plasma-Lyte A; Baxter]) for the maintenance of hydration, bethanechol (0.5 mg/kg PO q8h [Myocholine-Glenwood; Glenwood]) and phenoxybenzamine (0.5 mg/kg PO q12h [Phenoxybenzamin-HCl]) for supporting micturition. The urinary bladder was manually voided four times daily and physiotherapy was initiated. The cat was eating well, consuming both wet and dry food. Four days later the cat was euthanased owing to a lack of neurological improvement and poor prognosis.

The spinal cord was removed and immersion-fixed in 10% formalin. Macroscopic examination revealed severe right-sided segmental intramedullary haemorrhage in

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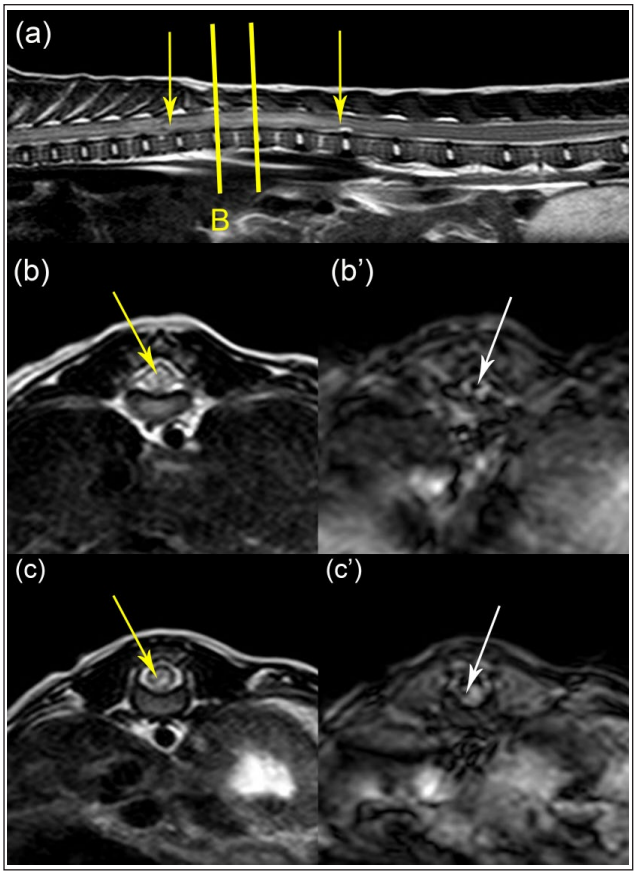


Figure 1 Thoracocolumbar spine of a 4-month-old Ragdoll cat. (a) T2-weighted (T2W) sagittal image. (b) T2W and (b') T2*W transverse images at the level T10–T11. (c) T2W and (c') T2*W transverse images at the level T11–T12. Note the heterogeneous hyperintense signal of the spinal cord in both sagittal and transverse T2W images (yellow arrows in a–c). (b',c') On both T2*W images, the white arrows are pointing towards a susceptibility artefact within the spinal cord, indicating intramedullary haemorrhage

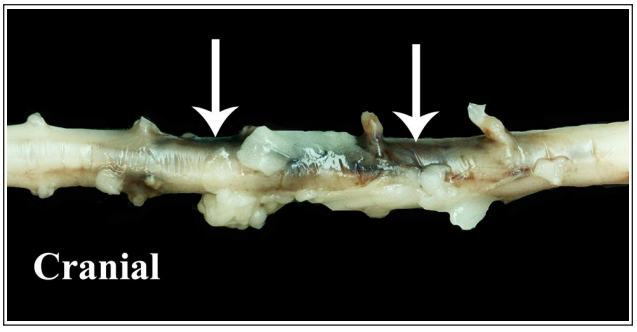


Figure 2 Macroscopic dorsal view of formalin-fixed spinal cord of a 4-month-old Ragdoll cat. Note the severe right-sided segmental haemorrhage and myelomalacia from T10 to L1 (white arrows)

