Small Intestinal Tumors

Essay

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Summary

Tumors of the small intestine differ from gastric or colonic neoplasms because of their low incidence rate and the occurrence of histological entities rarely seen in other gastrointestinal tract ***(Blanchard, 2000)***.

Benign and malignant small intestinal tumors are uncommon; most malignancies represent metastases .Primary small bowel tumors constitute 1% to 2% of all primary gastrointestinal malignancies ***(Blanchard, 2000)***.

Research into the natural history and prognosis of patients with small bowel cancer has been limited by the small number of cases and the heterogeneity of tumor types, including adenocarcinomas, carcinoids, sarcomas, Gastrointestinal stromal tumors and lymphomas. Each of these tumor subtypes has its own distinct clinical behavior and, therefore, dictates a different treatment approach. Unfortunately, malignant lesions are often discovered when they have metastasized to distant sites or at surgery when indicated for other diagnosis or intestinal obstruction ***(Zeh, 2005)***.

Preoperative diagnosis of primary small intestinal neoplasm as can be a challenge for both clinicians and radiologists. As a result of their infrequent occurrence, they invariably present difficult problem in diagnosis and management these problems are reflected mainly in delayed treatment and a very poor prognosis for such malignant tumors, their morphological changes however, shown in enteroclysis and CT, correlate pathological specimens ***(Merck,1995)***.

In patients with symptomatic disease, the correct diagnosis is achieved preoperatively in 43% small bowel enema or enteroclysis, computed tomography scan (CT) are the most effective diagnosis procedures ***(Chen, 2006).***

This ability to accurately image a small intestinal neoplasm, independently of its size, anatomical localization and growing tendency, represents a major improvement in the diagnosis and management of these neoplasms ***(Minardi, 1998).***

The few published series on small bowel neoplasms that are available cannot be used as generalizations for presentation of the individual histological subtypes. However, it does appear that adenocarcinomas are more frequently associated with pain and obstruction when compared to sarcomas and carcinoids**,** GIST present more commonly with acute GI bleeding ***(Jemal, 2007)***.

After the colon, the duodenum is the most common site of adenocarcinoma. Patients with familial adenomatous polyposis have a relative risk of more than 300 for duodenal adenocarcinoma but no elevated risk for gastric or non duodenal small bowel cancer. Molecular genetic studies of duodenal polyps in patients with familial adenomatous polyposis a high frequency of p53 over expression in dysplastic adenomas, although the frequency of TP53 and k-ras gene mutations was much lower ***(Arai, 1997)***.

The relative risk of small bowel adenocarcinoma is estimated to be between 15 and more than 100 in patients with Crohn's disease. Unlike most small-bowel adenocarcinomas, Crohn's related tumors generally occur in the ileum, reflecting the distribution of Crohn's disease. The risk of adenocarcinoma does not begin until at least 10 years after the onset of Crohn's disease,

and the adenocarcinoma typically occurs more than 20 years afterwards ***(Blanchard ,1996)***.

Patients with celiac disease appear to be at increased risk of small bowel lymphoma and adenocarcinoma. Patients with adult celiac disease appear a relative risk of 300 for the development of lymphoma and 67 for the development of adenocarcinoma. Small bowel adenocarcinomas associated with celiac disease appear to have an increased incidence of defective DNA mismatch repair compared with those not associated with celiac disease and are also associated with an earlier stage at diagnosis and a better prognosis ***(Green, 2001)***.

The prognosis (chance of recovery) and treatment options depend on the type of small intestine cancer, whether the cancer has spread to other places in the body, whether the cancer can be completely removed by surgery, whether the cancer is newly diagnosed or has recurred ***(Chen, 2006)***.

Because of its low prevalence, few clinical trials have been performed to assess the efficacy of chemotherapy for treating small bowel cancer; newer agents found to be effective for colorectal carcinoma also may be active for small-bowel adenocarcinoma. 5-FU refractory small bowel adenocarcinoma was treated with salvage irinotecan therapy

Also FOLFOX 4 regimen (i.e., combination infusion 5-FU, oxaliplatin, and leucovorin) was safely administered as adjuvant chemotherapy in patients with resected small bowel adenocarcinoma associated with celiac disease ***(Polyzos, 2003)***.

