

GASTROINTESTINAL STROMAL TUMOR OF THE STOMACH

- Rare soft tissue tumor of the GI tract, mesentery, and omentum (up to 3% of all GI cancers)
- Incidence 1-2/100,000; 6,000 cases reported each year in the United States
- Stomach 60- 70% of cases; small intestine 20%, rectum 5%, esophagus 2%
- M>=F; age 40-70 (median 60); no racial predilection
- Histologic subtypes include spindle, epithelioid, mixed

Pathology

- Once thought to be of smooth muscle origin, classified as leiomyosarcomas- today recognized as both smooth muscle and neural elements, and the cell of origin is now believed to be the interstitial cell of Cajal (ICC), an intestinal pacemaker cell.
- IHC staining for the trans-membrane receptor tyrosine kinase KIT (CD117), highlights the interstitial cells of Cajal in more than 95% of GISTs.
- Approximately two thirds of GISTs also express CD34.
- Do not express Desmin or S-100
- Tumor size ranges between 0.5 and 44 cm in diameter (median diameter, 6 cm).

Clinical features

- Mass-related symptoms (e.g., abdominal pain, bloating, and early satiety)
- Melena or anemia (from overlying mucosal ulceration)
- Tumor ulceration / rupture → peritonitis (not common)

Evaluation

- CT/ MRI / PET (intense uptake; predicting malignant potential)
- Endoscopy, with or without EUS. Because of the infrequency of mucosal involvement, it is rarely diagnostic.
- Biopsy is controversial, because of the risk of tumor rupture and intra-abdominal dissemination. It may be required, in disseminated disease, suspected lymphoma and enrollment in a trial of neoadjuvant therapy

Prognostic indicators

- Low risk of an aggressive disease course:
 - Tumor size < 2 cm in diameter
 - Mitotic count < 5 per high-power field (HPF)
- High risk of an aggressive disease course:
 - Tumor > 10 cm
 - Mitotic count > 10/HPF
- For all other tumors, the risk of aggressive disease is considered to be intermediate.

Treatment

Surgery is the mainstay treatment. Surgical Principles:

- Complete resection, with grossly negative margins and an intact pseudocapsule (avoid tumor rupture)
- The implications of positive microscopic margins is unclear
- Gastric segmental resection is preferred rather than enucleation
- No requirement for routine lymphadenectomy (usually no need for subtotal/total gastrectomy)
- Laparoscopic resection
- Locally advanced – En-block resection
- Patients with metastatic disease or too high risk for en-block resection may be treated primarily with imatinib.
- Borderline resectable lesions should be treated with imatinib until they exhibit a maximal response as documented by CT and PET; surgery may then be undertaken to resect any residual foci of disease.
- Isolated liver metastasis should be resected

Gleevec (Imatinib, STI-571)

- KIT protein functions as a transmembrane receptor that dimerizes in the presence of its ligand, known as a stem-cell factor, which leads to increased tyrosine kinase activity.
- In GIST this triggers a cascade of intracellular signals to either stimulate tumor cell proliferation or inhibit apoptosis.
- These findings led to the application of the orally bioactive tyrosine kinase inhibitor Imatinib mesylate, originally indicated for the treatment of chronic myelocytic leukemia.
- The role of adjuvant therapy with imatinib is under evaluation of The American College of Surgeons Oncology Group, for patients with high-risk and intermediate-risk GIST.

Prognosis

- The majority of patients will experience tumor recurrence despite undergoing complete resection of their primary tumor.
- The median time to recurrence after surgery is reported to range from 18–24 months
- 2-year survival of patients with metastatic disease is now reported to be approximately 70%

Summary

- Approximately 80% of patients with metastatic GIST benefit from imatinib.
- For patients with primary GIST, surgery remains the treatment of choice, and whether outcome is improved by adjuvant imatinib is currently under broad investigation.
- A combination of imatinib therapy and surgery also may be effective in a subset of patients with metastatic or unresectable primary GIST

References

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Aviad Hoffman, MD
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