Mesenchymal neoplasms of the gastrointestinal tract – what’s new?

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Bristol Royal Infirmary
Intra-abdominal spindle cell lesions: a review and practical aids to diagnosis

A Al-Nafussi & N A C S Wong
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Intra-abdominal spindle cell lesions are uncommon and often present a diagnostic challenge. An important group of such lesions are the gastrointestinal stromal tumours. Other intra-abdominal spindle cell lesions include fibromatosis, various sarcomas—in particular, leiomyosarcoma, liposarcoma, and malignant peripheral nerve sheath tumour—and, in women, endometrial stromal sarcoma. Less common lesions are inflammatory myofibroblastic tumours, the mesenteric spindle cell reactive lesions, retroperitoneal fibrosis, and solitary fibrous tumour. A variety of intra-abdominal tumours of nonmesenchymal origin may have a spindle cell/sarcomatoid morphology; these include sarcomatoid carcinoma, malignant melanoma and, in women, sarcomatoid granulosa cell tumour. Finally, metastatic sarcomas from pelvic or extra-abdominal organs need also be considered. A set of practical aids to the diagnosis of intra-abdominal spindle cell lesions is presented to assist pathologists dealing with such lesions, particularly with regards to the consideration of differential diagnoses.

Keywords: abdomen, connective and soft tissue, fibrosis, gastrointestinal neoplasms, neoplasms, stromal
Talk plan

• Summary from 2010 talk.
• What’s happened since 2010.
• GISTs then other neoplasm types.
• Diagnostic and clinical relevance.
Gastrointestinal stromal tumour (GIST)
a) Jee – IST

b) Ger – IST
Summary of 2010 GIST talk

- DOG1
- Prognostication
- Chemotherapy
- Wild type GISTs
Specificity of DOG1 (K9 clone) and protein kinase C theta (clone 27) as immunohistochemical markers of gastrointestinal stromal tumour

Newton A C S Wong & Golda Shelley-Fraser
Department of Histopathology, Bristol Royal Infirmary, Bristol, UK

DOG1 and CD117 are the antibodies of choice in the diagnosis of gastrointestinal stromal tumours

Marco Novelli,1* Sabrina Rossi,2* Manuel Rodriguez-Justo,1 Philippe Taniere,3 Beatrice Seddon,4 Luisa Toffolatti,2 Chiara Sartor,2 Pancras C W Hogendoorn,5 Raf Sciot,6 Martine Van Glabbeke,7 Jaap Verweij,8 Jean Yves Blay,9 Peter Hohenberger,10 Adrienne Planagan1 & Angelo P Dei Tos2

1Department of Pathology, University College London NHS Trust, London, UK, 2Department of Pathology, General Hospital of Treviso, Italy, 3Histopathology, University Hospital Birmingham NHS Foundation Trust, Birmingham, 4Department of Oncology, University College London NHS Trust, London, UK, 5Department of Pathology, Leiden Medical Center, the Netherlands, 6Department of Pathology, University of Leuven, Leuven, 7EORTC Data Center, Brussels, Belgium, 8Department of Medical Oncology, Erasmus University Medical Center, Rotterdam, the Netherlands, 9Department of Medical Oncology, Centre Leon Berard, Lyon, France, and 10Division of Surgical Oncology and Thoracic Surgery, Mannheim University Medical Center, Mannheim, Germany
CD117 + DOG1 + CD117 = it is a GIST!
Co-expression of CD117 and DOG1:

- Adenocarcinoma and squamous cell carcinoma (sarcomatoid)
- Neuroendocrine neoplasms
- Melanoma and synovial sarcoma
‘Since 2010’ – DOG1

- Co-expression of CD117 and DOG1:
  - Adenocarcinoma and squamous cell carcinoma (sarcomatoid)
  - Neuroendocrine neoplasms
  - Melanoma and synovial sarcoma
‘Since 2010’ – DOG1

- Co-expression of CD117 and DOG1:
  - Adenocarcinoma and squamous cell carcinoma (sarcomatoid)
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  - Melanoma and synovial sarcoma
+  +  =  it is a GIST!

