

การกระจายของมะเร็งลำไส้ใหญ่มาลำไส้เล็กส่วนต้นในผู้ป่วยที่มาด้วย Trousseau's syndrome

ปิยนันท์ ขนไมตรี¹ อัคริน สุดเจริญ¹ ปิยกรณ์ พูลแย้ม¹ วรุฒิ รุ่งแสงมบุญ¹ ภาณุณัฐ ม่วงน้อย¹ ชาญชัย เจริญพงศ์สุนทร¹
วรรณพร บุรีวงศ์² สันหิรี สุดชื่น² เทอดเกียรติ ตรวงศา³ มนัสนันท์ รวีสุนทรเกียรติ³

¹ภาควิชาอายุรศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ

²ภาควิชารังสีวิทยา มหาวิทยาลัยศรีนครินทรวิโรฒ

³ภาควิชาพยาธิวิทยา มหาวิทยาลัยศรีนครินทรวิโรฒ

บทคัดย่อ

การกระจายของมะเร็งลำไส้ใหญ่มักพบที่ต่อมน้ำเหลือง ตับ ปอด และเยื่อช่องท้อง การกระจายของมะเร็งลำไส้ใหญ่มาลำไส้เล็กส่วนต้นพบน้อยมาก กลไกการกระจายของมะเร็งลำไส้ใหญ่อานขามาลำไส้เล็กส่วนต้นเชื่อว่าเกิดจากการกระจายมาทางน้ำเหลืองผ่านต่อมน้ำเหลืองและ mesentery โดยมักพบต่อมน้ำเหลืองบริเวณ hepatoduodenal ligament โตร่วมด้วย ผู้นิพนธ์รายงานผู้ป่วยมะเร็งลำไส้ใหญ่ที่มีการกระจายมาลำไส้เล็กส่วนต้นที่มาด้วย Trousseau's syndrome

คำสำคัญ: มะเร็งลำไส้ใหญ่ มะเร็งกระจายมาลำไส้เล็กส่วนต้น Trousseau's syndrome

ผู้นิพนธ์ประสานงาน:

ปิยนันท์ ขนไมตรี

ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ

62 หมู่ 7 ถนนรังสิตนครนายก ตำบลองครักษ์ อำเภองครักษ์ จังหวัดนครนายก 26120

อีเมล: piyanant_n@yahoo.co.th

Duodenal metastasis from colonic cancer in patient presenting with Trousseau's syndrome

Piyanant Chonmaitree¹, Asawin Sudcharoen¹, Piyakorn Poonyam¹, Worawut Roongsangmanoon¹,
Panunat Muangnoi¹, Chanchai Charonpongsuntorn¹, Wanaporn Burivong², Sunsiree Soodchuen²,
Therdkiat Trongwongsa³, Manasanan Raveesunthornkiet³

¹Department of Medicine, Faculty of Medicine, Srinakharinwirot University

²Department of Radiology, Faculty of Medicine, Srinakharinwirot University

³Department of Pathology, Faculty of Medicine, Srinakharinwirot University

Abstract

In colon cancer, common sites of metastasis are regional lymph node, liver, lung and peritoneum. Duodenal metastasis is rare. Pathogenesis of duodenal metastasis from right-sided colon is lymphatic spreading via periduodenal lymph node and mesentery. Lymph node at hepatoduodenal ligament is the predictor of duodenal metastasis. We report a case of colonic cancer with duodenal metastasis who presented with Trousseau's syndrome.

Keywords: colon cancer, duodenal metastasis, Trousseau's syndrome

Corresponding Author:

Piyanant Chonmaitree

Department of Medicine, Faculty of Medicine,

Srinakharinwirot University

62 Moo 7, Rangsit Nakhon Nayok Road,

Ongkharak, Nakhon Nayok, 26120 Thailand

E-mail: piyanant_n@yahoo.co.th

Introduction

About 15-20% of colon cancer presents initially with distant metastasis.¹ Colon cancer usually metastasizes to regional lymph node, liver, lung and peritoneum. Colon cancer with duodenal metastasis is uncommon. We report a case of colonic cancer with duodenal metastasis who presented with Trousseau's syndrome.

