

LONG TERM SURVIVAL OF GASTRO-INTESTINAL STROMAL TUMOURS (GIST) IN 2 DOGS

C. MULLER⁽¹⁾, J. GUAGUÈRE-LUCAS⁽¹⁾, A. MULLER⁽¹⁾, E. GUAGUÈRE⁽¹⁾, P. DEVAUCHELLE⁽²⁾, F. DEGORCE-RUBIALES⁽³⁾, MN. LUCAS⁽³⁾, M. DELVERDIER⁽⁴⁾

(1) Clinique Vétérinaire Saint-Bernard - Lomme, (2) Centre de cancérologie vétérinaire - Maisons-Alfort, (3) LAPVSO - Toulouse, (4) École Nationale Vétérinaire - Toulouse, France.

Case 1

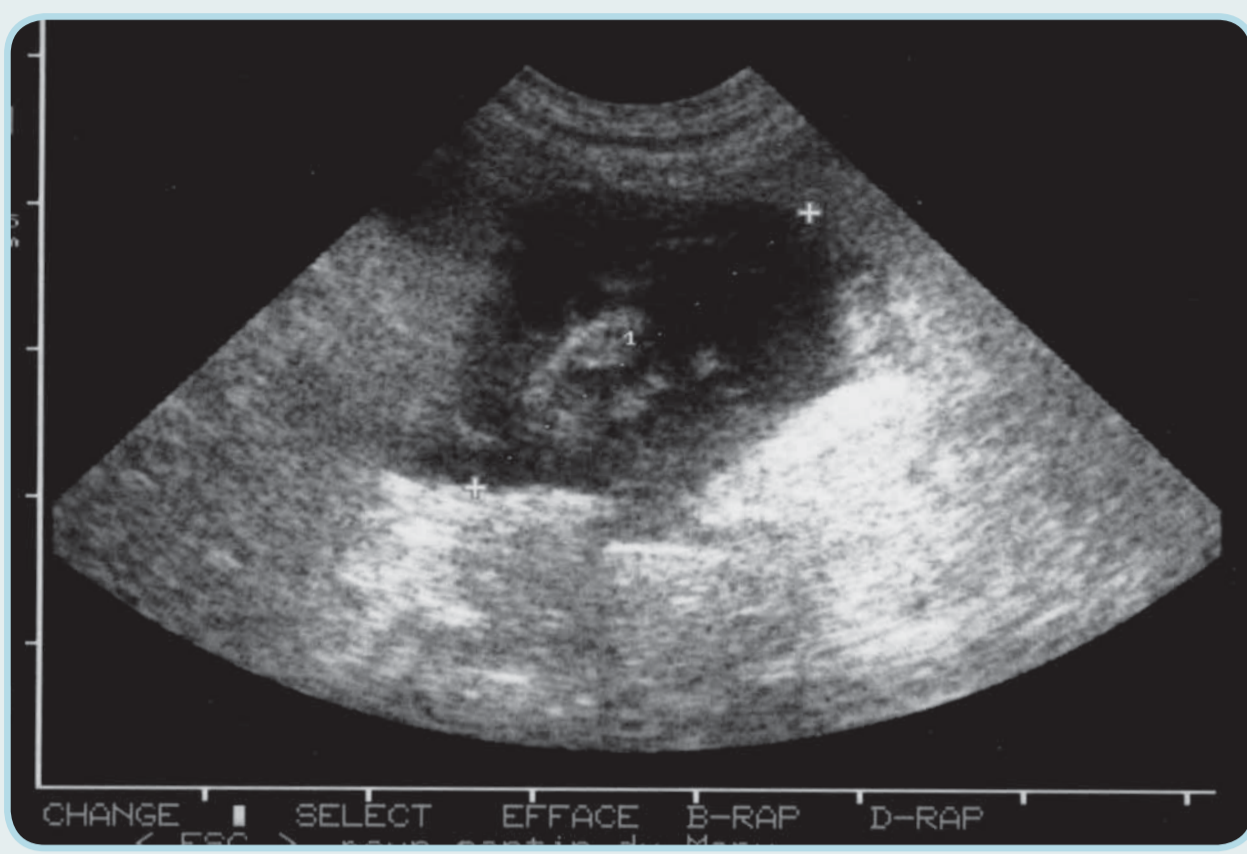


Photo 1: Abdominal ultrasonography : we can see an intestinal mass involving mucous and muscular layers.

