COMPANION OR PET ANIMALS

Hypoglycaemia associated with gastrointestinal and extragastrointestinal stromal tumour in two dogs

Joanna Lodzinska,1 Clara Ballber,2 Sionagh H Smith,3 Spela Bavcar1

SUMMARY

Gastrointestinal stromal tumours (GISTs) are uncommon mesenchymal tumours that originate from the interstitial cells of Cajal. As these tumours are difficult to distinguish from gastrointestinal smooth muscle tumours using standard histological techniques, their true prevalence may be underestimated. Metabolic and systemic consequences of GISTs are not well described in any species. More rarely, neoplasms with histological and immunohistochemical features similar to GISTs may occur outside the gastrointestinal tract, the so-called extragastrointestinal stromal tumours (EGISTs). EGISTs have never been described in the veterinary literature. In this article, the authors present and describe clinical findings, management and treatment of two dogs with clinical hypoglycaemia induced by histologically confirmed GIST and EGIST. Hypoglycaemia resolved immediately and long term after tumour excision. To the authors’ knowledge, this is the first report of hypoglycaemia associated with a canine GIST and the first case report of an EGIST in a dog.

BACKGROUND

Gastrointestinal stromal tumours (GISTs) are mesenchymal tumours that occur in the gastrointestinal tract (GIT) of dogs, cats,1,2 horses,3,4 human beings,5-8 and non-human primates.9 They can occur in any segment of the GIT; however, most of them develop in the stomach and small intestine. Clinically, they can lead to focal obstruction, vomiting and diarrhoea, as well as chronic low-grade GIT blood loss, resulting in iron deficiency anaemia. Surgical removal usually results in excellent outcomes, while only a few case reports have been published demonstrating a response to tyrosine kinase inhibitors.10-12

More rarely, neoplasms with histological and immunohistochemical features similar to GISTs may occur outside the GIT, the so-called extragastrointestinal stromal tumours (EGISTs).

These tumours are difficult to distinguish from gastrointestinal smooth muscle tumours such as leiomyoma or leiomyosarcoma,11 using standard histological techniques; therefore, their true prevalence may be underestimated. It has been established that GISTs can be differentiated by the expression of KIT (CD117), a receptor tyrosine kinase encoded by the proto-oncogene c-KIT.11-15 One study also suggests that the immunohistochemical application of discovered on GIST protein 1 (DOG1) achieves higher specificity and sensitivity than KIT for differentiating between canine GISTs and leiomyosarcomas. Inclusion of both DOG1 and KIT immunohistochemistry in diagnostic panels offers improved overall accuracy of canine GIST diagnosis.16

No previous cases of GIST-associated hypoglycaemia have been described in the veterinary literature. To the authors’ knowledge, there are also no case reports describing an EGIST in veterinary medicine.

Hypoglycaemia in dogs, defined as a blood glucose concentration of less than 3.3 mmol/l,17 can be a life-threatening disorder that necessitates swift and decisive treatment to prevent lasting neuronal damage. Most frequently reported causes of severe hypoglycaemia in adult dogs are insulinoma, excessive insulin administration and non-pancreatic neoplasia.18,19 Sepsis, severe hepatothropy and hypoadrenocorticism are usually associated with only a mild decrease in blood glucose concentration.20

In human medicine, non-islet cell tumour hypoglycaemia (NICTH) is a well-recognised paraneoplastic syndrome20 and has been described in association with GISTs in human beings.21 In dogs, NICTH has been described with neoplasms of hepatic,22,23 smooth muscle,24,25 mammary26 and renal origin,27,28 but not with neoplasms of the GIT. Different mechanisms have been proposed to explain the paraneoplastic syndrome. NICTH may be caused by increased tumour utilisation of glucose; decreased hepatic glycogenolysis or gluconeogenesis; or secretion of insulin or insulin-like growth factor 1 (IGF1) and insulin-like growth factor 2 (IGF2).29 However, in human medicine it has been established that IGF2 is the main cause of NICTH, including in GISTs.30 Two different studies suggest that IGF2 is also a relevant factor in dogs.23,28 Some mesenchymal and epithelial tumours can overexpress IGF2, resulting in the secretion of partially processed precursors of IGF2 (‘big’ IGF2). This molecule binds to insulin receptors, resulting in insulin-like hypoglycaemic effects.31 The purpose of this paper is to describe clinical findings and treatment in two dogs with marked hypoglycaemia associated with GIST and EGIST that resolved after tumour excision.