Case presentations

A 63-year-old woman presented with left-sided of neck and shoulder swelling for 2 days. The patient had no significant past medical history. Physical

examination revealed swelling at left-sided of neck, shoulder and arm, superficial vein dilatation at left-sided of chest and supraclavicular lymphadenopathy. There was no sign of inflammation. CT of neck showed a hyperdense clot in the left internal jugular vein, the left subclavian vein, the proximal left brachiocephalic vein, suggestive of venous thrombosis. Collateral vessels were seen at left axillary region and left chest wall. Fat reticulation along left cervical, left supraclavicular and left chest wall regions were seen. There was a 1.1-cm. of left supraclavicular lymph node (Figure 1).

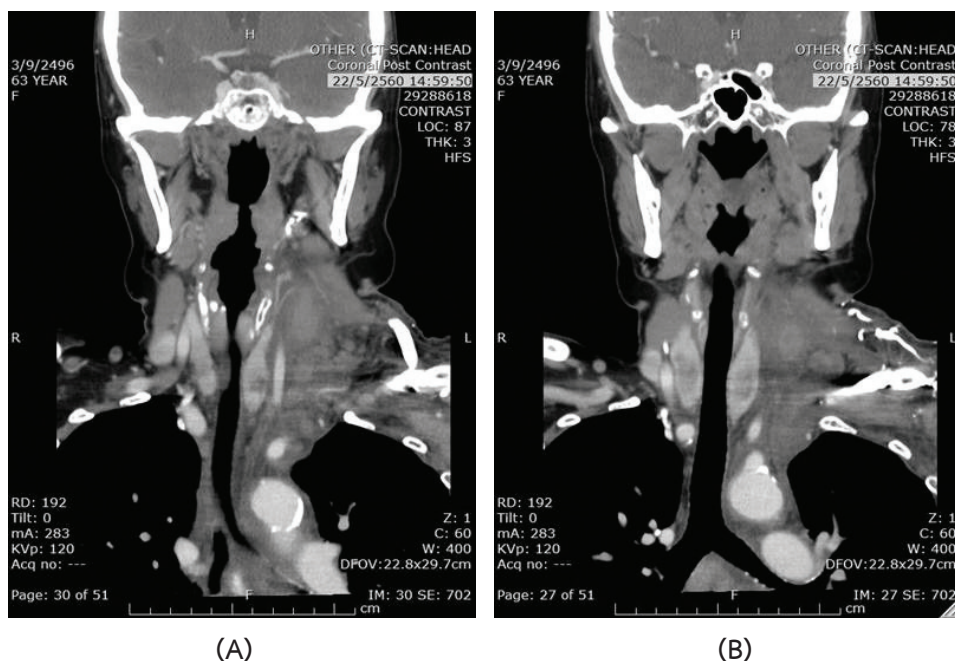


Figure 1 CT scan of neck with IV contrast venous phase coronal view showed (A) internal jugular vein thrombosis and multiple subcentimeter cervical lymphadenopathies (B) left supraclavicular lymphadenopathy.

Complete blood count showed hemoglobin 8.9 g/dL, WBC 13,400/mm³ with neutrophil 79%, and platelet 302,000/mm³. Coagulogram, blood urea nitrogen, creatinine and liver function test were normal. Hypercoagulable state was considered, protein C, protein S, antithrombin III, anticardiolipin IgM and IgG, β 2 glycoprotein IgM and IgG, lupus anticoagulant were

normal. CT whole abdomen revealed a short segment of circumferential thickening of large bowel from hepatic flexure extending to distal ascending colon with multiple pericolic lymphadenopathies. Multiple matted intraabdominal lymphadenopathies were seen, including lymph node at hepatoduodenal ligament (Figure 2).