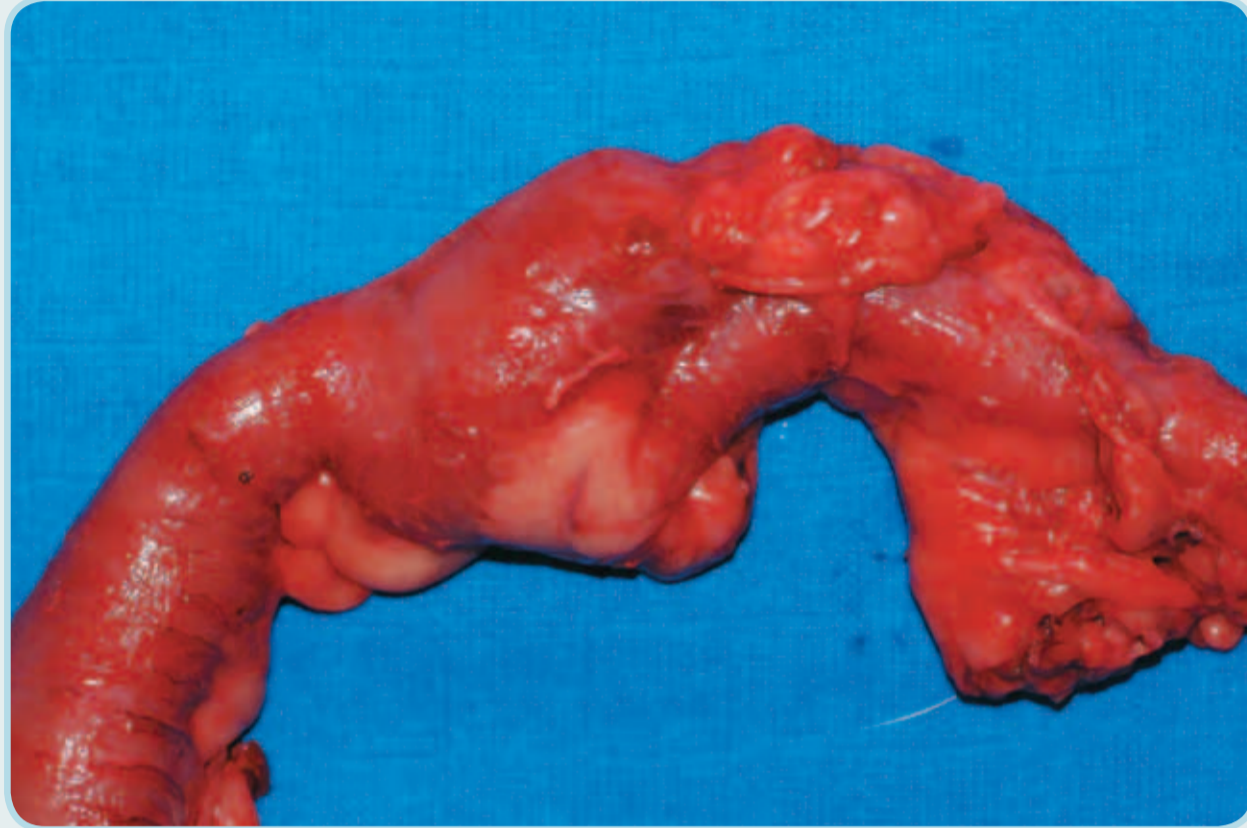


Photo 2: Intestinal mass after surgical resection.