CD117

DOG1
Summary of 2010 GIST talk

- DOG1
- Prognostication
- Chemotherapy
- Wild type GISTs
# Gastrointestinal stromal tumors: Pathology and prognosis at different sites

Markku Miettinen, MD, Jerzy Lasota, MD

## Table 1  Rates of metastases or tumor related death in GISTs of stomach and small intestine by tumors grouped by mitotic rate and tumor size

<table>
<thead>
<tr>
<th>Group</th>
<th>Size</th>
<th>Mitotic rate</th>
<th>Gastric GISTs</th>
<th>Jejunal and ileal GISTs</th>
<th>Duodenal GISTs</th>
<th>Rectal GISTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≤2 cm</td>
<td>≤5 per 50 HPFs</td>
<td>0 none</td>
<td>0 none</td>
<td>0 none</td>
<td>0 none</td>
</tr>
<tr>
<td>2</td>
<td>&gt;2 ≤ 5 cm</td>
<td>≤5 per 50 HPFs</td>
<td>1.9 very low</td>
<td>4.3 low</td>
<td>8.3 low</td>
<td>8.5% low</td>
</tr>
<tr>
<td>3a</td>
<td>&gt;5 ≤ 10 cm</td>
<td>≤5 per 50 HPFs</td>
<td>3.6 low</td>
<td>24 moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>&gt;10 cm</td>
<td>≤5 per 50 HPFs</td>
<td>12 moderate</td>
<td>52 high</td>
<td>34 high‡</td>
<td>57‡ high‡</td>
</tr>
<tr>
<td>4</td>
<td>≤2 cm</td>
<td>&gt;5 per 50 HPFs</td>
<td>0‡</td>
<td>50‡</td>
<td>§</td>
<td>54 high</td>
</tr>
<tr>
<td>5</td>
<td>&gt;2 ≤ 5 cm</td>
<td>&gt;5 per 50 HPFs</td>
<td>16 moderate</td>
<td>73 high</td>
<td>50 high</td>
<td>52 high</td>
</tr>
<tr>
<td>6a</td>
<td>&gt;5 ≤ 10 cm</td>
<td>&gt;5 per 50 HPFs</td>
<td>55 high</td>
<td>85 high</td>
<td>86 high‡</td>
<td>71 high‡</td>
</tr>
<tr>
<td>6b</td>
<td>&gt;10 cm</td>
<td>&gt;5 per 50 HPFs</td>
<td>86 high</td>
<td>90 high</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on previously published long-term follow-up studies on 1055 gastric, 629 small intestinal, 144 duodenal, and 111 rectal GISTs.\(^{12,15,18,30}\)

†Denotes tumor categories with very small numbers of cases.

‡Groups 3a and 3b or 6a and 6b are combined in duodenal and rectal GISTs because of small number of cases.

§No tumors of such category were included in the study. Note that small intestinal and other intestinal GISTs show a markedly worse prognosis in many mitosis and size categories than gastric GISTs.
Prognostication for GIST

- Miettinen/AFIP classification applies well to most adult GISTs
- Paediatric/wild type GISTs do better than predicted by AFIP system.
Standards and datasets for reporting cancers

Dataset for gastrointestinal stromal tumours (GISTs)

February 2011, amended February 2012

Coordinators:
Dr Elaine MacDuff, Western Infirmary Glasgow
Dr Shaun Walsh, Ninewells Hospital Dundee
Dr Robin Reid, Western Infirmary Glasgow
‘Since 2010’ – Prognostication

- Use 5 mm$^2$ rather than 50 HPFs
- TNM7 – Poor take-up (ESMO)
- Serosal tumour rupture (Joensuu)
clinical practice guidelines

Gastrointestinal stromal tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

The ESMO / European Sarcoma Network Working Group*

stage classification and risk assessment

The TNM classification has several limitations and is therefore not recommended.
‘Since 2010’ – Prognostication

• Use 5 mm$^2$ rather than 50 HPFs
• TNM7 – Poor take-up (ESMO)
• Serosal tumour rupture (Joensuu)
Standards and datasets for reporting cancers

Dataset for gastrointestinal stromal tumours (GISTs)

February 2011, amended February 2012

Coordinators:  Dr Elaine MacDuff, Western Infirmary Glasgow
                Dr Shaun Walsh, Ninewells Hospital Dundee
                Dr Robin Reid, Western Infirmary Glasgow
Progress in pathology

Risk stratification of patients diagnosed with gastrointestinal stromal tumor☆

Heikki Joensuu MD, PhD

Department of Oncology, Helsinki University Central Hospital, FIN-00029 Helsinki, Finland

Received 18 April 2008; revised 29 May 2008; accepted 13 June 2008
### Definition of the risk categories in the proposed Joensuu classification.