CASE PRESENTATION

Dog 1

A 13-year-old, male entire golden retriever presented to the referring emergency service with a history of intermittent diarrhoea and acute-onset weakness and collapse. Symptomatic hypoglycaemia (2.4-2.6 mmol/l; reference range 4.11-7.95 mmol/l).
causing weakness episodes was detected by the referring veterinary surgeon on multiple measurements, and the dog was referred to the Royal (Dick) School of Veterinary Studies (R(D)SVS) for investigation of hypoglycaemic episodes and a palpable cranial abdominal mass. The initial treatment by the referring veterinarian included 2.5 per cent glucose constant rate infusion. On physical examination the dog was quiet, alert and responsive. Ptyalism was noted and a large mass was palpated in the cranial abdomen. Initial investigations included complete blood count and serum biochemistry that revealed low urea and confirmed hypoglycaemia of 2.58 mmol/l (reference range 4.11–7.95 mmol/l). Despite glucose supplementation, the glucose was consistently low at 2.44 mmol/l and 2.6 mmol/l on subsequent measurements taken over a 24-hour period using a hand-held glucometer. To rule out hepatic dysfunction as cause of low urea and glucose, a bile acid stimulation test was performed, and this ruled out severe functional loss.

Abdominal ultrasound scan confirmed the presence of a large, round heterogeneous mass containing small cavities in the right cranial abdomen dorsal to the duodenum (figure 1). Its exact origin could not be established but neoplasia was considered the most likely differential diagnosis. No other abdominal abnormalities were identified (including in the liver) and thoracic radiography did not show any evidence of metastatic disease or any other abnormality. The patient was stabilised on glucose infusion and surgery was scheduled.

Ventral midline exploratory coeliotomy was performed. The mass was associated with the junction of the central and right pancreatic regions, and pancreatic origin was suspected but not surgically confirmed, given multiple adhesions to the duodenum, gastric wall and transverse colon. The common bile duct and the gastric pylorus were not involved. No other abnormalities were found during surgery and, given the normal liver morphology and lack of significant laboratory changes, liver biopsies were not taken. The mass was successfully excised and submitted for histopathology. Glucose supplementation was gradually discontinued 12 hours after the surgery. The hypoglycaemia resolved quickly and all the measurements during the postoperative period were within normal limits. The dog was managed on pain relief and discharged four days later.

Macroscopically, the mass was fluctuant to firm, mottled dark purple to grey and spherical, measuring 14 cm in diameter, with fat attached to its surface. On cut section, it was solid and mottled pink, red and orange, with a soft consistency. Histopathology of the mass confirmed an intra-abdominal malignant spindle cell tumour (sarcoma) that was completely excised with narrow margins and no evidence of pancreatic or GIT involvement. The only recognisable architecture consisted of fat and smooth muscle. This was effaced by a well-demarcated, expansile and encapsulated proliferation of spindle cells arranged in interlacing fascicles with a faint herringbone pattern. The spindle cells breached the capsule and invaded the surrounding fat. The spindle cells contained fibrillar, eosinophilic cytoplasm and elongated or ‘cigar shaped’ nuclei. Anisokaryosis was mild and the mitotic index averaged 3 per high power field (hpf) at 400 x. There were multifocal areas of necrosis and haemorrhage, with occasional cystic degeneration. Immunohistochemically, ~10 per cent of the spindle cells labelled strongly with antibody against CD117, confirming a diagnosis of EGIST.

In addition to surgical removal, treatment in this patient consisted of single-agent chemotherapy (four doses of doxorubicin (30 mg/m2) given every three weeks). Six months after the initial diagnosis, a new 8-mm nodule next to the pancreas was noticed on a routine recheck ultrasound. Fine needle aspirate (FNA) confirmed mesenchymal neoplasia, indicating probable recurrence of the previously diagnosed EGIST. Blood glucose levels were tested and were within normal limits on subsequent chemotherapy consultations. Five months later multiple pancreatic nodules and a liver mass were identified on ultrasound (figure 2). The owners opted for no further treatment and the dog was humanely euthanased at the referring practice.