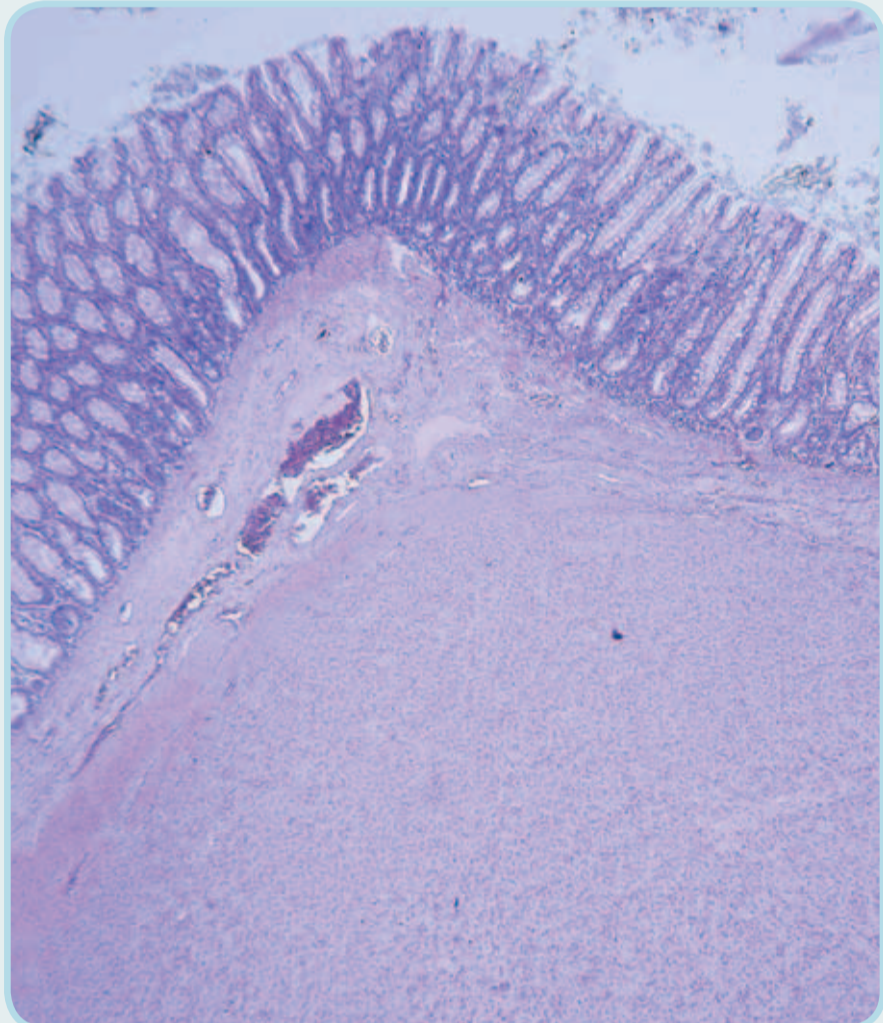


Photo 3: Spindle cells tumour located in inner circular intestinal muscularis externa (HE, X 25).

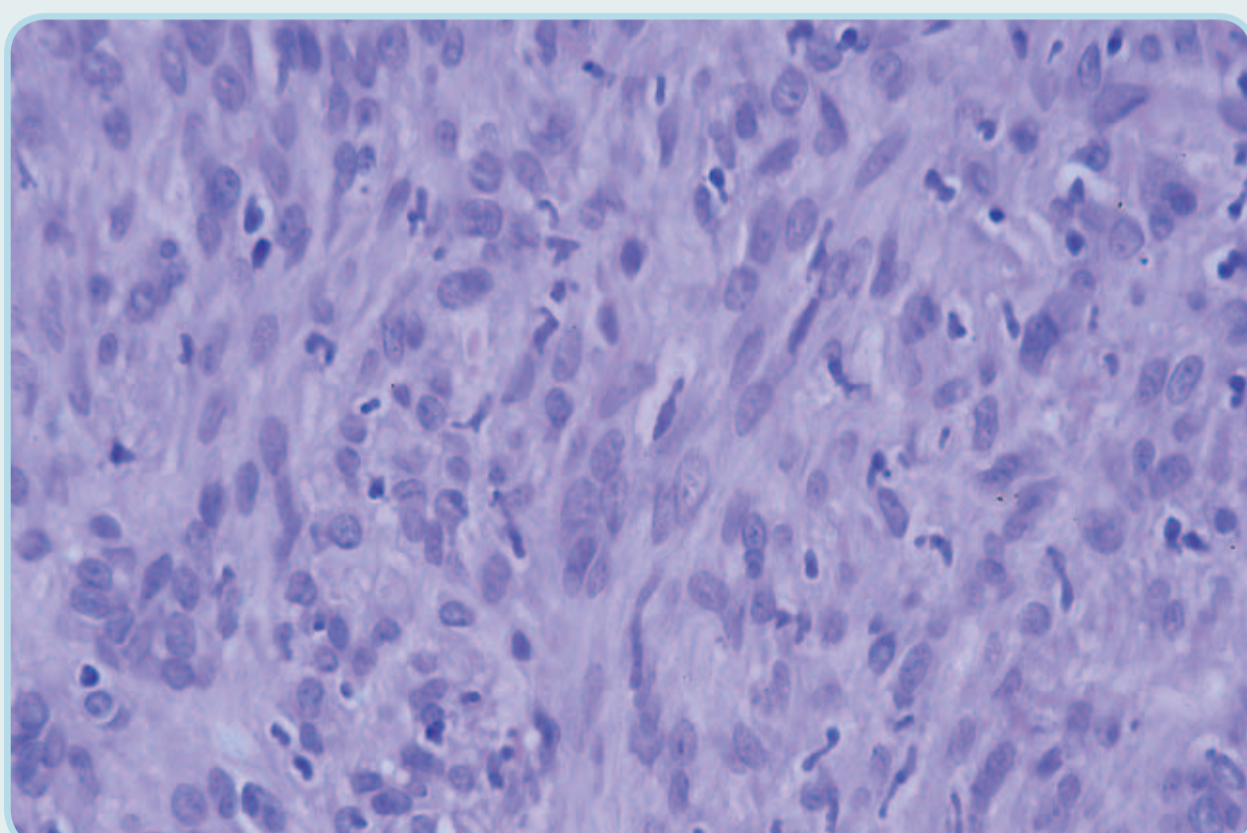


Photo 4: Spindle cells arranged in haphazardly interlacing fascicles with mononuclear cells infiltrate (HE, X 400).