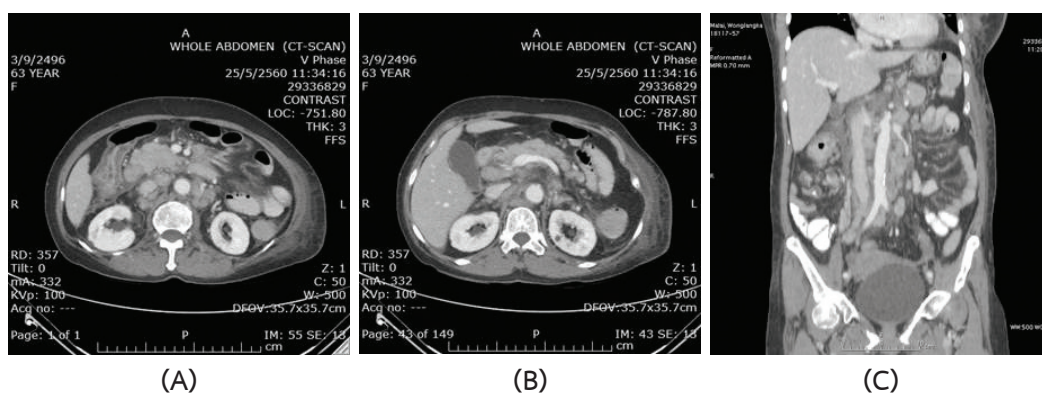


Figure 2 CT scan of abdomen with IV contrast venous phase (A) axial view showed circumferential thickening of colonic wall at hepatic flexure without direct duodenal invasion, (B) enlarged lymph node at hepatoduodenal area and (C) coronal view showed matted lymph nodes at paraaortic and portocaval areas.

Esophagogastroduodenoscopy demonstrated submucosal mass in the second part of duodenum, proximal to the

ampulla of Vater and colonoscopy showed circumferential mass at hepatic flexure (Figure 3).

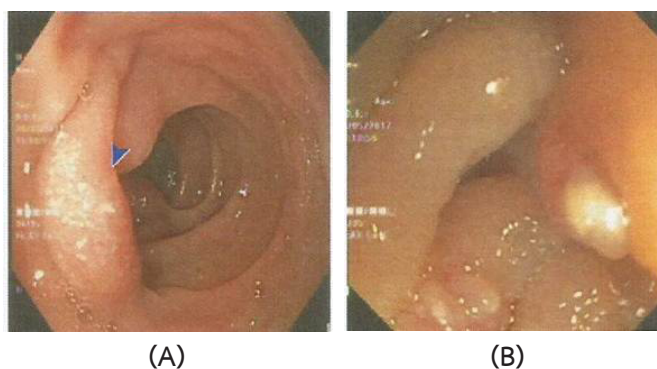


Figure 3 (A) Esophagogastroduodenoscopy showed submucosal mass in the second part of duodenum. (B) Colonoscopy showed circumferential mass at hepatic flexure.

Pathology from colonic mass showed poorly differentiated adenocarcinoma. The section of duodenal mucosa revealed preserved epithelial layer while colonic mucosa showed distinct transformation zone. Moreover, tumor clusters that found in the duodenum were confined to central lymphatic duct in the duodenal villi (highlight by D2-40 immunohistochemical

stain). The tumor cells in both sites had the same pathology, which were columnar cells arrange in dysplastic glands with hyperchromatic irregular nuclei. The immunophenotypes were also resemble in the two lesions (positive for CK7, CDX-2 and negative for CK20), which were favor colorectal in origin (Figure 4).