**Dog 2**
A 13-year-old, female neutered labrador was referred for investigation of an abdominal mass. A few episodes of vomiting and diarrhoea were reported but they had resolved by the time of presentation. The owner also reported a two-month history of progressive weight loss. On physical examination the patient was bright, alert and responsive with a body condition score of 2/9. A grade I/VI heart murmur was auscultated and abdominal palpation indicated the presence of a mass in the cranial abdomen. Initial investigations included complete blood count and serum biochemistry. Mild leucopenia with mild neutropenia (no left shift) and lymphopenia, and minimal (non-significant) normocytic-normochromic anaemia were noted. Biochemical abnormalities consisted of moderate elevations in both alanine transaminase and alkaline phosphatase. Mildly raised basal bile acids were not considered significant, but a bile acid stimulation test was not performed. Due to the non-specific presenting complaints and mild hypercholesterolaemia, total thyroxine (TT4) and thyroid stimulating hormone (TSH) were assessed but were not suggestive of hypothyroidism.

Abdominal ultrasound confirmed the presence of a very large cranial abdominal mass, for which the exact origin could not be established. Results of an FNA suggested chronic haemorrhage. CT of the abdomen indicated that the mass was most likely of gastric origin. Additional findings on thoracic CT images showed changes consistent with aspiration pneumonia, although there was no history or clinical signs typical of that. Electrolyte surgery was scheduled and the patient was discharged on the same day with a course of antibiotics to treat the presumed subclinical aspiration pneumonia before surgery. The dog re-presented to the R(D)SVS emergency service a few hours later due to a collapsing episode.
The dog was dull but responsive, with continued ptyalism. In addition, pyrexia and tachypnoea with increased inspiratory effort had developed. The heart rate was 104 beats per minute, with good-quality synchronous pulses, and blood pressure was 155 mmHg. Blood analysis revealed more severe lymphopenia and neutropenia with a glucose of 4.3 mmol/l (reference range 4.11–7.95 mmol/l). Oxygen therapy and intravenous antibiotic therapy were initiated and the patient was closely monitored. Two hours later the glucose levels had dropped to 3 mmol/l. At this point a dextrose bolus was administered, and repeat (every two hours) glucose measurements using hand-held glucometer were commenced. These were consistently low; therefore, a 5 per cent dextrose continuous rate infusion (CRI) was started.

The respiratory status of the patient remained stable in the following days, but glucose remained low despite CRI supplementation. Administration of an anti-inflammatory dose of dexamethasone achieved a mild improvement in glucose levels. However, they decreased again once dexamethasone was discontinued. Leucocytes returned to normal, although lymphopenia persisted. Once the respiratory status of the patient was stable, a ventral midline exploratory coeliotomy was performed. It revealed a mass arising from the dorsal aspect of the pyloric antrum with omentum wrapped around it; this was removed and submitted for histopathology. Glucose levels were closely monitored during surgery, and due to initial hypoglycaemia of 2.8 mmol/l supplemental dextrose injections were given. Once the mass was excised the consecutive glucose readings were within normal limits and no further supplementation was required. Recovery from the surgery was uneventful. The hypoglycaemia resolved completely after the mass excision and the patient was discharged four days later.

Macroscopically, the mass was ovoid and multinodular, measuring 14 cm in diameter at its widest dimension, with an attached fragment of omentum. Histopathologically it comprised an expansile, non-encapsulated but well-demarcated proliferation of spindle cells similar to those described above (figure 3). Anisokaryosis was moderate to marked but mitoses were rare. There were large areas of necrosis and some haemorrhage. The spindle cell proliferation merged with the muscularis layer of the pyloric stomach. Immunohistochemically, 20 per cent of the spindle cells labelled moderately strongly with antibody against CD117, supporting a diagnosis of GIST (figure 4). Different chemotherapy protocols were discussed but declined by the owners. At the last follow-up appointment (three months after initial diagnosis), the dog was free of clinical signs.