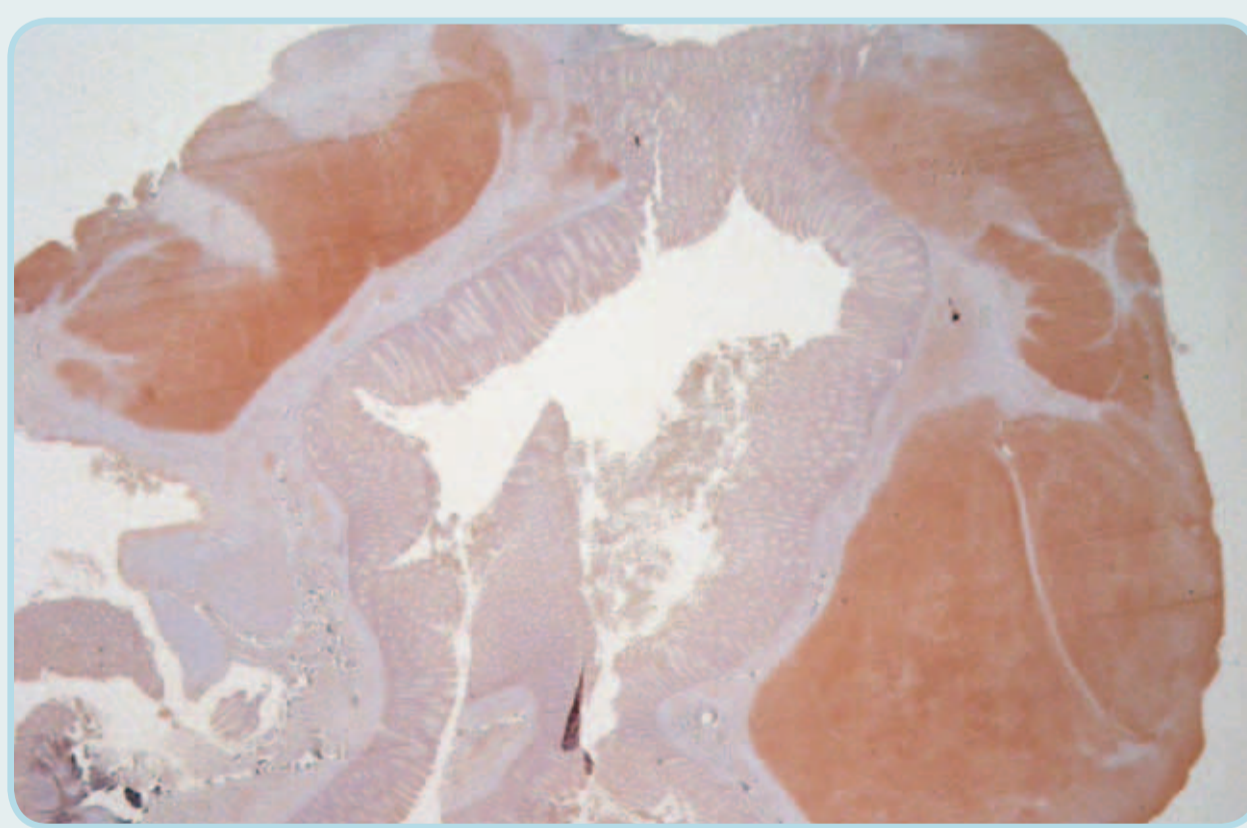


Photo 5: Caeco-colic area (anti - C-kit immunoperoxidase, x10): Marked expression of C-kit in the neoplastic tissue. On this section, the mass in the muscular layers of the gut is labelled while smooth muscle shows no evidence of staining.

A twelve-year-old Dachshund presented for vomiting appeared 3 days before. Abdominal palpation revealed moderate pain and a mobile median 4-cm-diameter mass.

The dog had also received ciclosporine at 5 mg/kg per day for 14 months because of granulomatous meningo-encephalomyelitis. Routine haematology and biochemistry profile showed only a moderate leukocytosis with neutrophilia.

Abdominal ultrasonography confirmed the presence of an intestinal mass involving the mucous and muscular layers and located in the caeco-colic region (photo 1). Localised peritonitis was also present.

Neither thoracic nor abdominal involvement could be demonstrated. The dog underwent large surgical resection with histologically healthy margins (20 cm of the ileum, the caecum and 10 cm of the colon) (photo 2).

Histopathological examination revealed a spindle cells intestinal sarcoma with a strong C-kit expression on the immunochemistry (actin negative) (photos 3 to 6). The definitive diagnosis was a GIST.