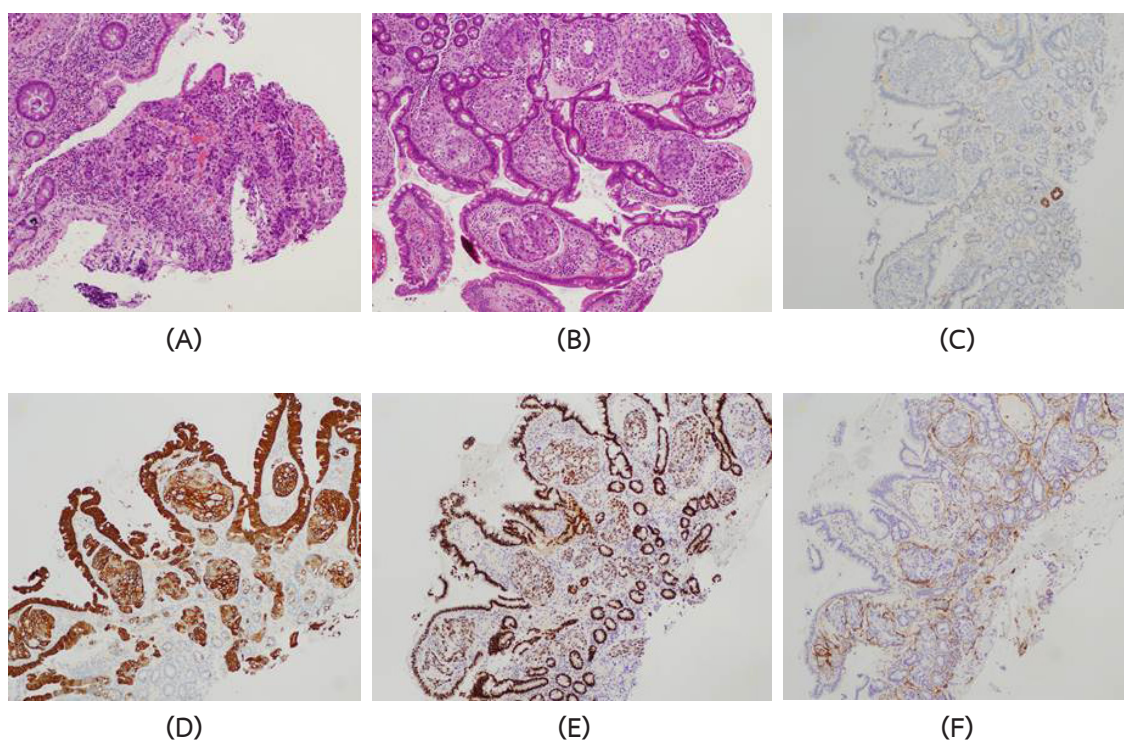


Figure 4 Pathology from duodenal submucosal mass. (A) H&E stain showed poorly differentiated adenocarcinoma of colon, (B) H&E stain showed tumor emboli in lymphatic vessels of duodenal villi. Tumor showed CK7 negative (C), CK 20 (D) and CDX2 (E) positive. D240 stain (F) highlight endothelium of lymphatic vessels around tumor cell cluster.

She was diagnosed with advanced stage of colonic cancer with Trousseau's syndrome. The patient was treated with enoxaparin and chemotherapy.

Discussion

Trousseau's syndrome is the hypercoagulable state in patient with malignancy. It was first described in 1865, by

Armand Trousseau, as migratory superficial thrombophlebitis.^{2,3} He was also diagnosed this syndrome 2 year later. In 1977, Sack reported that Trousseau's syndrome was chronic disseminated coagulation, platelet-rich microthrombi, microangiopathic hemolytic anemia, verrucous endocarditis, and thromboembolic problems.^{2,3} Recently, the definition of Trousseau's syndrome is ranging from classic descriptions to any kind of coagulopathy occurring in any kind of malignancy.² The incidence of Trousseau's syndrome varies widely. It is the second most common cause of death in cancer patients after cancer itself.³ Trousseau's syndrome can occur preceding or concomitantly the diagnosis of occult malignancy.² Common primary tumors of Trousseau's syndrome are lung, pancreas, colon, kidney and prostate.³ Our patient presented with internal jugular venous thrombosis concomitantly with adenocarcinoma of colon. Risk factors of Trousseau's syndrome are classified into 3 groups: patient-related, treatment-related and cancer-related features. Patient-related features include older age, prolonged immobility, prior history of thrombosis, elevated leukocyte and platelet counts, acute infection, comorbidity and obesity. Treatment-related features include chemotherapy, hormonal agents, growth factors, antiangiogenic agents, surgery and central venous catheterization. Cancer-related features include primary site of tumor, stage of cancer, compression or direct invasion of large vessels, mucin

