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胃腸道間質瘤(GIST, gastrointestinal stromal tumor)—小腸部位

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病史　該名55歲病患以前並無任何病史。根據病人主述，間歇性的解瀝青便已有4-5 天。沒有腹痛、嘔吐或體重減輕的症狀。該病患因為頭暈、心悸且近乎昏厥而被送到本院急診。在急診時意識清醒，血壓 110/70 mmHg，脈搏 110/min，WBC 12700/ul，Hb 7.9g/dl，PLT 252k/ul，其餘生化檢查均在正常範圍。住院當天胃鏡檢查僅發現輕微胃炎，並無任何出血點。因持續解瀝青便，且血壓降低及意識改變，故轉入加護病房。此時鼻胃管引流仍無上消化道出血的徵象，故強烈懷疑小腸出血，並即刻安排小腸血管攝影(SMA angiography)。血管攝影(Fig. 1)發現在空腸(jejunum)有一團圓形高度顯影的區域，疑似腫瘤(tumor stain)，並有出血現象。腹部電腦斷層(Fig. 2)也證實有一顆5 x 4cm 圓形腫瘤位於左側空腸位置。故緊急照會外科後立即開刀，術後診斷為小腸腫瘤併出血。病理診斷為胃腸道間質瘤(GIST, gastrointestinal stromal tumor), C-kit(+), 約5.0 x 4.7cm。術後第四天即順利出院。

討論　GIST 是一種胃腸道的間葉瘤(mesenchymal tumor)，在組織學及免疫組織染色上，有別於單純由肌肉或神經細胞來源的平滑肌肉瘤(leiomyoma)或神經鞘瘤(schwannoma)。好發於50-60歲中年人，好發部位在胃部佔60-70%，小腸佔25-30%，極少數發生在大腸、直腸或食道。其症狀表現包括消化道出血(GI bleeding)、消化不良(dyspepsia)、胃腸道阻塞(obstruction)。診斷上以內視鏡為主。因為該腫瘤的血管支配相當豐富，對於內視鏡不易到達的部位，血管攝影亦為診斷工具之一。據統計，有一半的病人發現腫瘤時，已有肝臟或腹膜轉移。GIST 不易由組織學上判斷良性或惡性，除非已造成鄰近器官、淋巴結或遠端轉移。故有人提出 mitotic index(mitotic rate>2/10 HPF)或 size >5cm 較易復發或轉移。GIST 在病理學上呈現一致的 C-kit (CD117)陽性(一種 type III receptor-tyrosine kinase)。由於 kit 突變(exon 11)導致過度活化，造成細胞增生。治療上除了開刀外，可用口服 Glivec(STI 571)(一種 tyrosine kinase inhibitor)來阻止腫瘤生長，其通常用於轉移性腫瘤，反應率(response rate)可達60%。

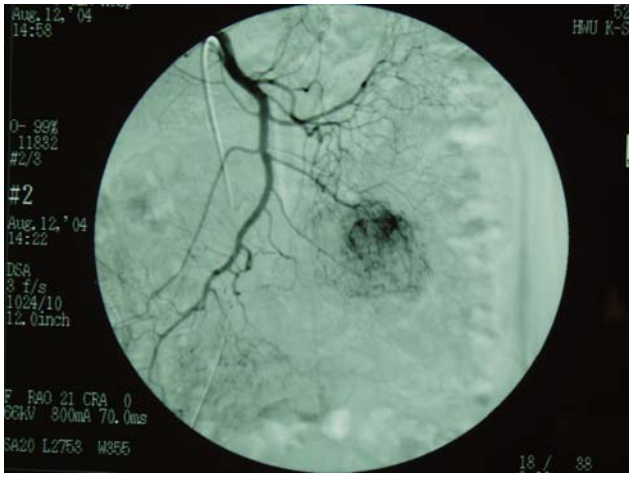

Fig. 1

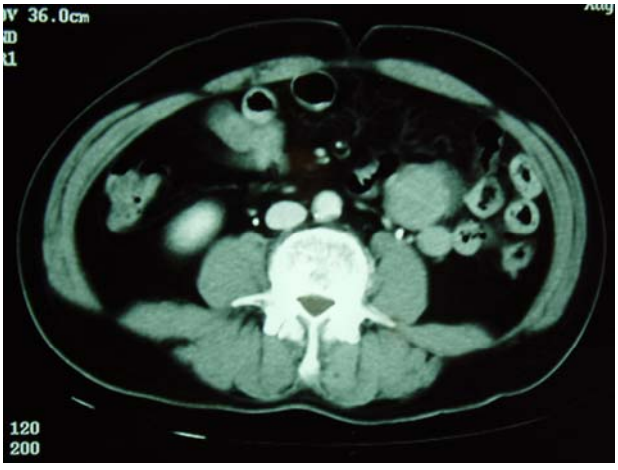

Fig. 2

參考資料:

1. Gastrointestinal stromal tumors: update. Arkh Patol. 2004;66:36-40.
Xie XY, Carter N, Darwin PE, Drachenberg CB.

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract. GIST have characteristic morphological features and are positive for KIT (CD117). Overexpression of KIT in the tumor cells results from constitutive activation of the KIT tyrosine kinase receptor. KIT activation leads to intracellular signaling that causes increased cellular proliferation and enhanced cell survival leading to tumor formation. A successful therapeutic strategy is available with the pharmacological agent SCI.-571 that blocks the intracellular effects of KIT activation. GIST are more common in the stomach (60-70%) and the small intestine (25-35%), with a minority of lesions occurring in the colon, rectum, appendix and esophagus. GIST differ histologically, immunohistochemically and genetically from leiomyomas, leiomyosarcomas and schwannomas. The pathologist plays an important role in the evaluation of these esions. Adequate gross and microscopic pathological evaluation are crucial in the determination of treatment and prognosis.

2. Gastrointestinal stromal tumors (GIST). Z Gastroenterol. 2004 ;42:327-31.
Reichardt P, Pink D, Mrozek A, Lindner T, Hohenberger P.

The vast majority of mesenchymal tumors originating from the GI tract consists of gastrointestinal stromal tumors (GIST), an entity just recently defined. The incidence is estimated to be around 10 - 20/1000000, the median age at diagnosis has been reported to be 55 to 65 years. GISTs most commonly occur in the stomach or duodenum, followed by the small intestine. About half of the patients present with metastatic disease at first diagnosis, predominantly in the liver or periteneum. GISTs are strongly and uniformly positive for CD117 (c-kit), a type III receptor-tyrosine kinase. Kit mutations, mostly in exon 11, leading to ligand independent constitutive activation are supposed to play a major role in the pathogenesis of GIST. Until recently no active systemic treatment was available for advanced gastrointestinal stromal tumors. Imatinib (STI571 =Glivec) is a rationally designed, orally available phenylaminopyrimidin analogue. The mechanism of action consists of a competitive interaction with the ATP-binding pocket of specific tyrosine kinases. Early results from clinical trials with response rates around 60 % and progression arrest in more than 80 % of patients resulting in fast relief of symptoms, confirm the high activity of this novel treatment. The role of adjuvant treatment after potentially curative resection of GIST is currently evaluated in ongoing clinical trials. Patients with progressive disease while under treatment with Imatinib should be enrolled in studies testing novel treatment strategies as RAD001, PKC412 or SU11 248.

闌尾惡性腫瘤(腺癌)

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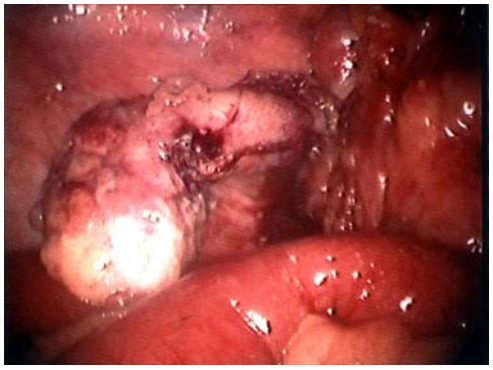
病例報告

一位 65 歲男性病人因右下腹疼痛、食慾變差及發燒，持續了 2 天，到本院急診求診。在本院急診處，抽血檢查顯示，白血球升高，高達 16000；理學檢查發現右下腹明顯壓痛及局部復膜炎徵像，包括反彈痛和肌肉僵硬，發燒(38.1C)。X 光檢查發現在右下腹有腸氣，亦即有局部腸阻塞的現象。綜合以上症狀及徵像，診斷為急性闌尾炎，因此建議病人開刀治療。我們以腹腔鏡進行手術，手術中，發現(1)骨盆腔積膿(2)闌尾底部潰爛(3)闌尾腫脹及有膿瘍覆蓋在上面。我們仍以腹腔鏡將闌尾切除，並將骨盆腔予以沖洗。術後，病人復原良好，於 4 天後出院。門診追蹤時，病人恢復很好，而且手術傷口無感染現象。但是，很意外地，病理報告為闌尾惡性腫瘤(腺癌)，而且侵犯肌肉層，屬於 Duke’s B1 (Stage I)，因此我們建議病人接受根除性右側結腸切除手術。