Evidence of intestinal rupture was seen on histology and was consistent with the local peritonitis and the abdominal pain. The dog received no adjuvant therapy. Chronic diarrhoea by malassimilation persisted and was poorly responsive to medical and nutritional classical therapy.

The dog was euthanized 2 years after diagnosis because of severe weight loss and persistent diarrhoea. No sign of recurrence was observed on necropsy.

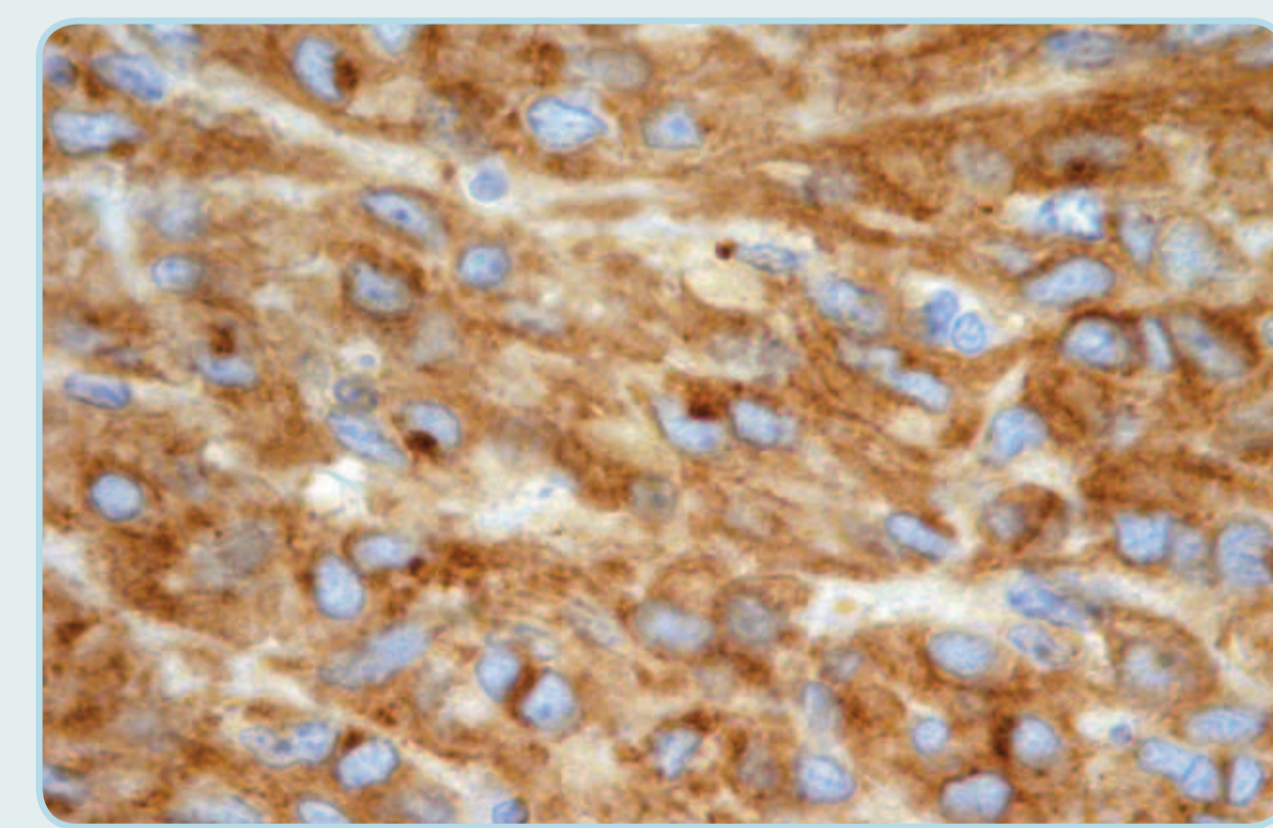


Photo 6: Expression of C-kit in neoplastic cells (anti - C-kit immunoperoxidase, x1000): The immunohistochemical expression of C-kit is cytoplasmic and diffuse, with a mild or moderate intensity, and, for some cells, paranuclear and punctiform, with a marked intensity.

Case 2

An eight-year-old Giant Schnauzer presented for tenesmus and blood on defecation.

A 3-cm-diameter mass could be detected on rectal palpation (4 cm inside the rectum) (photo 7). Clinical examination, biochemistry profile and haematology were unremarkable. Colonic video-endoscopy revealed no other abnormality. Abdominal ultrasonography and thoracic radiographs were normal.

The dog underwent complete resection and the histopathological examination showed a spindle cells rectal sarcoma, positive for C-kit expression (negative for actin) (photo 8).

The final diagnosis was a GIST. An adjuvant fractionated radiotherapy was decided because of the impossibility to achieve a very large resection.

A total dose of 48 Gray in 4 weeks was administered by a linear accelerator on a Monday-Wednesday-Friday schedule (photo 9).