**DISCUSSION**

As far as the authors are aware, there are no previous reports of GIST-associated hypoglycaemia in dogs. To date, only one case report of GIST-associated hypoglycaemia in a veterinary patient has been published, and that was in a horse. However, GISTs are a relatively new entity. An immunohistochemical review of previously diagnosed gastrointestinal leiomyomas and leiomyosarcomas has resulted in most of these tumours being reclassified as GISTs. All the cases describing hypoglycaemia secondary to leiomyomas/sarcomas were published before this new classification. Therefore, it is possible that some of these previous cases were actually GISTs.

Paraneoplastic syndromes are common manifestations of many malignancies and have been reported with GIST. Multiple articles on GIST-associated hypoglycaemia are available in human medicine, but no information on its systemic effects is available in the veterinary literature. Hypoglycaemia was a common presenting abnormality in both of the dogs reported here. In dog 1, the hypoglycaemia was considered to be the most likely cause of the clinical signs (weakness and collapse), given the lack of other physical and laboratory abnormalities. However, other unrelated causes (such as a transient arrhythmia or syncopal episode) were not ruled out. Liver dysfunction was considered an unlikely explanation for the hypoglycaemia. A bile acid stimulation test was not consistent with severe liver
dysfunction and no imaging abnormalities were identified in the liver. Furthermore, the dog became normoglycaemic after the tumour was resected, providing more support for a paraneoplastic mechanism.

During surgery the mass was adjacent to the pancreas, but pancreatic involvement was not confirmed histopathologically. A concomitant, undetected insulinoma cannot be ruled out as a potential cause for hypoglycaemia as insulin levels were not measured, but the presence of two different neoplasms is considered unlikely.

Interestingly, histopathological examination of the mass in dog 1 did not indicate a direct connection between the mass and the GIT. EGISTs have been described in human medicine widely but nothing has been reported in the veterinary literature. In recent years, interstitial cells of Cajal (ICC) or ICC-like cells have been found in extraintestinal organs. For example, in the genitourinary tract, KIT-positive specialised pacemaker cells have been described in the human bladder, urethra, uterus and prostate. The presence of these cells in various organs or soft tissue could provide an explanation for the rare cases of GISTs that occur as primary tumours outside the GIT, such as in the mesentery, omentum, retroperitoneum, liver, gall bladder, vagina, uterus, urinary bladder or prostate. In some of these tumours, the origin remains unclear.

In addition to its hypoglycaemia, dog 2 was also diagnosed with aspiration pneumonia and, considering the clinical findings (dyspnoea, pyrexia), laboratory abnormalities (neutropenia) and timeframe, sepsis with secondary hypoglycaemia was a possibility. However, hypoglycaemia persisted after sepsis resolved. It also responded to glucocorticoid administration and, as with dog 1, resolved after mass removal, such that sepsis as a sole cause was unlikely.

The main limitation of this report is the fact that the exact underlying mechanism for the hypoglycaemia was not determined. Given that the main cause of NICTH seems to be the secretion of IGF2, this should ideally have been measured to confirm the source of hypoglycaemia. Consequently, other causes of hypoglycaemia (insulinoma or liver disease in dog 1 and sepsis in dog 2), although unlikely, cannot be completely excluded. Furthermore, while an antibody panel was not applied in these two cases, both samples labelled strongly with antibody against CD117 which, given the other histological features, was excluded. Furthermore, while an antibody panel was not applied in these two cases, both samples labelled strongly with antibody against CD117 which, given the other histological features, was considered sufficiently diagnostic of GIST and EGIST.

To the authors’ knowledge these are the first cases describing hypoglycaemia associated with GIST and EGIST in dogs. GIST and EGIST should be considered as a differential diagnosis in dogs presenting with an abdominal mass and hypoglycaemia.

Learning points

► Extragastrintestinal stromal tumours (EGISTs) do occur in dogs.

► Gastrointestinal stromal tumour (GIST) and EGIST should be considered as a differential diagnosis in dogs presenting with an abdominal mass.

► GIST and EGIST should be considered as a differential diagnosis in dogs presenting hypoglycaemia.