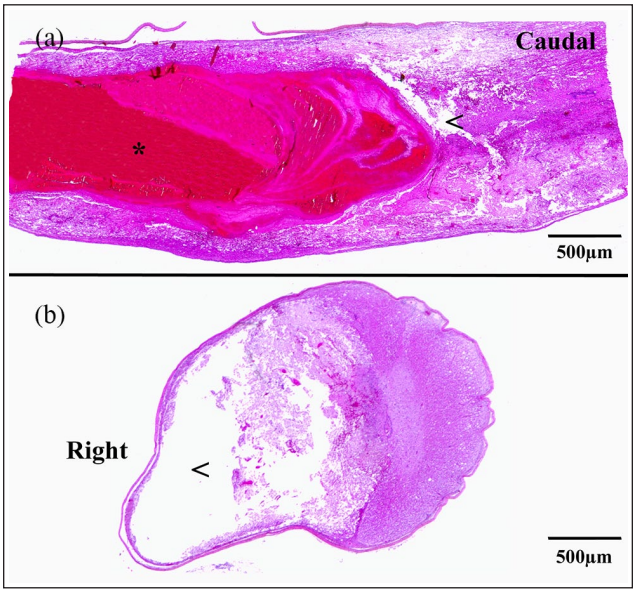


Figure 3 Photomicrography. Haematoxylin and eosin staining of (a) longitudinal and (b) transverse view of the spinal cord at the level of T13 showing haemorrhagic myelomalacia in a 4-month-old Ragdoll cat. Note the severe haemorrhage (*) and the necrosis (<)

the spinal cord segments T10–L1 (Figure 2) and right-sided malacia caudal to L1. Lesions were associated with severe swelling of the right half of the spinal cord and midline shift to the left. No extradural haemorrhage was detected. Cranial to T10, two round, well-defined haemorrhages were visible in the dorsal funiculi and around the central canal. Representative longitudinal and transversal sections were embedded in paraffin and sectioned at 4 µm and stained with haematoxylin and eosin for histopathology (Figures 3 and 4). A large focal and severe intramedullary space-occupying haemorrhage displacing neuroparenchyma was observed (Figure 3a). The haemorrhage was surrounded by oedematous and necrotic neuroparenchyma with swollen axons and hypereosinophilic neurons (Figure 4a). Focally, necrosis had progressed to cystic malacia and was infiltrated by numerous gitter cells (Figure 4b) and neutrophils (Figure 4a), and had multiple areas of mineralisation. A trajectory-like, longitudinal optically empty cavity was detected containing some eosinophilic droplets at the edges (Figure 4c). Cranial to the space-occupying haemorrhage, the central canal was dilated and contained erythrocytes and macrophages. The spinal cord changes were compatible with a traumatic lesion encompassing vascular disruption and spinal cord contusion and suspected perforation. However, no further evidence was found in surrounding tissues of blunt trauma, vertebral fracture, disc extrusion or injection puncture (SC or intramuscular [IM] haemorrhages).

Discussion

Traumatic injuries, including disc herniation,[4] lumbar puncture during CSF collection[5,6] and incorrect microchip