The dog was still alive 18 months later, without any sign of recurrence.

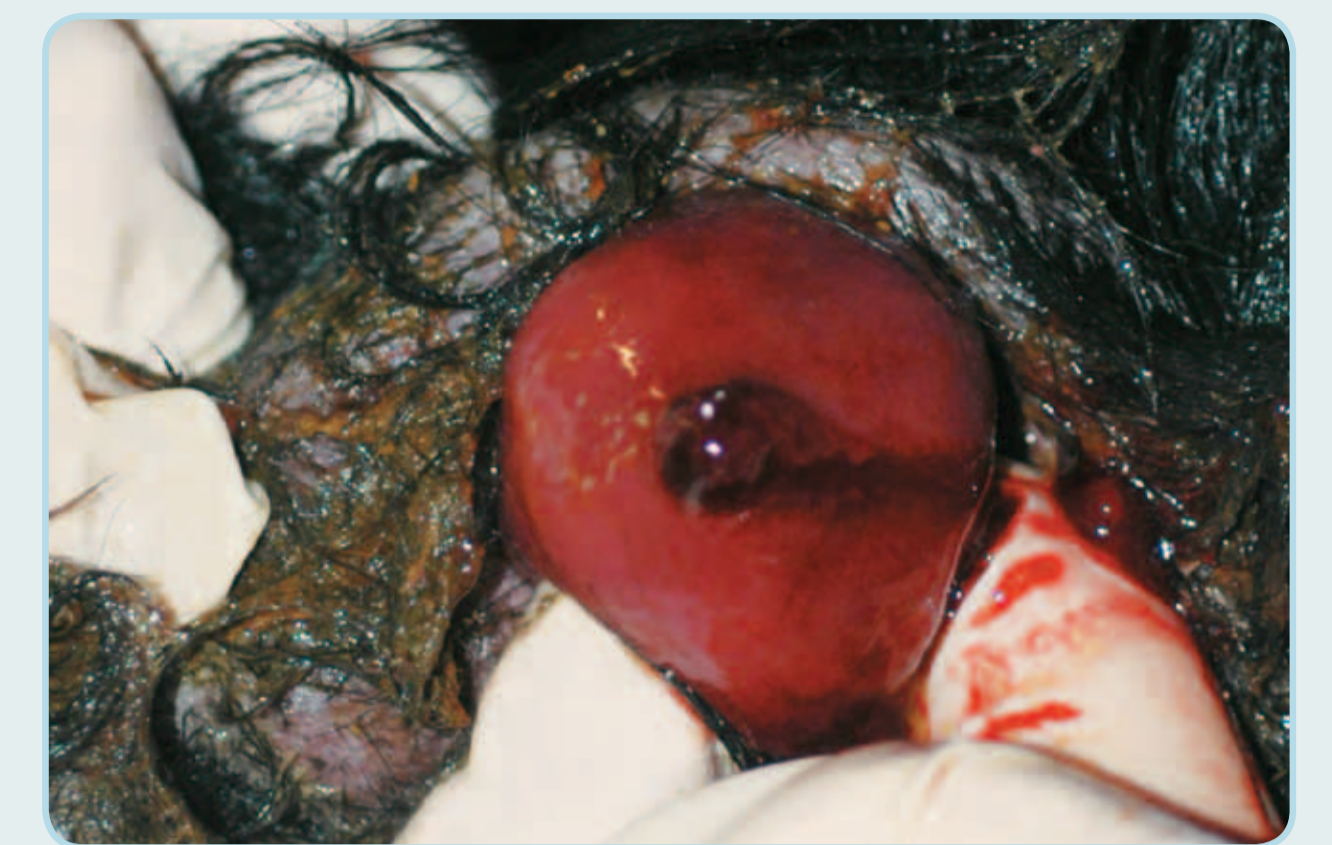


Photo 7: An ulcerated mass can be observed on rectal eversion.