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Tumour size (cm)</th>
<th>Mitotic index (per 50 HPF&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>Primary tumour site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low risk</td>
<td>≤2.0</td>
<td>≤5</td>
<td>Any</td>
</tr>
<tr>
<td>Low risk</td>
<td>2.1—5.0</td>
<td>≤5</td>
<td>Any</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>≤5.0</td>
<td>6—10</td>
<td>Gastric</td>
</tr>
<tr>
<td></td>
<td>5.1—10.0</td>
<td>≤5</td>
<td>Gastric</td>
</tr>
<tr>
<td>High risk</td>
<td>Any</td>
<td>Any</td>
<td>Tumour rupture</td>
</tr>
<tr>
<td></td>
<td>&gt;10.0</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td>Any</td>
<td>&gt;10</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td>&gt;5.0</td>
<td>&gt;5</td>
<td>Any</td>
</tr>
<tr>
<td></td>
<td>≤5.0</td>
<td>&gt;5</td>
<td>Non-gastric</td>
</tr>
<tr>
<td></td>
<td>5.1—10.0</td>
<td>≤5</td>
<td>Non-gastric</td>
</tr>
</tbody>
</table>

<sup>a</sup> HPF, high-power field.
Validation of the Joensuu risk criteria for primary resectable gastrointestinal stromal tumour — The impact of tumour rupture on patient outcomes

P. Rutkowski a,*, E. Bylina a, A. Wozniak b, Z.I. Nowecki c, C. Osuch d, M. Matlok e, T. Świtaj a, W. Michej f, M. Wroński g, S. Głuszek h, J. Kroc i, A. Nasierowska-Guttmejer j, H. Joensuu k

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b Laboratory of Experimental Oncology, Catholic University Leuven, Leuven, Belgium
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e 1st Department of Surgery, Jagiellonian University, Cracow, Poland
f Department of Pathology, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland
g Department of Gastroenterological Surgery, Medical University of Warsaw, Poland
h Jan Kochanowski University, Kielce, Poland
i Pfizer Poland, Warsaw, Poland
j Department of Pathology, Central Hospital of Ministry of Internal Affairs, Warsaw, Poland
k Department of Oncology, Helsinki University Central Hospital, Helsinki, Finland
Tumour rupture

• Candidate for adjuvant Rx?
• Mention in report!
Summary of 2010 GIST talk

- DOG1
- Prognostication
- Chemotherapy
- Wild type GISTs
‘Since 2010’ – Chemotherapy

• Adjuvant imatinib:
  – High risk (+/- moderate)
  – ?tumour rupture
  – Three years
  – Mutation analysis
Mutations of tyrosine kinases (TKs)

# PRIMARY RESISTANCE / SENSITIVITY

## IMATINIB:

<table>
<thead>
<tr>
<th>Sensitive primary mutations</th>
<th>Resistant primary mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>KIT</em> exon 11</td>
<td><em>KIT</em> exon 9 (but dose escalation)</td>
</tr>
<tr>
<td>Upstream small mutations &gt;</td>
<td><em>KIT</em> exon 17</td>
</tr>
<tr>
<td>downstream large deletions</td>
<td><em>PDGFRA</em> exon 18 (e.g. D842V)</td>
</tr>
<tr>
<td>Wild type</td>
<td>Wild type</td>
</tr>
</tbody>
</table>

## SUNITINIB:

<table>
<thead>
<tr>
<th>Sensitive primary mutations</th>
<th>Resistant primary mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>KIT</em> exon 9</td>
<td><em>KIT</em> exon 11</td>
</tr>
<tr>
<td>Wild type</td>
<td><em>PDGFRA</em> exon 18 (D842V)</td>
</tr>
</tbody>
</table>
Summary of 2010 GIST talk