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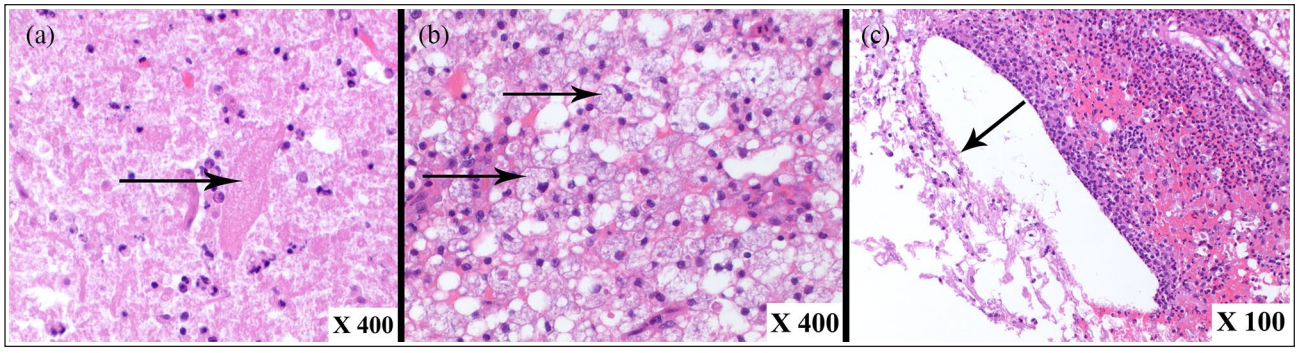


Figure 4 Photomicrography. Haematoxylin and eosin staining of the spinal cord between T10 and L1 of a 4-month-old Ragdoll cat. (a) Note the area of necrosis in the grey matter with a necrotic neuron (arrow) and infiltration by neutrophils; (b) large aggregations of numerous enlarged phagocytic cells with vacuolar cytoplasm called gitter cells (arrows); and (c) a longitudinal empty space close to the haemorrhage that contains some eosinophilic droplets (arrow) at the edges and could be compatible with an injection trajectory

placement,[7,8] are the most commonly reported cause for haematomyelia in small animals. In the absence of trauma, conditions described to be associated with intramedullary spinal cord haemorrhage include neoplasia, vasculitis,[9] parasite infection[10] and haemophilia.[11]

In the present case, intramedullary haemorrhage developed <24 h after trauma and this correlates well with the description of rapidly developing parenchymal haemorrhages after experimental SCI. Indeed, in rats, two studies focused on MRI findings after SCI,[12] and these found a good correlation between MRI and histopathological findings.[13] MRI was used to visualise the evolution of spinal cord changes in the very early phase of SCI. One study reported that the volume of haemorrhage increased linearly with time (0.15% per min, relative to the initial volume) and up to 45% within 5 h of SCI in rats. Haemorrhage was initially found in 12.5% of the cross-sectional area of the lesion epicentre, increasing exponentially to approximately 25% of the epicentre cross-section within hours of injury.[14] Haemorrhage severity in the present case suggests that intraspinal injection led to a significant vascular disruption. A 2019 study by Jeong et al[15] documented the characteristics of intraspinal bleeding in eight Beagles. In the acute phase (1–3 days), the authors observed a hyperintense signal in T2W images and a mixed signal in T1W images, as seen in the present case with hypointense foci in T2W images. Although T1W and T2W images provide high resolution for intramedullary changes, the signal for haemorrhage varies with time due to degradation of haemoglobin.[15] The presence of a signal void on T2* images, as described in the present case, is therefore more sensitive for detecting haemorrhage than pulse sequences.[16,17]

Owing to the exaggerated movement of the cat during the injection, traumatic disorders such as vertebral fracture or ANNPE were considered as potential causes for paraplegia. Similar severe neurological damage is seen in paediatric human patients that have experienced forceful shaking, referred to as 'shaken baby syndrome'. Lesions in the thoracic and lumbar spine are usually due to hyperflexion or hyperextension of the vertebral column. Most infants have metaphyseal lesions that occur as a result of the sudden acceleration and deceleration during shaking. The vertebral bodies are usually involved, most commonly leading to various degrees of compressive fractures.[18] In the present case, no abnormalities affecting the intervertebral discs or the vertebrae were found. Therefore, vertebral fracture, disc herniation or ANNPE were unlikely underlying causes of intraspinal haemorrhage.

