Surgical treatment for carcinoids - What’s New & What’s Next?

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Lymphatic mapping helps define resection margins for midgut carcinoids.
Background

• Midgut Carcinoid:
  • Uncommon Disease
  • Vague symptoms

• Delayed/ Retrograde Diagnosis
  • Bowel obstruction
  • Flushing & Diarrhea
Treatment of Primary Disease

Surgery, Surgery, Surgery

Margins

Lymphatic

Blood Supply
Common Intra-operative Findings

- Partial Bowel Obstruction
- Massive Mesenteric Lymphadenopathy
- Mesenteric Vessels Encasement
- Intestinal ischemia
- Multiple "Primary" tumors
- Liver or other Metastasis
Traditional Surgical Approach

- Bowel lymph travels bi-directionally along subserosal channels
- Resection margins classically 5 cm to get lymphatics of bowel
How much to resect?
New concept---Sentinel Lymph Node & Lymphatic Mapping

Breast Cancer

Melanoma

GI Tract Malignancy?
• Boggy and Massive Lymphadenopathy

• Alternative Sub-Serosal Lymphatic Pathways

• Multiple “Primary” Tumors

• True, True, & True but Unrelated?

• Untold Story?
Hypothesis

• Massive Lymphadenectomy ---- Obstruction of normal “radial” mesenteric lymphatics --- Detour --- “Longitudinal” alternating intra-intestinal sub-serosal pathways --- returns into unobstructed mesenteric lymphatics

• Multiple “Primary”

• Recurrences at or adjacent to resection sites
Drop metastasis developed on route of Lymphatic detour
Method

• Resects Tumor(s) with “Adequate “Margins using Lymphatic Mapping
• Conservation of Bowel Length
• Mesenteric Lymphadenectomy
• Restore Blood Supply
• Spare Ileocecal Valve Whenever Possible based on Mapping
Lymphatic drain crossing ileo-cecal valve
Lymphatic drain doesn’t across ICV
Results

• 303 Patients for cyto-reductive operations (11/2006-10/2011)
• 112 patients underwent mapping (35 REDO)
• 98 patients with midgut primary
• 45 patients with tumor near ileo-cecal valve

• 92% resection margins modified
• 44% ileo-cecal valve preserved
• 54% Disease found at or near the anastamosis
• 0 % had anaphylactic reaction
Conclusion

• Time-effective & Safe
• Better cytoreduction
• No “arbitral” margins
• Ileo-cecal valve sparing

• Less local recurrence
• Less diarrhea
• Better quality of life
• Improve long term survival
An important step for maximum debulking and restoring blood supply to the ischemic bowel secondary to an extensive mesenteric lymphadenopathy and vascular encasement
Intraoperative chemotherapy

Dissolvable foam soaked in chemotherapeutic agent

Liver resection cavities
Mesentery defects after dissection
Pelvis
Diaphragm
SPECIMEN SITE: omentum
TESTING LABORATORY: PTI-Southside
TUMOR TYPE: Gastrointestinal: Small Intestine
LAB ADDRESS: 2516 Jane Street, Pittsburgh, PA 15203

TESTING INFORMATION

SINGLE AGENTS: 7
COMBINATION AGENTS: 3

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<th>Responsive</th>
<th>Intermediate Response</th>
<th>Non-Responsive</th>
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<td>DOXORUBICIN/FLUOROURACIL ETOPOSIDE</td>
<td>SUNITINIB PACLITAXEL CISPLATIN DOXORUBICIN</td>
<td>FLUOROURACIL/TEMOZOLOMIDE FLUOROURACIL CISPLATIN/ETOPOSIDE TEMOZOLOMIDE</td>
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62 consecutive Mid gut carcinoid Patients for cyto-reductive operations (1/2007-12/2009)
32 patients underwent intra-op chemo
30 patients without tx as control

5 year survival rates are the same so far

18.8% (6/32) vs 53.3% (16/30) need re-exploration
56.3% (9/16) vs 33.3% (2/6) had local recurrence
6.25% (2/32) vs 30% (9/30) had local recurrence
A new approach for evaluating ischemic bowel following extensive mesenteric lymphadenectomy for midgut carcinoid
Results

Between 6/2006 and 10/2010, a total of 12 patients underwent staged 2\textsuperscript{nd} look laparoscopies; six were conducted to evaluate the integrity of anastomoses between ischemic looking bowel segments following extensive mesenteric lymph node dissection.