- DOG1
- Prognostication
- Chemotherapy
- Wild type GISTs
Kinase Mutations in GISTs

"Wild-type"

PDGFRA

Exon 18

Exon 12

Exon 17

Exon 13

KIT

Exon 11

Exon 9

Paediatric GISTs
(all wild type)
Wild type GISTs in adults

- Syndromic (Neurofibromatosis 1, Carney triad and Carney Stratakis)
- Sporadic / non-syndromic
Wild type GISTs in adults

• Syndromic (Neurofibromatosis 1 and Carney syndromes)
• Sporadic / non-syndromic
Since 2010 – Wild type GISTs

“Pediatric-type” Gastrointestinal Stromal Tumors in Adults: Distinctive Histology Predicts Genotype and Clinical Behavior

Tanya A. Rege, MD, PhD,* † Andrew J. Wagner, MD, PhD,‡ Christopher L. Corless, MD, PhD,§ ‖ Michael C. Heinrich, MD, ‖ ‖ and Jason L. Hornick, MD, PhD* †

Abstract: Gastrointestinal stromal tumors (GISTs) rarely affect children, mainly girls. Pediatric GISTs typically arise in the stomach as multifocal tumors with a multinodular growth pattern, epithelioid morphology, lymph node metastases, an absence of KIT and PDGFRA gene mutations, and indolent behavior. Occasional GISTs in adults show similar features. Such tumors are not widely recognized. GISTs with a multinodular growth pattern in patients over the age of 18 years were retrieved from surgical and consultation files. Hematoxylin and eosin-stained slides were reviewed, immunohistochemistry was performed, and KIT (exons 9, 11, 13, and 17) and PDGFRA (exons 12, 14, and 18) genes were screened for mutations. Clinical follow-up was obtained. Sixteen cases were identified, affecting 13 women and 3 men (median age, 31.5 y; range, 19 to 56 y), all in the stomach. The mean tumor size was 5.4 cm (range, 1.8 to 11 cm); 4 were multifocal. All tumors showed a multinodular or plexiform architecture and epithelioid (N = 3) or mixed epithelioid and spindle cell (N = 13) morphology. Five tumors had vascular invasion; 6 had focal necrosis. Mitotic activity ranged from 3 to 156/50 high-power fields (8 tumors had >50 high-power fields). Nineteen (87%) were KIT positive (N = 5), liver (N = 3), and peritoneum/omentum (N = 3). Primary tumors from 7 patients with metastases were Armed Forces Institute of Pathology low risk, very low risk, or no risk of recurrence. None of the metastatic tumors responded to treatment with imatinib mesylate. One patient died of disseminated liver and intra-abdominal metastases and the remaining patients were alive at last follow-up. Gastric GISTs in adults with a multinodular or plexiform growth pattern and epithelioid or mixed morphology are similar to pediatric GISTs. Unlike conventional adult GISTs, this distinctive subset predominantly affects women, often metastasizes to lymph nodes, and lacks mutations in KIT and PDGFRA. Current risk assessment criteria do not reliably predict behavior for this group. Although metastases are common and most tumors are imatinib resistant, they pursue a relatively indolent clinical course. Recognition of “pediatric-type” GISTs in adults is critical for prognosis, appropriate therapy, and follow-up.

Key Words: gastrointestinal stromal tumor, KIT, PDGFRA, tyrosine kinase inhibitor, sarcoma, soft tissue tumor

Wild type GISTs in adults

- Syndromic (Neurofibromatosis 1 and Carney syndromes)
- Sporadic / non-syndromic
• Gastric
• Epithelioid/MCT
• **Multinodular**
• Multifocal
• Nodal spread
• Wild type
• Imatinib resistant
• Poorly predicted by AFIP system
• Gastric
• Epithelioid/MCT
• Multinodular
• Multifocal
• Nodal spread
• Wild type
• Imatinib resistant
• Poorly predicted by AFIP system
Nodes and GISTs