Contributors Conception and design: JL, CB. Acquisition of data: JL, SHS. Analysis and interpretation of data: JL, CB, SHS, SB. Drafting the article: JL, CB. Revising the article for intellectual content: JL, CB, SHS, SB. Final approval of the completed article: JL, CB, SHS, SB.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon request.

ORCID iD Joanna Lodzinska http://orcid.org/0000-0003-2205-1952

REFERENCES

1 Gillespie V, Baer K, Farrell J, et al. Canine gastrointestinal stromal tumours: immunohistochemical expression of CD34 and examination of prognostic indicators including proliferation markers Ki67 and AgNOR. Vet Pathol 2011;48:283–91.

2 LaRock RG, Ginn PE. Immunohistochemical staining characteristics of canine gastrointestinal stromal tumors. Veterinary pathology 1997;34:303–11.

3 Morini M, Gentilini F, Pietra M, et al. Cytological, immunohistochemical and mutational analysis of a gastric gastrointestinal stromal tumour in a cat. J Comp Pathol 2011;145:152–7.

4 Suva A, Shimoda T. Intestinal gastrointestinal stromal tumour in a cat. The Journal of Sci 2017;79:562–6.

5 Gupta A, Gupta S, Tandon A, et al. Gastrointestinal stromal tumor causing ileo-ileo intussusception in an adult patient with presentation with review of literature. Pan Afr Med J 2011;8:29.

6 Kim CI, Day S, Yeh KA. Gastrointestinal stromal tumors: analysis of clinical and pathologic factors. Am Surg 2001;67:135–7.

7 Occhionorelli S, Maitaritonno M, Pennella A, et al. Gastro-intestinal stromal tumour (GIST): case report. G Chir 2001;22:65–9.

8 Zhao X, Yue C. Gastrointestinal stromal tumour. J Gastrointest Oncol 2012;3:189–208.

9 Wong D, Hepworth K, Yaeger M, et al. Imaging diagnosis-hypoglycaemia associated with cholangiocarcinoma and peritoneal carcinomatosis in a horse. Vet Radiol Ultrason 2015;56:19–12.

10 Saturday GA, Lasota J, Frost D, et al. KIT-positive Gastrointestinal Stromal Tumor in a 22-year-old Male Chimpanssee (Pan troglodites). Vet Pathol 2005;42:362–5.

11 Russell KN, Mehler SJ, Skorupski KA, et al. Clinical and immunohistochemical differentiation of gastrointestinal stromal tumours from leiomyosarcomas in dogs: 42 cases (1990–2003). J Am Vet Med Assoc 2007;230:1329–33.

12 Elliott JW, Swinbourne F, Parry A, et al. Successful treatment of a metastatic, gastrointestinal stromal tumour in a dog with toceranib phosphate (Palladia). J Small Anim Pract 2017;58:416–8.

13 Irie M, Takeuchi Y, Ohtake Y, et al. Imatinib mesylate treatment in a dog with gastrointestinal stromal tumours with a c-kit mutation. J Vet Med Sci 2015;77:1535–9.

14 Kobayashi M, Kuroki S, Ito K, et al. Imatinib-associated tumour response in a dog with a non-resectable gastrointestinal stromal tumour harbouring a c-kit exon 11 deletion mutation. Vet J 2013;198:271–4.

15 Maas CP H, Ter Haar G, van der Gaag I, et al. Reclassification of small intestinal and cecal smooth muscle tumours in 72 dogs: clinical, histologic, and immunohistochemical evaluation. Vet Surg 2007;36:302–13.

16 Dailey DD, Erhart EJ, Duval DL, et al. DOG1 is a sensitive and specific immunohistochemical marker for diagnosis of canine gastrointestinal stromal tumours. J Vet Diagn Invest 2015;27:268–77.

17 Ettinger SJ, Feldman EC, Cote E. Textbook of veterinary internal medicine : diseases of the dog and the cat. 8th edn. St. Louis, Missouri: Elsevier, 2017.

18 Leifer CE, Peterson ME. Hypoglycaemia, 1984: 873–89.

19 Leifer CE, Peterson ME, Matus RE, et al. Hypoglycaemia associated with nonislet cell tumor in 13 dogs. J Am Vet Med Assoc 1985;186:53–5.