All initially ischemic looking bowel segments restored normal perfusion and all anastomoses remained intact. All staged 2\textsuperscript{nd} look laparoscopies were concluded in 5-10 minutes without any complications or prolonged hospital stays.
Radio-guided exploration facilitates surgical cytoreduction of Neurendocrine tumors.
Common Pre-operative Imaging Studies

Octreoscan: 90% positive
MIBG Scan: 70% positive
CT Scan
MRI
PET
Radio-guided Surgery

• Sentinel lymph node biopsy
  • Breast Cancer
  • Melanoma
  • Lung Cancer
• Tumor marker-guided 2nd look
• Minimally invasive Parathyroidectomy
• Neuroendocrine Tumors
Adoption of gamma probe use intraoperatively

• Target-directed dissection
  • Time saving, less tissue damage and blood loss

• Most minimally invasive procedure possible
  • Small incision, minimal dissection, rapid recovery

• Real time differentiation
  • Scar, desmoplastic tissue, viable vs nonviable tumor

• Enhance the degree of debulking
  • Identify and locate tumor burden missed by surgeon

• Confirmation of target removal
  • Ex vivo count of specimen, in vivo count of field
Results

46 patients had gamma probe guided explorations
3 patients injected with $^{99m}$Tc,
3 patients injected with $^{123}$I MIBG (3)
40 patients injected with $^{111}$In pentetreotide.

37 out of 40 (93%) of the $^{111}$In-pentetreotide guided explorations the gamma probe was deemed helpful
5 out of 6 neck and mediastinum explorations the gamma probe was essential
$^{123}$I MIBG was not useful in all three patients
The optimal doses and interval between injection and exploration of $^{111}$In pentetreotide is 6 mCi injected 6-7 days prior to surgery.
Discussion

• Useful and powerful adjunct, especially for re-exploration and unusual anatomic locations

• Essential for neck and mediastinal lymph node metastasis

• Great potential for rectal carcinoid: defining lymphatic drainage and proximal margins

• Isotope selection, injection dose and timing of exploration are the keys for a successful outcome
Comparison of patients with metastatic small bowel neuroendocrine tumors (distant disease) between the NOLANETS clinic and the SEER national database

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<td>SEER</td>
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<td>67%</td>
<td>48%</td>
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New technology: Irreversible Electroporation (IRE)

High voltage electrical pulses

Low energy direct current

Permanent cell membrane disruption

Without heat
Potential New Approaches

For extremely advanced diseases or carcinomatosis:
Biopsy of primary, lymph node and liver metastasis

Biological / chemo-sensitivity tests &/or
Immunological prep: Anti-CEA/SM Designer T-cells

Neo-adjuvant biological or immuno or chemo therapy

Post- treatment Surgical exploration: cytoreduction;
Electrooperations with intralesional-chemotherapy;
Intra /prei tumor injection of Anti-SM Designer T cells;
Intra-operative chemo-infusion: divers’ approach
- Functioning vs Nonfunctioning tumors
- Local/ regional vs Distant diseases
- Surgical vs Non-surgical treatment
- Combine surgical non surgical txs and the sequences
- Surgical procedures for pancreatic primaries
  A). Enucleation
  B). Beger’s procedure
  C). Whipple
  D). Central pancreatectomy
  E). Distal pancreatectomy with or without en bloc resection of adjacent organs
  F). Total pancreatectomy for MEN I patients
  G). Ablations
“Start by doing what is necessary, then what is possible, and suddenly you are doing the impossible.”

― St. Francis of Assisi
Thank You!!

Questions?