

Case Report

Trousseau syndrome accompanied by cholangiocellular carcinoma: Report of two

Ryuichi Yamamoto^{1)*}, Shingo Kato¹⁾, Masatomo Takahashi¹⁾,
Shino Ono¹⁾, Tomoya Sakurada¹⁾, Sumiko Nagoshi¹⁾,
Ko Nishikawa²⁾, Koji Yakabi¹⁾

1)Department of Gastroenterology and Hepatology, Saitama Medical Center, Saitama Medical University

2)Department of the Gastroenterology, Ageo Central General Hospital

Two cases of Trousseau syndrome associated with cholangiocellular carcinoma have been reported. The first patient, a 82-year-old woman, received chemotherapy with weekly gemcitabine after the placement of a self-expanding metal stent for palliation of unresectable malignant biliary obstruction. She was admitted to our hospital because of dizziness in October 2010. A computed tomography (CT) showed fresh cerebral infarcts in the area of left middle cerebral artery and in the right temporal lobe. The final diagnosis was Trousseau syndrome accompanied by cholangiocellular carcinoma. She died 36 days after admission. The second patient, a 69-year-old woman, was admitted to our hospital because of disturbed consciousness. Her CT showed a cerebral infarct in the right temporal lobe. An enhanced abdominal CT showed a malignant tumor in left hepatic lobe. A fine needle biopsy showed a cholangiocellular carcinoma. The final diagnosis was Trousseau syndrome accompanied by cholangiocellular carcinoma. She died 25 days after admission.

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Introduction

The association between cancer and venous thrombosis was first recognized more than 100 years ago by Trousseau¹⁾. Cancer-related coagulopathy is known as Trousseau syndrome with a poor prognosis^{1, 2)}. The exact incidence of thromboembolic disease in association with cholangiocellular carcinoma is not known. However, the occurrence of Trousseau syndrome in the setting of advanced cholangiocellular carcinoma has rarely been reported³⁾. In this report,

the authors describe two patients with cholangiocellular carcinoma complicated by Trousseau syndrome, a clinical state consistent with disseminated intravascular coagulation (DIC).

Case reports

Case 1

A 82-year-old woman was diagnosed with cholangiocellular carcinoma involving the confluence of the right and left hepatic duct (T3N1M0, stage III) (Fig. 1A, B, C). After placement of a self-expanding metallic stent for palliation of unresectable malignant biliary obstruction, she received chemotherapy with gemcitabine. Gemcitabine was administered weekly as an intravenous 30 min infusion of 800 mg/m² for 3 consecutive weeks followed by 1-week of rest

* Author :Department of Gastroenterology and Hepatology, Saitama Medical Center, Saitama Medical University

1981, Kamoda, Kawagoe City, Saitama 350-8550, Japan

E-mail: ryuichi5118@gmail.com

○ The authors declare that there are no conflicts of interest associated with the present study.