20 Bodnar TW, Acevedo MI, Petropoulos M. Management of non-islet-cell tumor hypoglycaemia: a clinical review. J Clin Endocrinol 2014;99:713–22.

21 Beckers MMJ, Sleip PHTJ, van Doorn J. Hypoglycaemia in a patient with a gastrointestinal stromal tumour. Clin Endocrinol 2003;59:402–4.

22 Battaglia L, Petterino C, Zappulli V, et al. Hypoglycaemia as a paraneoplastic syndrome associated with renal adenocarcinoma in a dog. Vet Res Commun 2005;29:671–5.

23 Zini E, Glaus TM, Minuto F, et al. A non-resectable gastrointestinal stromal tumour harbouring a c-kit exon 11 deletion mutation. Vet J 2013;198:271–4.

24 Beaudry D, Knapp DW, Montgomery Y, et al. Hypoglycaemia in four dogs with smooth muscle tumours. J Vet Intern Med 1995;9:415–8.

25 Boari A, Barreca A, Bestetti G, et al. Hypoglycaemia in a dog with a leiomyoma of the gastric wall producing an insulin-like growth factor II-like peptide. Eur J Endocrinol 1995;132:744–50.

26 Rossi G, Ernico G, Perez P, et al. Paraneoplastic hypoglycaemia in a diabetic dog with an insulin growth factor type-2-producing mammary carcinoma. Vet Clin Pathol 2010;39:480–4.

27 Swain JM, Pirie RS, Hudson NPH, et al. Insulin-Like growth factors and recurrent hypoglycaemia associated with renal cell carcinoma in a horse. J Vet Intern Med 2005;19:613–6.
28 Snead EC. A case of bilateral renal lymphosarcoma with secondary polycythaemia and paraneoplastic syndromes of hypoglycaemia and uveitis in an English Springer Spaniel. *Vet Comp Oncol* 2005;3:139–44.

29 Withrow SJ, MacEwan EG. Small animal clinical oncology. 3rd edn. Philadelphia: W. B. Saunders, 2001.

30 Richford B, Van Den Berg G, Van Den Graaf W. Non-islet cell tumour hypoglycaemia in a patient with a gastrointestinal stromal tumour. *Acta Oncol* 2005;44:764–6.

31 de Groot JWB, Richford B, van Doorn J, et al. Non-islet cell tumour-induced hypoglycaemia: a review of the literature including two new cases. *Endor Relat Cancer* 2017;14:979–93.

32 Freeman L, Becvarova I, Cave N, et al. WSAVA nutritional assessment guidelines. *J Feline Med Surg* 2011;13:516–25.

33 Haga HA, Ytrehus B, Miettinen M. Gastrointestinal stromal tumors and leiomyomas in the dog: a histopathologic, immunohistochemical, and molecular genetic study of 50 cases. *Vet Pathol* 2003;40:42–54.

34 Bagley RS, Levy JK, Malarkey DE. Hypoglycemia associated with intra-abdominal leiomyoma and leiomyosarcoma in six dogs. *J Am Vet Med Assoc* 1996;208:69–71.

35 Cohen M, Post GS, Wright JC. Gastrointestinal leiomyosarcoma in 14 dogs. *J Vet Intern Med* 2003;17:107–10.

36 Gueris HM, Holcombe RF. A case of advanced gastrointestinal stromal tumor (GIST) presenting with paraneoplastic syndrome. *J Clin Oncol* 2004;22.

37 Tsikrikas S, Manolakopoulos S, Deutsch M, et al. Unusual combination of paraneoplastic manifestations in a patient with metastatic gastrointestinal stromal tumor (GIST). *Scand J Gastroenterol* 2008;43:1012–5.

38 Dimitriadis GK, Gopalakrishnan K, Rao R, et al. Severe paraneoplastic hypoglycaemia secondary to a gastrointestinal stromal tumour masquerading as a stroke. *Endocrinol Diabetes Metab Case Rep* 2015;2015.

39 Escobar GA, Robinson WA, Nydam TL, et al. Severe paraneoplastic hypoglycaemia in a patient with a gastrointestinal stromal tumor with an exon 9 mutation: a case report. *BMC Cancer* 2007;7:13.

