

GIPS Slide Seminar - An Umcimbi of GI Pathology

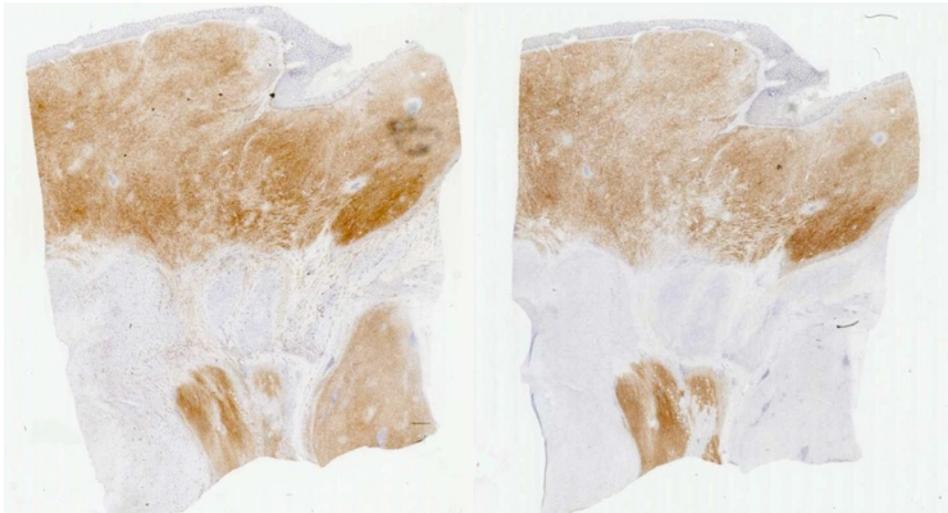
CASE 3

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Clinical history:

38 year old male with a sigmoid tumour, lymph node and lung metastases, as well as separate presacral mass. Sections provided from the sigmoid tumor –



CD34

CD117

Sections show a spindle cell tumour extending from the submucosa through the full thickness of the colonic wall. Tumour cells are diffusely CD34 and CD117 positive.

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Diagnosis of Gastrointestinal tumour

- 1) Clinical information (Age, site and any history of NF1 or familial GISTs)

2) Radiology

3) Morphology (macro + micro)

4) Immunocytochemistry

5) Mutation analysis

1. Clinical information

- Age:
- Any age but GISTs typically present > 40 years.
 - Paediatric GISTs very uncommon and tend to be wild type.

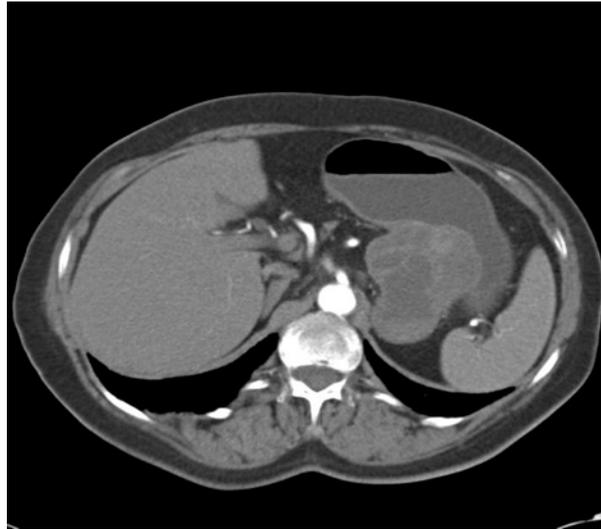
Site:

• Stomach	60-70%
• Small bowel	25-35%
• Large bowel	5%
• Oesophagus	2-3%
• Abdominal cavity	5%
<small>(mesentery, omentum, retroperitoneum, gallbladder, pancreas)</small>	

- GISTs are uncommon in the oesophagus and large bowel.

Neurofibromatosis (NF1): • Patients may get multiple GISTs which are typically wild type (for KIT and PDGFR α)

2) Radiology



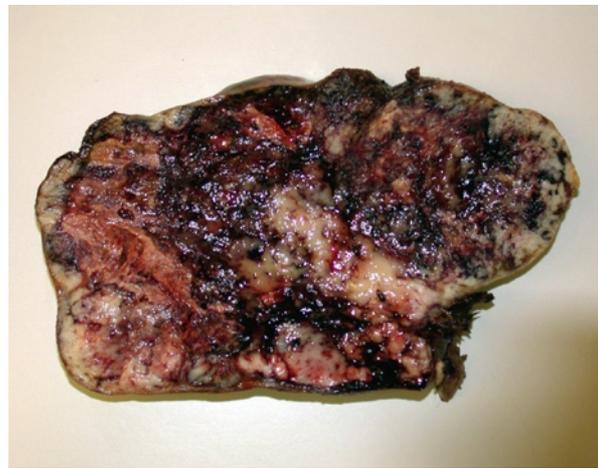
- Imaging very useful in separating carcinomas from sarcomas.
- Not always so useful in subcategorising sarcomas (except liposarcomas).
- Pattern of metastases can be very helpful (lymph node metastases uncommon, lung metastases rare in GISTs).

3) Morphology

- Macroscopic:
- Classical dumbbell morphology (submucosal and subserosal components) with central “pore” over mucosal surface.
 - Large malignant GISTs often just “sarcomatous” appearance.