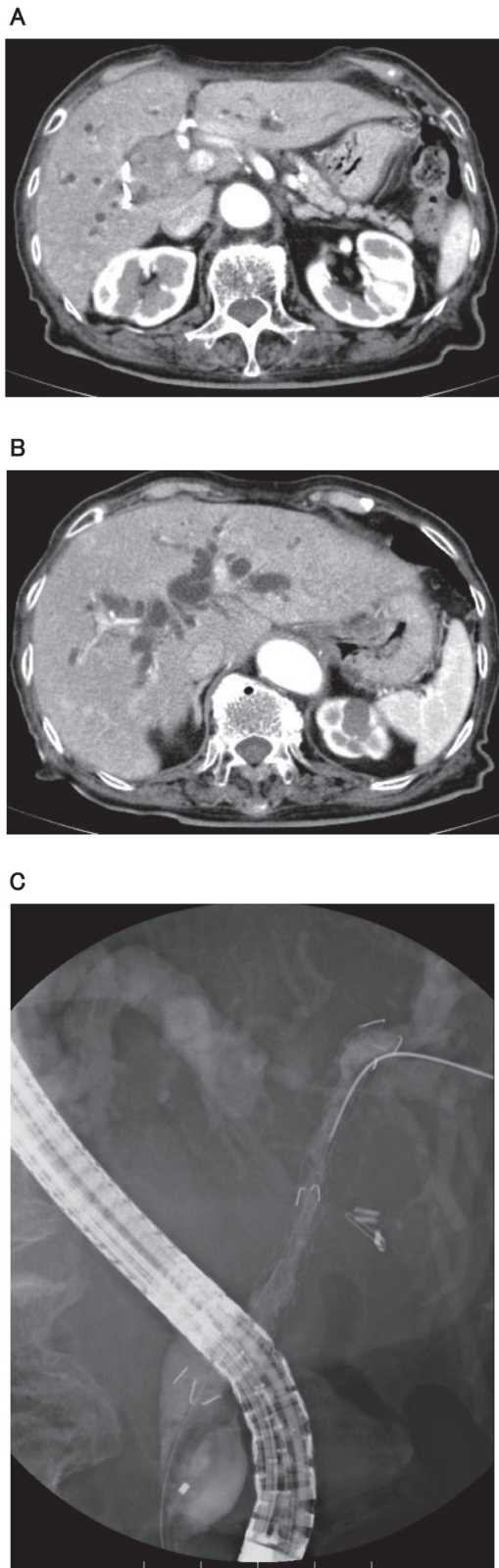


Fig 1. Enhanced abdominal CT revealed a cholangiocellular carcinoma centrally located in the right lobe of the liver (A) and dilatation of bi-lateral intrahepatic bile duct (B). An uncovered metallic stent was placed in the common bile duct in order to dilate the stenosis of right intrahepatic bile duct (C).

(28-day cycle). Her clinical condition was progressively getting worse despite six courses of chemotherapy. She was admitted to our hospital because of dizziness in October 2010. A computed tomography(CT) showed fresh cerebral infarcts in the area of left middle cerebral artery and in the right temporal lobe (Fig. 2). The platelet count was $20.2 \times 10^4/\mu\text{L}$ after chemotherapy, but the platelet count was $5.7 \times 10^4/\mu\text{L}$ and prothrombin time (PT) was 18 seconds (international normalized ratio (INR) was 1.56) on admission. The fibrinogen concentration was 101 mg/dL, and fibrinogen degradation products (FDP) measured 80 $\mu\text{g}/\text{mL}$. These findings suggested DIC. The patient was treated with nafamostat mesilate. However, the patient died 36 days after admission. The final diagnosis was Trousseau syndrome accompanied by cholangiocellular carcinoma.

Case 2

A 69-year-old woman was admitted to our hospital because of disturbed consciousness in May 2010. The Glasgow coma scale score upon admission was E2V2M4. The CT showed a new broad cerebral infarct in the right temporal lobe (Fig. 3A). The patient's MRI (diffusion weighted sequence) demonstrated a new area of acute cerebral infarction in the right temporal lobe (Figure 3B). The platelet count was $6.3 \times 10^4/\mu\text{L}$, her PT was 17.3 seconds (INR was 1.43), the fibrinogen concentration was 259 mg/dL, and FDP measured 80 $\mu\text{g}/\text{mL}$ over. These findings suggested DIC. An enhanced abdominal CT showed a malignant tumor (10 cm \times 8.5 cm) in left hepatic lobe (Fig. 4A, B). Fine needle biopsy showed cholangiocellular carcinoma (Fig. 5). She was treated with nafamostat mesilate.

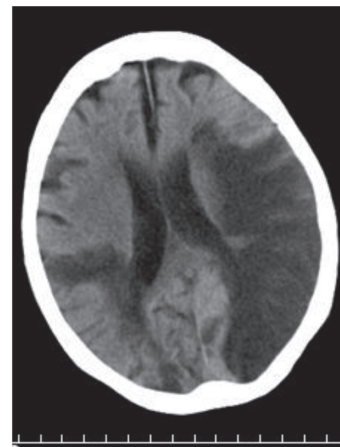


Fig 2. CT shows new cerebral infarcts in the area of left middle cerebral artery and in the right temporal lobe.

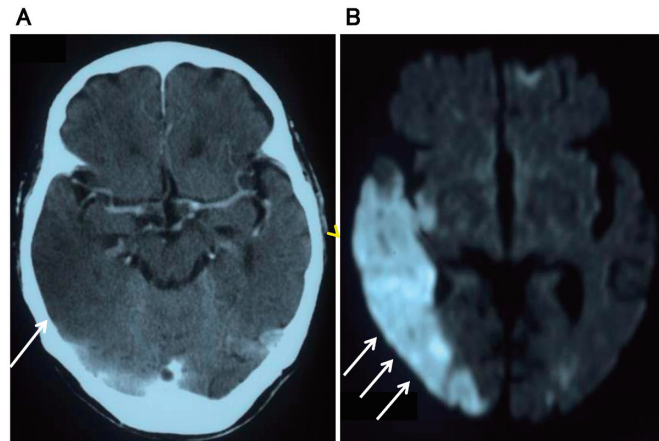


Fig 3. CT shows a new broad cerebral infarct in the right temporal lobe (A). MRI (diffusion weighted sequence) demonstrated a new area of acute cerebral infarct in the right temporal lobe (B).