• If gastric, epithelioid/mixed cell type and younger female, should surgeon harvest nodes?
• Block any lymph nodes available.
• Gastric
• Epithelioid/MCT
• Multinodular
• Multifocal
• Nodal spread
• Wild type
• Imatinib resistant
• Poorly predicted by AFIP system
• SDHB loss

• Expression of IGFR1

• BRAF V600E mutation
Expression of the Receptor for Type I Insulin-like Growth Factor (IGF1R) in Gastrointestinal Stromal Tumors
An Immunohistochemical Study of 1078 Cases With Diagnostic and Therapeutic Implications

Jerzy Lasota, MD,* Zengfeng Wang, PhD,* Su Young Kim, MD,† Lee Helman, MD,† and Markku Miettinen, MD*

Abstract: A majority of gastrointestinal stromal tumors (GISTs) carry gain-of-function KIT or platelet-derived growth factor receptor α (PDGFRA) mutations. However, no mutational activation of KIT or PDGFRA has been identified in pediatric

Key Words: gastrointestinal stromal tumor, insulin-like growth factor 1 receptor, IGF1R, GIST, immunohistochemistry, succinate dehydrogenase, pediatric GIST

• SDHB loss

• Expression of IGFR1

• BRAF V600E mutation
Wild type GISTs

- Immunohistochemical marker(s) for wild type GISTs
- BRAF and IGFR1 targeted treatment
No mutation

‘Heterozygous mutation

Artefact?
Wild type GISTs

- Immunohistochemical marker(s) for wild type GISTs
- BRAF and IGFR1 targeted treatment
Gastrointestinal smooth muscle neoplasms

- ‘Post GIST era’
- Diagnosis (new IHC markers)
- Classification
- Grading
Gastrointestinal smooth muscle neoplasms

• Colorectal mucosal leiomyomas
• Retroperitoneal uterine-like leiomyomas [can be DOG1+] 
• (Intra)mural smooth muscle neoplasms
Smooth muscle IHC markers

• SMA, Desmin, Caldesmon

• Smoothelin and PLAP?
Smooth muscle IHC markers

- Caldesmon vs. smoothelin vs. PLAP
- 31 GI smooth muscle neoplasms (3 leiomyosarcomas)
- 111 other mesenchymal neoplasms (16 neoplasm types)
Leiomyoma: 27/27
Leiomyosarcomas: 4/4 (focally reduced)
GIST: 11/20
Angiomyolipoma: 5/5
Glomus tumour: 6/7
Leiomyoma: 27/27
Leiomyosarcomas: 4/4 (focally reduced)
Angiomyolipoma: 1/5
DSCRT: 1/1
SMOOTH ELLIN

Leiomyoma: 27/27
Leiomyosarcomas: 4/4 (focally reduced)
Angiomyolipoma: 1/5
Glomus tumour: 4/7
Smooth muscle IHC markers

- Sensitivity: 100% for all three markers
- Specificity:
  - Caldesmon 80%
  - PLAP 96%
  - Smoothelin 91%
Smooth muscle IHC markers

• PLAP antibodies:
  – 8A9 monoclonal (Dako)
  – A0268 polyclonal (Dako)
  – PL8-Fm6 monoclonal (Biogenex)
Review Article

Primary leiomyosarcomas of the gastrointestinal tract in the post-gastrointestinal stromal tumor era

Gitika Aggarwal MD\textsuperscript{a}, Suash Sharma MD\textsuperscript{a}, Mei Zheng MD\textsuperscript{a}, Michelle D. Reid MD\textsuperscript{b}, John H. Crosby MD\textsuperscript{a}, Sherman M. Chamberlain MD\textsuperscript{c}, Asha Nayak-Kapoor MD\textsuperscript{c}, Jeffrey R. Lee MD\textsuperscript{a,d,e,*}

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\textsuperscript{b} Department of Pathology, Emory University, Atlanta, GA
\textsuperscript{c} Department of Medicine, Medical College of Georgia, Georgia Health Sciences University, Augusta, GA
\textsuperscript{d} Institute of Molecular Medicine and Genetics, Medical College of Georgia, Georgia Health Sciences University, Augusta, GA
\textsuperscript{e} Department of Pathology, Charlie Norwood Veterans Affairs Medical Center, Augusta, GA