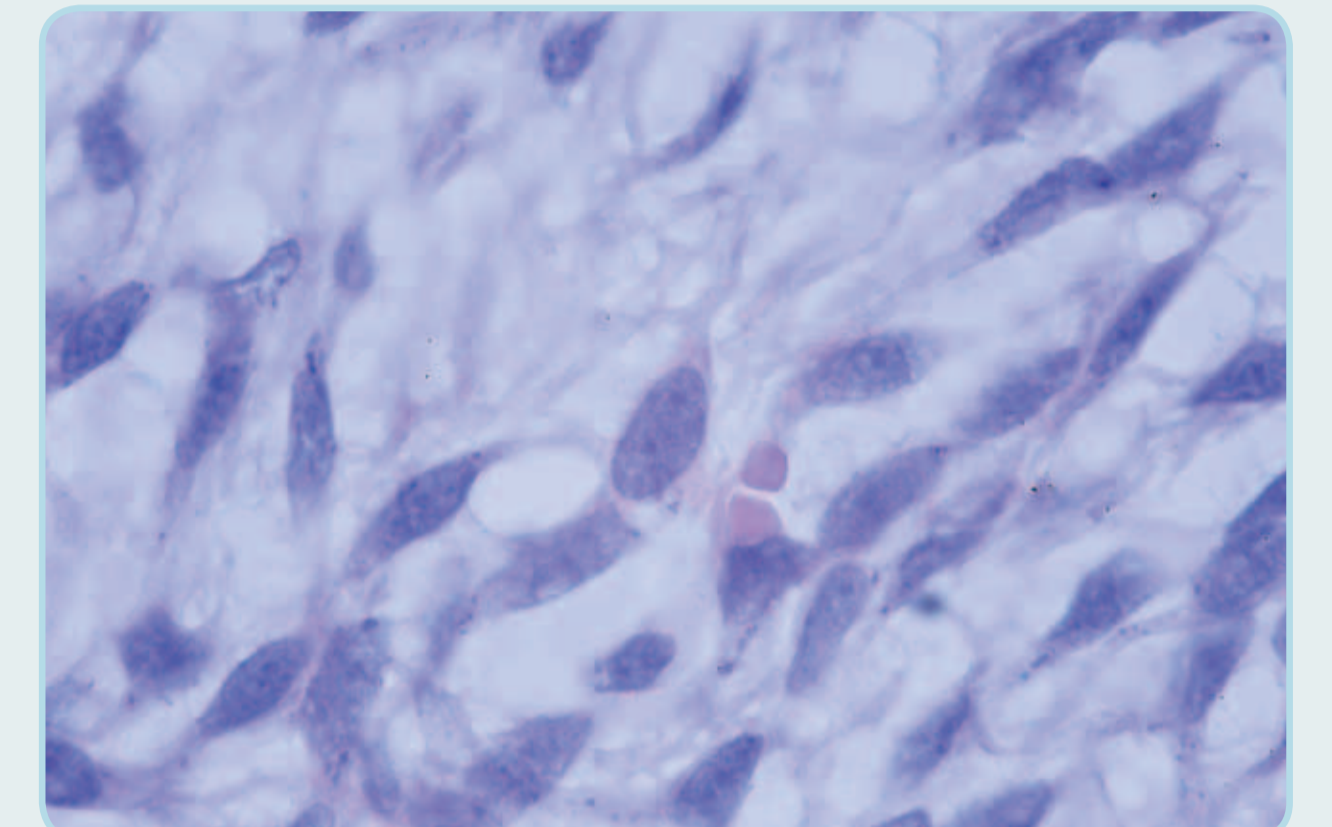


Photo 8: Spindle cells with scanty eosinophilic elongated cytoplasm and symmetrical, oval, blunt-ended and "cigar"-shaped nucleus. The chromatin is stippled with one or two small nucleoli. Slight cellular pleomorphism, no mitotic activity. Cells are distorted by abundant myxoid stroma (HE, X 1000).



Photo 9: The dog was placed in the linear accelerator after anesthesia.

Gastro-intestinal stromal tumours are uncommon in veterinary medicine. Immunochemistry allows now to differentiate them from leiomyosarcomas by evaluating the expression of C-kit mutation, which could be important for prognosis. These two cases give an example of long-term follow-up after surgical resection.

DISCUSSION

GIST are the most common mesenchymal tumours of the gastro-intestinal tract in humans. The mutation C-kit is immunohistochemically identified in most cases and allows confirmation of the diagnosis. The two main locations are the stomach and the small intestine, GIST are sporadically reported in the rectum in humans. The outcome depends on tumour size and mitotic activity and can be good for completely resected tumours.

In veterinary medicine, immunochemistry has developed recently and it is now possible to differentiate between leiomyosarcomas (smooth muscles tumours) and GIST, the latter are defined most of the time by a positive expression of C-kit mutation (CD 117), as in humans. GIST are probably derived from the interstitial cells of Cajal (ICC).

These cells have a diffuse distribution and play a role of control for the leiomyocytes (figure 1). Some GIST can be positive for the C-kit mutation only and, sometimes, they can be positive for actin, likely when ICC are distributed along the muscular layer.

GIST develop most commonly in the caecum and large

intestine; fewer are identified in the stomach and small intestine.