Because these are uncontrolled studies with few patients, drawing conclusions regarding the benefit of chemotherapy for small bowel adenocarcinoma, either in the metastatic or adjuvant setting, is difficult. In patients with a good performance status, any attempts using the regimens mentioned seem reasonable ***(Polyzos, 2003)***.

The efficacy of cytotoxic chemotherapy for small bowel sarcomas, no survival benefit with the addition of adjuvant chemotherapy after surgery Also chemotherapy in patients with metastatic GI soft tissue sarcomas have also yielded disappointing results ***(Bettini,2003).***

Evidence indicates that in general, small bowel sarcomas and GISTs are more resistant to chemotherapy than sarcomas in other sites. Greater expression of multi drug resistance proteins in GISTs compared with non-GI leiomyosarcomas ***(Bettini, 2003).***

Unlike conventional chemotherapy, the recently developed novel agent imatinib mesylate (also known as STI571 and Gleevec) has shown promising activity in GISTs. Imatinib is a small molecule that selectively inhibits the tyrosine kinas activity of bcr-abl, c-kit, and PDGFR ***(Bettini, 2003).***

Multinational studies of 147 subjects with advanced GISTs were randomized to receive 400 mg or 600 mg of imatinib daily. Results demonstrated a 54% partial response rate and 28% stable disease, with a median duration of response greater than 24 weeks and no differences in response between the two doses ***(Bettini, 2003).***

Another study of imatinib for Research and Treatment of Cancer, indicated a 54% partial response rate and 37% stable disease rate, with a duration of response greater than 10 months, among 35 subjects with GISTs so these studies have led to the US Food and Drug Administration approval of imatinib for advanced GISTs. However, its effect on survival and its role in the adjuvant setting remain to be defined by the results of ongoing randomized clinical trials ***(Van Oosterom, 2002)***.

The FDA has recently as targeted therapy for patients in whom imatinib fails in the form of disease progression or inability to tolerate the drug ***(Van Oosterom, 2002)***.

Surgical resection provides the only hope of cure for patients with small bowel adenocarcinomas. Several studies have shown that patients who undergo resection have an improved 5 year survival rate of 40-60%. Surgery is indicated for palliation in patients with symptomatic advanced disease, such as intestinal obstruction ***(Blair, 1996)***.

Radiation although no survival benefit is achieved with adjuvant radiotherapy after surgery for small bowel adenocarcinoma or sarcoma, radiotherapy may be useful as a palliative procedure for pain relief or obstructive symptoms in patients with advanced disease. Also, radiotherapy may be of benefit for controlling chronic tumor related blood loss. While postoperative radiotherapy has been shown to improve local control for sarcomas of the extremities, its role for GIST and GI sarcomas is not clear. Adjuvant Brach therapy and intraoperative

radiation are also being investigated for treatment of GI sarcomas ***(Blair, 1996)***.

No standard medication regimen demonstrates benefit in an adjuvant or metastatic setting for small bowel adenocarcinoma. Because of the similarity to colorectal adenocarcinoma, a regimen containing 5-FU with leucovorin may be used. Newer agents active in colorectal carcinoma, such as irinotecan and oxaliplatin, may also be considered, in combination with 5-FU. Small bowel sarcomas, most of which are c-kit –positive GISTs, are resistant to cytotoxic chemotherapy. However, patients with advanced disease may be treated with imatinib ***(Bauer, 1997)***.

الملخص العربي

تختلف اورام الأمعاء الدقيقة عن اورام المعدة والقولون في قلة حدوثها بالقناة الهضمية ؛ والتأخر في ظهور اعراضها وعلاماتها الجسمانية ؛وصعوبة تشخيصها . وغالباً يؤدي الي التأخر في علاجها؛ **وبالتالي سوء في معدل الاستشفاء.**

تعتبر الفحوص التصويرية والمعملية ومناظير الجهاز الهضمي وأخذ العينات وفحصها بالعين المجردة
والمجهرية من أهم وسائل تشخيص **اورام** الأمعاء الدقيقة.

يتفاوت علاج هذه الأورام من العلاج الجراحي أو الاشعاعي أو الكيماوى حسب مرحلة اكتشاف نوع الورم المصاب به المريض.

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Contents

List of figures