DOI 10.1007/s00423-006-0092-y

Original Article

True smooth muscle neoplasms of the gastrointestinal tract: morphological spectrum and classification in a series of 85 cases from a single institute

Abbas Agaimy - Peter H. Wünsch

Received: 20 March 2006 / Accepted: 20 July 2006 / Published online: 21 September 2006
© Springer-Verlag 2006
<table>
<thead>
<tr>
<th>AFIP series</th>
<th>Leiomyomas</th>
<th>Leiomyosarcomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oesophagus</td>
<td>48 [“mitoses were rare”]</td>
<td>3 [all &gt;50/50hpf]</td>
</tr>
<tr>
<td>(Stomach)</td>
<td>3 [all 0/50hpf]</td>
<td>1 [25/50hpf]</td>
</tr>
<tr>
<td>Duodenum</td>
<td>4 [max 1/50hpf]</td>
<td>5 [five &gt; 50/50hpf one 6/50hpf]</td>
</tr>
<tr>
<td>Jejunum/Ileum</td>
<td>9 [max 3/50hpf]</td>
<td>16 [all &gt; 35/50hpf except one]</td>
</tr>
<tr>
<td>Colon</td>
<td>0</td>
<td>7 [all &gt; 100/50hpf except one]</td>
</tr>
<tr>
<td>Rectum</td>
<td>3 [all 0/50hpf]</td>
<td>8 [all &gt;28/50hpf]</td>
</tr>
</tbody>
</table>
Intramural GI smooth muscle neoplasms

• Clearer distinction between leiomyomas and leiomyosarcomas.

• Borderline/Low grade LMS/STUMP neoplasms are rare and should be treated with complete surgical excision.

<table>
<thead>
<tr>
<th>Grading principles for leiomyosarcomas (LMS) based on French Federation of Cancer Centres (FNCLCC) criteria</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differentiation</td>
<td></td>
</tr>
<tr>
<td>Well-differentiated LMS</td>
<td>1</td>
</tr>
<tr>
<td>Conventional LMS</td>
<td>2</td>
</tr>
<tr>
<td>Pleomorphic, poorly differentiated, and epithelioid LMS</td>
<td>3</td>
</tr>
<tr>
<td>Mitotic index</td>
<td></td>
</tr>
<tr>
<td>&lt;10/10 HPF</td>
<td>1</td>
</tr>
<tr>
<td>10–19/10 HPF</td>
<td>2</td>
</tr>
<tr>
<td>≥20/10 HPF</td>
<td>3</td>
</tr>
<tr>
<td>Tumour necrosis</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>&lt;50% of the tumour</td>
<td>1</td>
</tr>
<tr>
<td>&gt;50% of the tumour</td>
<td>2</td>
</tr>
</tbody>
</table>

Grade by total of score points: 2–3 = grade 1 (low grade) 4–5 = grade 2 (intermediate grade) 6–8 = grade 3 (high grade)
‘New’ entities

• RNFP
• GNET
Reactive Nodular Fibrous Pseudotumor of the Gastrointestinal Tract and Mesentery
A Clinicopathologic Study of Five Cases

Rhonda K. Yantiss, M.D., G. Petur Nielsen, M.D.,
Gregory Y. Lauwers, M.D., and Andrew E. Rosenberg, M.D.

Although the majority of mesenchymal lesions of the gastrointestinal tract are neoplastic in nature, nonneoplastic reactive processes may involve the gastrointestinal tract and mesentery, causing diagnostic confusion with more aggressive neoplasms, such as fibromatosis or gastrointestinal stromal tumors. In this study, we report a series of fibroinflammatory lesions of the gastrointestinal tract that we think represent a relatively cohesive group of tumors and describe the clinical and pathologic features of this entity, which we have termed “reactive nodular fibrous pseudotumor.” The tumors affected five patients (four male and one female patient) who ranged in age from 48 to 71 years (mean 56 years). Two patients presented with acute abdominal pain without a significant past medical history, two had incidental lesions discovered during evaluation for other medical conditions, and one was found to have an abdominal mass. Three patients had a history of abdominal surgery. The tumors were multiple in three patients and solitary in two patients. All patients had no residual disease following surgical resection (mean follow-up 16.3 months) and one patient who had an incomplete surgical resection had stable disease at 26 months. In summary, we report a series of distinct intraabdominal fibroinflammatory pseudotumors that we have collectively termed “reactive nodular fibrous pseudotumors.” These lesions are uncommon and may infiltrate the bowel wall, thereby mimicking primary bowel neoplasms or intraabdominal fibromatosis. Recognition of these nonneoplastic lesions is important, as they pursue a benign clinical course, but may be confused with other mesenchymal neoplasms that require more aggressive treatment.