from adenocarcinoma and tissue factor expression.³ Pathophysiology of Trousseau's syndrome is not well defined. Tumors produce two substances with procoagulant activity, tissue factor-like procoagulant and cancer procoagulant. Tissue factor is a transmembrane protein that forms a complex with factor VII to activate factor IX and X. Many cancer cells have high levels of tissue factor and can induce monocyte or macrophage to release tissue factor.² Inflammatory cytokines from cancer cells induce tissue factor expression on vascular cells. Cancer procoagulant is a calcium-dependent cysteine protease. It directly converts factor X to factor Xa. Mucin from adenocarcinoma can directly activate factor X and interact with L-selectin and P-selectin which generate platelet-rich thrombi. Other proposed mechanisms are hypoxic conditions within tumor and expression of the MET oncogene. Production of procoagulant factors (tissue factor, plasminogen activator inhibitor-1) is enhanced. In addition, inflammatory cytokines can activate endothelial and platelet adhesion molecules. Management of Trousseau's syndrome is elimination of the causative tumor with immediate anticoagulation. Unfractionated heparin (UFH), low molecular weight heparin (LMWH) or fondaparinux can be used. Meta-analysis of 11 studies showed that LMWH has statistically significant reduction in mortality at 3 months follow-up comparing with heparin.⁴ Additional, blood test monitoring and hospitalization are not required. There

is no study comparing efficacy of enoxaparin, dalteparin or tinzaparin. Fondaparinux has higher rates of recurrence comparing with enoxaparin.^{5,6} Fondaparinux has long half life and reversal agent is lacking. LMWH is preferred over UFH and Fondaparinux for initial treatment. Anticoagulant should be continued for at least 3-6 months. LMWH is preferred over vitamin K antagonist or direct oral anticoagulants for long term anticoagulation.⁶

Small bowel cancer is uncommon. Global incidence is 1 per 100,000 populations.¹ Small bowel metastasis is more common than primary neoplasms however distant metastasis to small bowel is quite rare.^{1,7} Common primary neoplasms that metastasize to duodenum include melanoma, lung cancer, renal cell carcinoma, breast cancer, cervical cancer, thyroid cancer, hepatocellular carcinoma and Merkel cell carcinoma^{1,7} Most of duodenal metastasis is located in bulb and periampullary region.

Colon cancer commonly metastasizes to regional lymph node, peritoneum, liver, lung, and occasionally metastasizes to bone, brain, thyroid, adrenal gland.¹ Duodenal metastasis from right-sided colon is rare because tumor is usually diagnosed earlier. Colon cancer can cause delay duodenal metastasis after resection of primary tumor. Pathogenesis of duodenal metastasis from right-sided colon is lymphatic spreading via periduodenal

lymph node and mesentery. Lymph node at hepatoduodenal ligament is the predictor of duodenal metastasis.⁷ Direct invasion is less likely.^{1,8,9} Our patient had enlarged lymph node at hepatoduodenal ligament and no evidence of direct duodenal invasion. Lymphatic spread is a likely the route of metastasis in our patient.

Symptoms and signs of colon cancer with duodenal metastasis may be similar to primary duodenal cancer. The most common presenting symptom is epigastric pain worsening after meal. Other symptoms are weakness, fatigue, weight loss, nausea and vomiting. Duodenal lesions in patient with a history of colon cancer should raise the possibility of metastasis. Endoscopy is the initial investigation for diagnosis. The endoscopic finding of duodenal metastasis are submucosal mass with or without ulceration, multiple nodules and raised plaques.⁷ Volcano-like lesion (submucosal mass with elevation and ulceration at apex) is the specific feature of metastasis neoplasms in gastrointestinal tract.⁷ Our patient, endoscopy revealed submucosal mass at duodenum and metastasis from colonic cancer was confirmed by pathology. Data about treatment is limited due to rarity of disease. The mainstay of treatment is chemotherapy. Our patient was diagnosed with advanced stage of colonic cancer due to cervical lymphadenopathy, chemotherapy was given.

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