中華癌醫會誌 (J. Chinese Oncol. Soc.) 25(6), 461-468, 2009

journal homepage:www.cos.org.tw/web/index.asp

Case Report

Aggressive Gastrointestinal Stromal Tumor Associated with Pituitary Acromegaly

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Abstract.

In this case report, we report a 52-year-old man presented with repeated hematochezia separated by a 7-month interval. Computed tomography (CT) showed a 4.7-cm mildly enhanced tumor at the distal ileum suggestive of gastrointestinal stromal tumor (GIST). Diagnosis of GIST was confirmed from typical histological and immunohistochemical staining after laparotomy segmental resection of the tumor at the distal ileum. Endocrinology clinic referral for a previous incidentally found pituitary tumor pointed to pituitary acromegaly owing to acromegalic appearance which was appreciated biochemically by elevated random growth hormone (GH), glucose tolerance test (GTT), elevated insulin-like growth factor-1 (IGF-1) and histopathologically after transsphenoidal adenomectomy. Suprisingly, just two months after the laparotomy surgery, a 2.2-cm hypoechoic liver nodule with increased uptake by positron emission tomography (PET) was detected which was not evident in the latest image studies. This is an unusual case with intense aggressive and malignant behavior of the GIST that could be stimulated by high IGF-1 concentrations associated with acromegaly through the activation of MAPK and PI3K bypassing KIT tyrosine kinase which underlies GIST.

Keywords **:** acromegaly, gastrointestinal stromal tumor, insulin-like growth factor

病例報告

肢端肥大症合併高度惡性表現的胃腸道基質瘤

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中文摘要

此篇病例報告中，我們報告一位在接受內視鏡檢查治療後 7 個月再次復發解血便的 52 歲男性病患。腹部電腦斷層攝影檢查發現於迴腸末端疑似胃腸道基質瘤的 4.7 公分腫瘤。經開腹手術切除後病理切片及免疫染色證實為胃腸道基質瘤。後因之前健檢意外發現的腦下垂體腫瘤而轉介至內分泌科門診，在此之前因無症狀病患未曾接受進一步檢查，病人的外觀呈現疑似肢端肥大症的臉部特徵且血清中生長激素，第一型

類胰島素生長因子及葡萄糖耐受性試驗皆呈現肢端肥大症的表現，在接受經鼻內視鏡經蝶竇手術亦證實為腦下垂體巨腺瘤所導致的肢端肥大症。令人訝異的於開腹手術後的 2 個月時於腹部超音波追蹤檢查時發現一顆之前無跡象的 2.2 公分低迴音性肝臟腫瘤，並於正子斷層攝影時呈現高信號而臨床上斷定為胃腸道基質瘤的轉移腫瘤。這是一個臨床少見具高侵襲性及高度惡性表現的胃腸道基質瘤，可能是透過肢端肥大症的血液中高濃度第一型類胰島素生長因子異常刺激於胃腸道基質瘤 c-kit tyrosine kinase 變異而持續活化的 mitogen-activated protein kinase (MAPK)及 phosphatidylinositol 3 kinase (PI3K)共同訊息通路所導致的細胞迅速增生。

關鍵字: 肢端肥大症、胃腸道基質瘤、第一型類胰島素生長因子

INTRODUCTION

Acromegaly is an endocrine disorder characterized by sustained hypersecretion of growth hormone (GH) with concomitant elevation of insulin-like growth factor I (IGF-I) associated with premature mortality from cardiopulmonary diseases and certain malignancies. In particular, there is a two-fold increased risk of developing colorectal cancer. Possible mechanisms underlying this association include elevated levels of circulating GH and IGF-I, but several other plausible processes may be relevant.

CASE REPORT

A 52-year-old man with history of impaired fasting glucose and hypertension diagnosed since December, 2006, which were well controlled with lifestyle modification, metformin 500 mg qd and amlodipine 5 mg qd. He suffered from bloody stool passage in May, 2009 with resultant decrement of hemoglobin level from 14.0 g/dl to 12.1 g/dl. Esophagoduodenogastroscopy (EGDscopy) and colonoscopy detected a gastric ulcer (A2) and a 0.3-cm transverse-colon Isp-type polyp, respectively. Pathology revealed chronic active ulcer with *Helicobacter*-like organism and tubular adenoma, respectively. The patient received triple therapy for eradication of *Helicobacter pylori* infection and then proton pump inhibitors for 3 months to cure gastric ulcer. However, recurred bloody stool and blood clot passage developed in December, 2009 for which EGDscopy and colonoscopy was performed, with negative findings. Tc99-RBC scintigraphy revealed intermittent extravasation from the terminal ileum or more proximal site, then videocapsule endoscopy was implemented which showed small intestinal bleeding and lymphangiectasis but was unable to locate the actual bleeding site. Abdominal CT (Figure 1) with contrast enhancement was further arranged, and found a 4.7-cm mildly enhanced tumor at or abutting the distal ileum suggestive of gastrointestinal stromal tumor (GIST) in March, 2010. The patient received laparotomy ileum segmental resection of a well- encapsulated 4.5-cm solid tumor at the anti-mesenteric site with a deep ulcer of 0.7-cm on the overlying intestinal mucosa which probably caused the small intestinal bleeding. Microscopically, the tumor was composed of proliferative spindle cells with hyperchromatic nucleus and frequent mitoses (>40/50 HPF)(Figure 2A), intestinal mucosa and section margins were free and there was no evident lymph node metastasis. Immunohistochemical staining showed strong reactivity to C-kit, CD34(+), S100(-) and Desmin(-), which confirmed GIST (Figure 2B).

Endocrinology clinic referral for an incidental pituitary tumor (11 mm) documented in December, 2007

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