Key Words: Reactive nodular fibrous pseudotumor—Fibroinflammatory tumor—Fibromatosis—Sclerosing mesenteritis—Mesentery—Gastrointestinal tract—Differential diagnosis.

CLINICAL CASE

Reactive nodular fibrous pseudotumor: A first report of gastric localization and clinicopathologic review

Pseudotumeur fibreuse nodulaire réactionnelle : à propos d’un premier cas de localisation gastrique et revue clinico-pathologique

G. Gauchotte\textsuperscript{a,\,*}, A. Bressenot\textsuperscript{a}, T. Serradori\textsuperscript{b}, P. Boissel\textsuperscript{b}, F. Plénat\textsuperscript{a}, K. Montagne\textsuperscript{a}

\textsuperscript{a} Laboratoire de pathologie, hôpitaux de Brabois, CHRU, 5, allée du Morvan, 54511 Vandoeuvre-lès-Nancy, France
\textsuperscript{b} Department of digestive surgery, hôpitaux de Brabois, CHRU, Vandoeuvre-lès-Nancy, France

Available online 16 September 2009
RNFP

- Hx of intra-abdominal injury.
- Well circumscribed.
- Serosal/subserosal.
- (Myo)fibroblastic.
- Keloidal / collagen bundles.
- Chronic inflammation.
Table 2. Results of Immunohistochemical Investigations

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE1/AE3</td>
<td>foc+</td>
<td>dif+</td>
<td>-</td>
<td>foc+</td>
<td>foc+</td>
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Abbreviations: dif+, diffusely positive; foc+, focally positive; SMA, smooth muscle actin; MSA, muscle-specific actin; PI, proliferative index; ALK-1, anaplastic lymphoma kinase-1, ND, not done.
RNFP

• Hx of intra-abdominal injury.
• Well circumscribed.
• Serosal/subserosal.
• (Myo)fibroblastic.
• Keloidal / collagen bundles.
• Chronic inflammation.
• Non-neoplastic (IgG4 related?)
Malignant Gastrointestinal Neuroectodermal Tumor: Clinicopathologic, Immunohistochemical, Ultrastructural, and Molecular Analysis of 16 Cases With a Reappraisal of Clear Cell Sarcoma-like Tumors of the Gastrointestinal Tract

David L. Stockman, MD,* Markku Miettinen, MD,† Saul Suster, MD,* Dominic Spagnolo, MBBS, FRCPA, MD,‡§ Hugo Dominguez-Malagon, MD,|| Jason L. Hornick, MD, PhD,¶ Volkan Adsay, MD,# Pauline M. Chou, MD, PhD,** Benhur Amanuel, MBBS, FRCPA,‡§ Peter VanTuinen, PhD,* and Eduardo V. Zambrano, MD*

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GNET

• Clear cell sarcoma-like tumours of the GIT (CCSLTGT).

• NOT to be confused with clear cell sarcoma of soft parts.

• Small bowel >> Stomach and large bowel
GNET

• Compared with clear cell sarcoma of soft parts (melanoma marker +ve).
• Autonomic NS primitive neural stem cell?
• Poor prognosis.
Summary

- **GIST:**
  - DOG1 and CD117
  - Tumour rupture
  - Adjuvant therapy
  - Wild type GISTs
Summary

• PLAP and smoothelin.
• FNCLCC grading of LMS.
• If myofibroblastic and inflamed, remember IgG4.
• If ?melanoma, consider GNET.