腹腔鏡可見闌尾底部潰爛腫脹及有膿瘍覆蓋在上面

討論

闌尾腫瘤少見，最常見的闌尾腫瘤是 carcinoid tumor(類癌)，佔 85％。原發性闌尾腺癌佔所有腸胃道腫瘤不到 0.5%。在 1963 年 Collins 統計 71000 個人類闌尾切片，僅發現 57 例原發性闌尾腺癌，約佔 008%。大多數病人的臨床症狀是右下腹痛或是右下腹腫瘤，因此超過一半的病人術前的診斷是急性闌尾炎。因為闌尾內徑狹窄，所以在疾病早期，闌尾就容易被腫瘤阻塞。其次，闌尾缺乏環狀肌肉纖維，所以容易破裂，造成腫瘤早期就容易擴散，最常見的轉移處是腹腔，其次是淋巴結、肝、腹壁及肺臟。有很高的比例會發現第二腫瘤，尤其是在腸胃道內。Mayo Clinic 的研究，發現有 35%比例會發現第二腫瘤；但是 Cortina 在 1995 發表只有 15%比例會發現第二腫瘤。所以，一但診斷原發性闌尾腺癌，就必須找尋第二腫瘤。

至於治療方面，必須考慮一些因子：(1)癌症細胞組織型態 (2)癌症分期 (TNM 分期) (3)是否有淋巴或神經侵犯 (4)Colonic type or cystic type。若是(1)分化不良型(Poorly differentiated) (2)Advanced disease(指侵犯深度超過 submucosa) (3)有淋巴或神經侵犯 (4)Colonic type(因為容易有 lymph node 轉移)，就考慮根除性右側結腸切除手術，再根據手術切除標本的病理檢查，決定是否要接受輔助性療法(化學療法或放射線療法)。若不是以上狀況，則建議單純闌尾切除，再加上門診追蹤就好。

Referrence

1: Dis Colon Rectum. 2004 Apr;47(4):474-80. Epub 2004 Feb 25.
Appendiceal adenocarcinoma: long-term outcomes after surgical therapy.
Ito H, Osteen RT, Bleday R, Zinner MJ, Ashley SW, Whang EE.
Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.
PURPOSE: Appendiceal adenocarcinomas are very rare. We analyzed contemporary outcomes associated with surgical therapies for these malignancies. METHODS: Retrospective outcomes for patients treated at a tertiary academic medical center from 1981 through 2001 were analyzed. RESULTS: A total of 36 patients (22 females (61 percent) mean age, 52 years) with appendiceal adenocarcinoma were treated. Eighty-eight percent of patients presented with symptoms of acute appendicitis. Eighteen (50 percent) patients underwent curative resection (7 primary right hemicolectomies, 10 appendectomies + subsequent right hemicolectomy, and 1 appendectomy alone). Mean length of follow-up was 55 months. Overall five-year survival rate was 46 percent. The five-year survival rate after curative resection was 61 percent and after palliative surgery was 32 percent ($P < 0.05$). Among patients who underwent curative resection, factors associated with improved five-year survival rates included histologic type (79 vs. 32 percent for colonic vs. mucinous types, respectively; $P < 0.05$), T stage (75 vs. 47 percent for T1 and 2 vs. T3 and 4, respectively; $P < 0.05$), and tumor grade (100 vs. 46 percent for well-differentiated tumors vs. moderately or poorly differentiated tumors, respectively; $P < 0.05$). CONCLUSIONS: Patients undergoing surgery for appendiceal adenocarcinoma can be stratified according to prognostic variables. The role of adjuvant therapies for patients with poor prognostic factors needs to be evaluated in a multi-institutional setting.
2: J Gastroenterol. 2002;37(3):210-4.
Early appendiceal adenocarcinoma. A review of the literature with special reference to optimal surgical procedures.
Hata K, Tanaka N, Nomura Y, Wada I, Nagawa H.
Department of Surgical Oncology, The University of Tokyo, Japan
A rare case of early colonic adenocarcinoma of the appendix confined to the mucosa is reported. The patient remained well 5 years after simple appendectomy. We also review the Japanese literature on early colonic adenocarcinoma of the appendix. Twenty-seven cases of early colonic adenocarcinoma of the appendix, including ours, have been reported in Japan. In 20 of these patients, right hemicolectomy or ileocecal resection was performed. Eighteen patients were available for lymph node evaluation. Lymph nodes were negative for metastasis in 17 of the 18. Only one patient, with poorly differentiated adenocarcinoma invading the submucosa, had lymph node metastases. Our study shows that well-differentiated adenocarcinoma invading the submucosa, or adenocarcinoma of any differentiation confined to the mucosa, may be feasibly treated with simple appendectomy.