40 Guiteau J, Fanucchi M, Folpe A, et al. Rectal gastrointestinal stromal tumor mimicking a primary prostatic lesion. *Can J Urol* 2008;15:4112–4.

41 Funihata M, Fujimori T, Murua I, et al. Malignant stromal tumor, so called “gastrointestinal stromal tumor”, with rhabdomyomatous differentiation occurring in the gallbladder. *Pathol Res Pract* 2005;201:609–13.

42 Herawi M, Montgomery EA, Epstein JJ, et al. Gastrointestinal stromal tumors (GISTs) on prostate needle biopsy: a clinicopathologic study of 8 cases. *Am J Surg Pathol* 2006;30:1389–95.

43 Huizinga JD, Faussone-Pellegrini MS. Interstitial cells of Cajal in the human urinary bladder: concept of vesical pacemaker. *Urology* 2004;64:809–13.

44 Ciortea SM, Radu E, Regalia T, et al. C-Kit immunopositive interstitial cells (Cajal-type) in human myometrium. *J Cell Mol Med* 2005;9:407–20.

45 Fiaszecka Piotrowska A, Rolle U, Solari V, et al. Interstitial cells of Cajal in the human normal urinary bladder and in the bladder of patients with megacystis-microcolonic intestinal Hyperperistalsis syndrome. *BJU Int* 2004;94:143–6.

46 Shafik A, El-Sibai O, Shafik AA, et al. Identification of interstitial cells of Cajal in human urinary bladder: concept of vesical pacemaker. *Urology* 2004;64:809–13.

47 Van der AA F, Roskams T, Blyweert W, et al. Interstitial cells in the human prostate: a new therapeutic target? *Prostate* 2003;56:250–5.

48 van der AA F, Roskams T, Blyweert W, et al. Identification of kit positive cells in the human urinary tract. *J Urol* 2004;171:2492–6.

49 Dickson BG, Srigley JR, Pollett AE, et al. Rectal gastrointestinal stromal tumor mimicking a primary prostatic lesion. *Can J Urol* 2008;15:4112–4.

50 Krska Z, Pesková M, Povyšil C, et al. Gist of pancreas. *Prague Med Rep* 2005;106:201–8.

51 Lee C-H, Lin Y-H, Lin H-Y, et al. Gastrointestinal stromal tumor of the prostate: a case report and literature review. *Hum Pathol* 2006;37:1361–5.

52 Madden JE, Burchette JL, Raj GV, et al. Anterior rectal wall gastrointestinal stromal tumor presenting clinically as prostatic mass. *Urol Oncol* 2005;23:68–72.

53 Ninomiya K, Goldblum JR, Albores-Saavedra J, et al. Extragastrointestinal (soft tissue) stromal tumors: an analysis of 48 cases with emphasis on histologic predictors of outcome. *Mod Pathol* 2000;13:577–85.

54 Van der AA F, Sciot R, Blyweert W, et al. Gastrointestinal stromal tumor of the prostate. *Urology* 2005;65:388.

55 Voelzke BB, Sakamoto K, Hantel A, et al. Gastrointestinal stromal tumor: involvement in urologic patients and recent therapeutic advances. *Urology* 2002:60:218–22.

56 Wingen CB, Pauwels PA, Debiec-Rychter M, et al. Uterine gastrointestinal stromal tumour (GIST). *Gynecol Oncol* 2005;97:970–2.

57 Takahashi RH, Matsubayashi J, Yokotsuka M, et al. An intrapelvic extraintestinal gastrointestinal stromal tumor of undetermined origin: diagnosis by prostate needle biopsy. *Pathol Res Pract* 2012;208:736–40.

Copyright 2019 British Veterinary Association. All rights reserved. For permission to reuse any of this content visit http://www.bmj.com/company/products-services/rights-and-licensing/permissions/

Veterinary Record Case Reports subscribers may re-use this article for personal use and teaching without any further permission.

Subscribe to Vet Record Case Reports and you can:

► Submit as many cases as you like
► Enjoy fast sympathetic peer review and rapid publication of accepted articles
► Access all the published articles
► Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit vetrecordcasereports.bvapublications.com for more articles like this and to become a subscriber