At the time of the diagnostic work-up, feline infectious peritonitis (FIP) was considered to be a potential underlying or concurrent disease, supported by hyperglobulinaemia and neutrophilic pleocytosis, despite a normal Pandy test (precipitation of proteins, mainly globulins, in phenol). Typically, FIP causes pyogranulomatous inflammation located around the meninges, with or without evidence of vasculitis,[19] findings that were not confirmed at necropsy. Therefore, neutrophilic pleocytosis and neutrophilic infiltration of the spinal cord were interpreted as a reaction to neuroparenchymal necrosis. Accordingly, neutrophilic pleocytosis has been described in the CSF of cats with myelomalacia secondary to fibrocartilaginous embolism,[20] and mild neutrophilic infiltration of the spinal cord has been histologically described in a cat with haemorrhagic myelomalacia.[21] These findings were therefore consistent with an iatrogenic needle injury and potential injection.

Iatrogenic needle injuries to the central nervous system (CNS) without injection have been previously reported in the veterinary literature following CSF collection attempts in dogs,[5,6] microchip implantation in a dog[7] and a cat,[8] and after attempted IM injection in one cat.[3] Iatrogenic injection into the CNS has been described

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after attempted IM injection in a lamb and an alpaca.[22] In human patients, myelopathies secondary to various needle-associated injuries have been occasionally described, including intramedullary contrast injection,[23] CNS migration of a broken acupuncture needle[24] and spinal cord infarction following a self-inflicted needle-stick injury.[25]

MRI features of needle-associated CNS injuries, without injection, have been previously described in four dogs and one cat, respectively.[3,5] MRI, performed between 8 h and 5 days after the incident, succeeded to demonstrate the needle trajectory either in the brainstem or in the paraspinal musculature in all cases.[3,5] In one dog, the findings were confirmed histopathologically.[5] The lack of visible needle trajectory on MRI in the present case can be related to the small size of the cat (body weight 1.9 kg) or a smaller needle compared with other cases.

In the present case, the CNS injury was most likely related to an intraspinal injection and not just the puncture wound of a needle. Although a fine-needle trajectory could have been missed on MRI, the fact that no high water lesion was detected in the paraspinal soft tissues indicates that the 0.3 ml volume was likely injected directly into the vertebral canal or even the spinal cord.

Cervical myelomalacia after intraspinal injection has been previously reported in a 2-day-old lamb and a 16-week-old alpaca.[22] Interestingly, these two other cases were also young animals, but any correlation of intraspinal injection incidents with age is hard to find. Young animals might be less used to routine medical procedures and therefore overreact more than adult animals, resulting in increased risk of ineffective restraint and possible injury. Anatomical peculiarities, such as lower bone density or larger intervertebral disc spaces, might also predispose young animals to this type of injury. Therefore, proper handling techniques are crucial and should be used during any procedure in order to prevent injury to the animal or veterinary staff. Additionally, in cats, feline injection-site sarcomas (FISSs) represent a very serious adverse reaction to injections. Although mainly described following vaccination, the occurrence of FISSs has been linked to different types of drugs. Feline vaccination guidelines have been recently updated by experts of the American Animal Hospital Association and the American Association of Feline Practitioners, and injections in the interscapular or thoracic region are no longer recommended. In order to facilitate amputation with sufficient margins, clinicians are encouraged to perform injections in the distal limbs or tail.[26] Following these guidelines would have prevented the complication described in this cat.

In the above-mentioned lamb, no MRI was performed, but histopathological examination identified the injection trajectory as a well-defined, unilateral area of liquefactive necrosis within the spinal cord, while in the alpaca the injection site was evident in the paraspinal tissue, although direct communication with the spinal cord was lacking.[22] Similarly to our patient, the spinal cord damage in one of these two large animal cases was characterised by a well-demarcated, unilateral focus of liquefactive necrosis and a white matter degeneration within a part of the opposite cervical spinal side. Wallerian degeneration was also present. In the other case, moderately severe acute unilateral myelomalacia of the white and grey matter was observed.