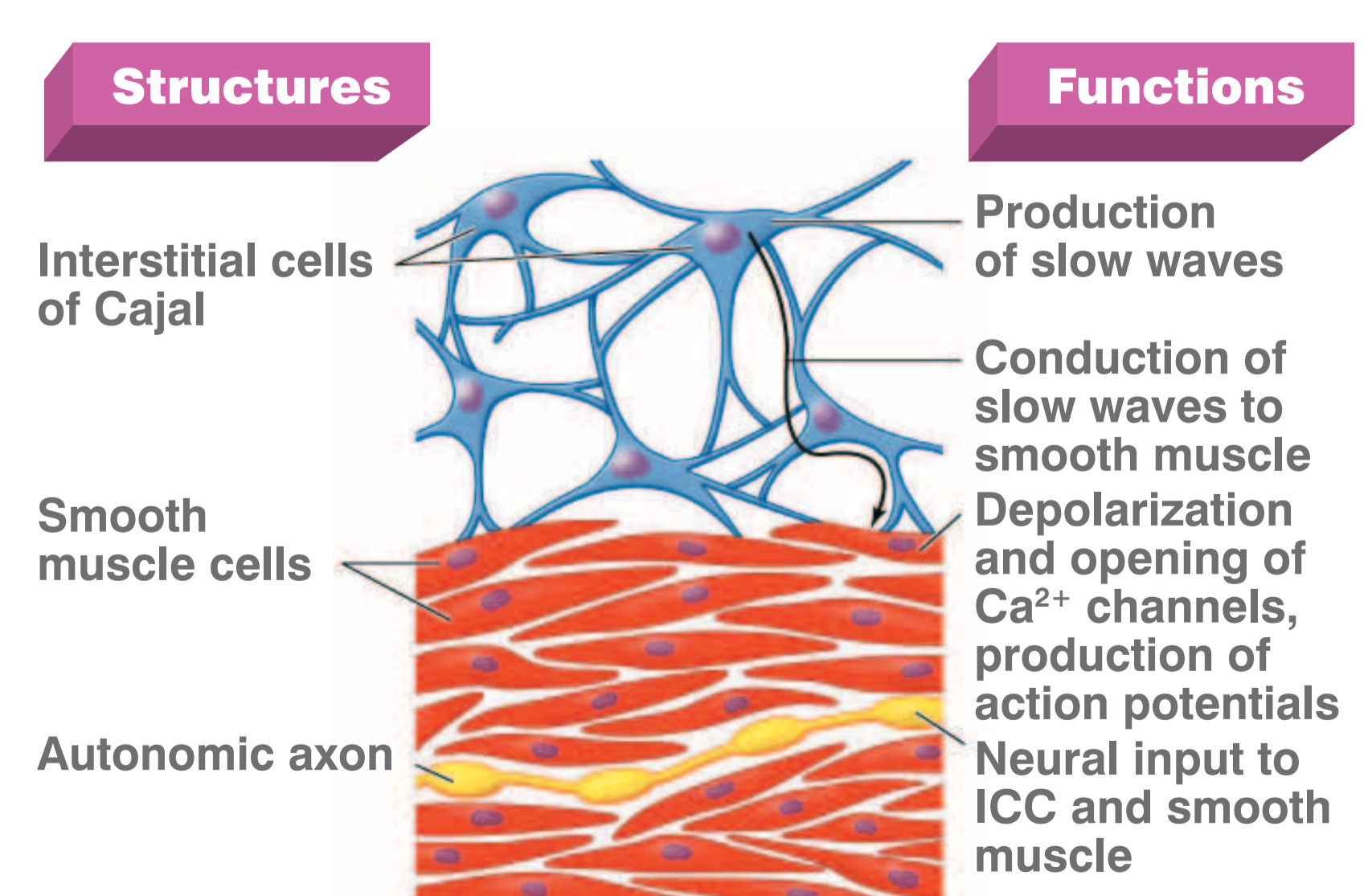
Both gastro-intestinal tumours (leiomyosarcomas and GIST) have a non specific clinical presentation: lethargy, weight loss, dysorexia and bleeding. However, perforation and sepsis, secondary to tumour invasion, seem to occur only with GIST, which are more likely locally invasive.

As a consequence, GIST can result in perioperative death because of local involvement, but their long-term prognosis seems better than leiomyosarcomas if margins are clean after surgery. In case of unresectable tumour, local recurrence or metastatic disease, human patients can receive a tyrosine kinase inhibitor (imatinib mesylate), if C-kit mutation is present.

This treatment shows prolonged survival times compared with classical chemotherapy.

Tyrosine kinase inhibitors are currently evaluated in veterinary medicine for tumours with C-kit expression, such as mast cells tumours, but studies are needed to evaluate them in metastatic or unresectable GISTs.

Figure 1: Interstitial cells of Cajal



CORRESPONDENCE :
 CLAUDE MULLER
 Clinique Vétérinaire Saint-Bernard
 598, avenue de Dunkerque
 F-59160 Lomme - France
 Phone: 33 3 20 93 67 55
 Fax: 33 3 20 22 87 32

CLINIQUE VÉTÉRINAIRE
 SAINT-BERNARD