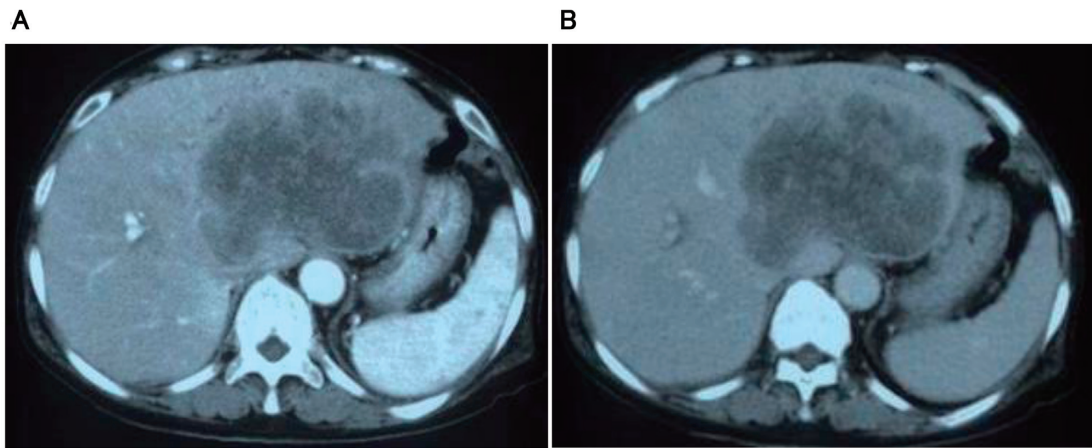


Fig 4. Enhanced abdominal CT showed a malignant tumor (10 cm×8.5 cm) in left hepatic lobe. The huge mass slightly enhanced on the arterial phase (A) and on the portal phase (B) revealed cholangiocellular carcinoma.

However, she died 25 days after admission. The final diagnosis was Trousseau syndrome accompanied by cholangiocellular carcinoma.

Discussion

In 1865, Trousseau first described the relationship between neoplastic and thromboembolic disease⁴. Since then, a variety of thromboembolic events including spontaneous, recurrent or migratory vascular thrombosis, microangiopathy, acute bleeding diathesis, and DIC in cancer patients have been termed Trousseau syndrome⁵. The prevalence of the syndrome was reported to be from 1% to 11%². Non-bacterial thrombotic endocarditis, which has been reported to occur in up to 1.3% of patients dying of cancer, comes within the disease spectrum of Trousseau syndrome⁶. Several cases with occurrence of Trousseau syndrome in the setting of advanced cholangiocellular carcinoma

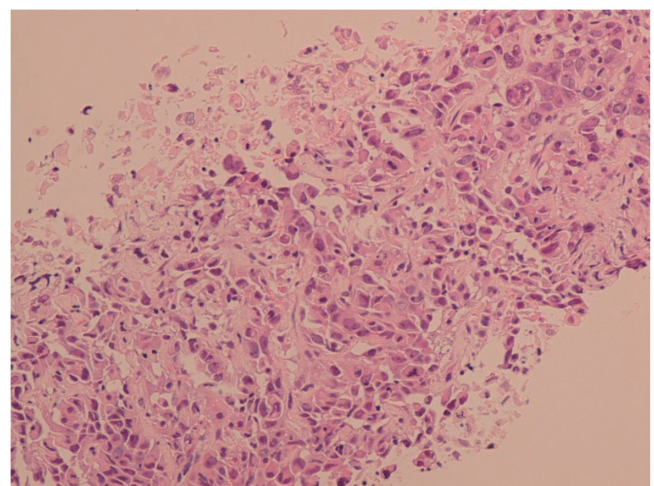


Fig 5. Photomicrograph of liver biopsy specimens. Moderately differentiated adenocarcinoma was shown in the hematoxylin-eosin stain (original magnification ×400). Pathological findings showed cholangiocellular carcinoma.

have been reported^{3, 9, 10)}.

Routine coagulability tests were not helpful in the prediction of the development of thromboembolic disorder except for decreased platelet counts. Although screening tests for coagulation are optimized toward the detection of a hemorrhage, they are of limited value in the hypercoagulable state of patients with neoplasms⁷⁾.