Although an injection trajectory was not visible in the post-mortem examination, we suspected a direct injection into the spinal cord in between two vertebrae. Severe haemorrhage could, in part, be responsible for not detecting injury trajectory. A 6-day delay between injection and necropsy could have also contributed to failure in detecting signs of needle penetration during post-mortem examination. Nevertheless, the longitudinal empty cavity in the spinal cord at the T11 level containing some eosinophilic droplets at the edges was suggestive of a potential needle trajectory and deposit of fluid. A similar unexplained finding, described as 'a pale, Luxol fast blue combined with the periodic acid–Schiff negative, eosinophilic, homogenous paucicellular fluid', was reported in the lamb with intraspinal injection.[22]

As no neurological improvement was observed, the cat described in this case report was euthanased at the request of the owner after 5 days. Owing to the paucity of clinical reports, prognostic factors for recovery in this type of injury are lacking. In veterinary medicine, negative prognostic factors in other types of SCI include the absence of deep pain sensation,[27–29] extensive intramedullary T2 hyperintensity[30] and long attenuation of CSF in sagittal single-shot turbo spin echo pulse sequences.[31]

Prognosis in needle-associated SCI in humans seems to be fair to good. Generally, lesions are due to a small-sized needle (acupuncture) and therefore motor disturbances are rarely described.[32] In these cases, surgery, either in order to remove the needle or an extramedullary haematoma, has a better outcome than conservative treatment (with signs of recovery in 10/21 vs 0/4 patients, respectively).[32] Other well-known SCIs occur secondary to neuraxial blocks.[33] Outcome after traumatic CNS injury varies in the veterinary literature between poor and good. Concerning four dogs with iatrogenic brainstem injury following CSF collection, one dog died because of respiratory arrest, two were euthanased owing to uncertain recovery and sudden deterioration 12 days after diagnosis, and one was lost to follow-up after 10 days of hospitalisation, during which time the dog recovered voluntary urination and ambulation with assistance.[5] However, the outcome was good for a brainstem injury in a young cat.[3]

The authors could not find any report of intraspinal injection in human medicine. Only inadvertent

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intrathecal injections are rarely described and outcomes vary from no neurological signs to death.[34] In dogs, an experimental study showed that an intrathecal injection of methylprednisolone did not impact the neurological state, but revealed histological changes such as meningeal thickening and lymphocytic infiltrates in vessels. In one dog, spinal cord necrosis was evident.[35] Finally, both large animals with intramedullary injections were euthanased owing to a lack of neurological improvement,[22] as in the present case report, suggesting a poor outcome in the case of an accidental intramedullary injection.

The main limitation of this case report is the lack of detection of a clearly identifiable needle trajectory to confirm the diagnosis. Nevertheless, the acute neurological deficits after injection, the absence of other traumatic causes and the histopathological findings strongly support our presumptive diagnosis of SCI due to intraspinal injection.

Conclusions

To our knowledge, this is the first report of a presumed intraspinal injection causing haematomyelia and myelomalacia in a cat, and the first that describes the clinical, MRI and post-mortem features of an iatrogenic needle SCI and suspected injection in a young cat. As a result of the SCI and presumed intraspinal injection, a combination of haemorrhagic and oedematous lesions was observed, potentially leading to spinal shock. The acute onset of signs after the thoracolumbar parenteral injection attempt, the MRI and histopathological findings, which were in agreement with two cases of iatrogenic traumatic CNS needle injuries and injections in the literature, and the absence of a vertebral fracture, strongly support our presumptive diagnosis.

Meticulous care and adequate restraint should be assured during any procedure in cats. Moreover, injections in the thoracic area should be avoided in feline patients, to reduce the risk of FISSs. This case report illustrates the need for in-depth training in proper cat-handling techniques. Outcomes for traumatic incidents of the spinal cord appear to be poor, particularly if, in addition to the needle injury, substances are injected into the spinal cord.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). No animals or humans are identifiable within this publication and therefore additional informed consent for publication was not required.

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