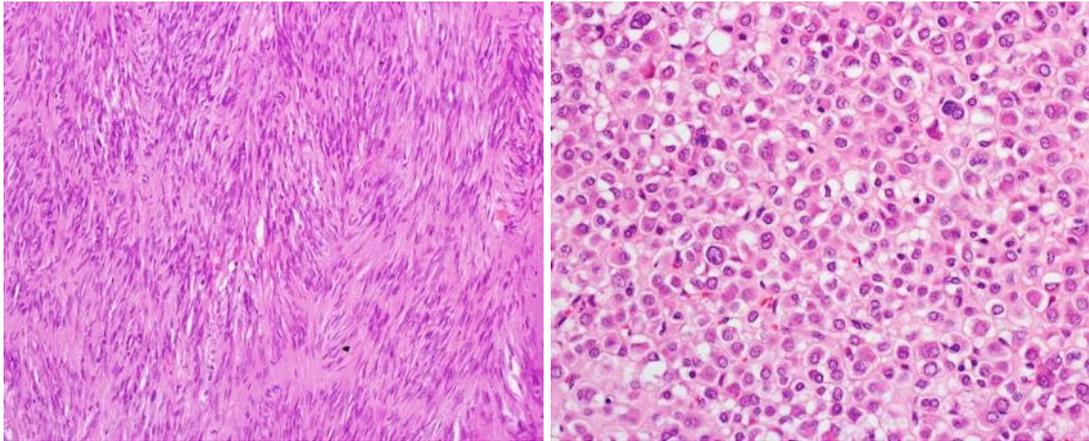


Classical dumbbell shaped GIST



Malignant GIST

- Microscopic:
- Classical spindle cell or epithelioid morphology but can show a broad spectrum of histological appearances.
 - Peinuclear vacuolation is very typical.

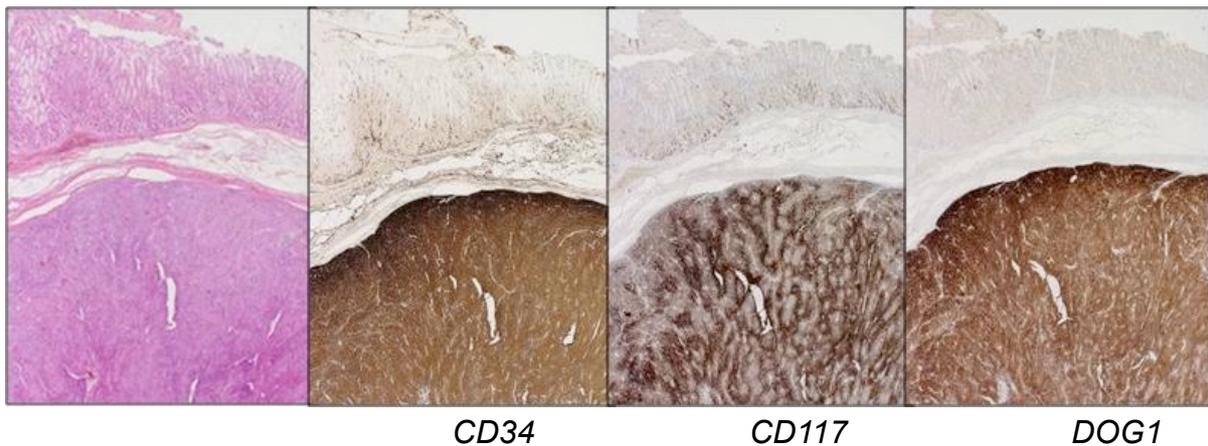


Spindle cell

Epithelioid

4) Immunohistochemistry:

- Antibodies of choice are now CD117 and DOG1¹.
- DOG1 most sensitive and specific.



CD34

CD117

DOG1

- CD117 can stain a variety of other tumour types which may be on the differential diagnosis (including melanoma² and Kaposi sarcoma³).
- For many years CD34 was an important antibody in the diagnosis of GISTs but it also stains many other tumours and has been superseded by DOG1.

5) Mutation analysis

- > 90% of GISTs have a mutation in either the KIT or PDGFR α genes.
- <10% of GISTs are wild type for both these genes. Such tumours are typically seen in paediatric patients and patients with NF1.
- Mutation analysis is becoming increasingly important in both GIST diagnosis and management (choice of medication and dosage).

References

General reference:

Gastrointestinal stromal tumours--an update for histopathologists.
Wong NA. Histopathology. 2011 Nov;59(5):807-21.

Specific references:

1. DOG1 and CD117 are the antibodies of choice in the diagnosis of gastrointestinal stromal tumours. Novelli M, Rossi S, Rodriguez-Justo M, Taniere P, Seddon B, Toffolatti L, Sartor C, Hogendoorn PC, Sciot R, Van Glabbeke M, Verweij J, Blay JY, Hohenberger P, Flanagan A, Dei Tos AP. Histopathology. 2010 Aug;57(2):259-70.
2. Case of rectal malignant melanoma showing immunohistochemical variability in a tumor. Seya T, Tanaka N, Shinji S, Shinji E, Yokoi K, Horiba K, Kanazawa Y, Yamada T, Oaki Y, Tajiri T. J Nihon Med Sch. 2007 Oct;74(5):377-81.
3. Gastrointestinal Kaposi's sarcoma: CD117 expression and the potential for misdiagnosis as gastrointestinal stromal tumour. Parfitt JR, Rodriguez-Justo M, Feakins R, Novelli MR. Histopathology. 2008 Jun;52(7):816-23.