The full mechanism of cancer-induced coagulopathy has not yet been clarified. Recently, several mechanisms of activated coagulability associated with malignancy have been suggested. The release of thromboplastin-like substances, fibrin deposition, direct factor X activation by tumor proteases, destruction of endothelial tissue, and tissue factors have been reported⁹⁾.

Useful treatment for Trousseau syndrome has not yet been established. However, low molecular weight heparin, compared with unfractionated heparin, has been recommended because of the reduction of cancer-related mortality without the increase of thromboembolism and bleeding events^{2, 9)}.

Finally, Trousseau syndrome should be kept in mind in the case of multiple cerebral infarction of an unknown origin. A malignant status defines a patient's prognosis in cases of Trousseau syndrome.

References

- 1) Callender N, Rapaport SI. Trousseau's syndrome. *West J Med* 1993;158:364-71.
- 2) Walsh-McMonagle D, Green D. Low-molecular-weight heparin in the management of Trousseau's syndrome. *Cancer* 1997;80:649-55.
- 3) Jang JW, Yeo CD, Kim JD, Bae SH, Choi JY, Jung ES, et al. Trousseau's syndrome in association with cholangiocarcinoma: positive tests for coagulation factors and anticardiolipin antibody. *J Korean Med Sci* 2006;21:155-9.
- 4) Trousseau A. *Phlegmasia Alba Dolens*. Clinique medicale de l'Hotel-Dieu de Paris, London: New Sydenham Society 1865;3:94.
- 5) Sack GH Jr, Levin J, Bell WR. Trousseau's syndrome and other manifestations of chronic disseminated coagulopathy in patients with neoplasm: clinical, pathophysiologic, and therapeutic features. *Medicine (Baltimore)* 1977;56:1-37.
- 6) Rogers LR, Cho ES, Kempin S, Posner JB. Cerebral infarction from non-bacterial thrombotic endocarditis. Clinical and pathological study including the effects of anticoagulation. *Am J Med* 1987;83:746-56.
- 7) Min KE, Gyorkey F, Sato C. Mucin-producing adenocarcinomas and nonbacterial thrombotic endocarditis. Pathogenetic role of tumour mucin. *Cancer* 1980;45:2374-82.
- 8) Hemostatic abnormalities and malignant diseases. *Lancet* 1986;1:303-4.
- 9) Tasi SH, Juan CJ, Dai MS, Kao WY. Trousseau's syndrome related to adenocarcinoma of the colon and cholangiocarcinoma. *Eu J Neurol* 2004;11:493-6.
- 10) Kikui S, Yanagimoto S. Trousseau syndrome accompanied by cholangiocellular carcinoma. A case report. *Neurol Med* 2006;64:276-9.

胆管細胞癌に伴ったTrousseau症候群の2例

山本 龍一¹⁾, 加藤 真吾¹⁾, 高橋 正朋¹⁾, 大野 志乃¹⁾, 櫻田 智也¹⁾, 名越 澄子¹⁾, 西川 稿²⁾, 屋嘉比 康治¹⁾

Trousseau症候群の原因となる悪性腫瘍には固形癌が多く、その中では婦人科腫瘍が最も多いとされており胆管細胞癌に伴ったTrousseau症候群の報告は稀である。

今回、われわれは脳梗塞で発見され胆管細胞癌に伴ったTrousseau症候群の2例を経験した。症例1は、82歳・女性。胆管癌に伴う閉塞黄疸に対し内視鏡的胆管ステント留置後ゲムシタビン単独療法施行中であった。めまいにて入院した。頭部CTにて左前頭葉の脳梗塞所見及び、採血検査にて血小板の低下が認められ、胆管癌に伴ったTrousseau症候群と診断した。nafamostat mesilateの持続点滴施行するも入院36日後死亡した。症例2は、69歳・女性。意識レベル低下、歩行困難にて入院となった。頭部CTにて右前頭葉に多発脳梗塞所見、腹部造影CTにて肝左葉に計10 cm大の造影効果の乏しい腫瘤を認め、腫瘍生検にて胆管細胞癌の診断であった。胆管細胞癌に伴ったTrousseau症候群と診断しnafamostat mesilateの持続点滴施行するも入院25日後死亡した。癌患者において脳梗塞が発症した際は、常にTrousseau症候群の可能性を考慮すべきである。

1) 埼玉医科大学 総合医療センター 消化器・肝臓内科 〒350-8550 埼玉県川口市鴨田 1981

2) 上尾中央総合病院 消化器内科

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