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Resection of pheochromocytoma extending into the right atrium in a patient with multiple endocrine neoplasia type 2A

患上多發性內分泌瘤II A型的病者切除向右心房生長的嗜鉻細胞瘤

We report the first case of successful surgical resection of a malignant pheochromocytoma with tumour extension into vena cava and right atrium in a patient with multiple endocrine neoplasia type 2A. A 21-year-old woman with genetic confirmation of multiple endocrine neoplasia type 2A syndrome was diagnosed with a very rare case of malignant pheochromocytoma with tumour thrombus extension into vena cava and right atrium causing Budd-Chiari syndrome. It posed a challenge to the surgeons with regard to complete tumour resection and vascular control. Reviewing the limited literature, surgical resection by means of cardiopulmonary bypass with hypothermic circulatory arrest has been reported with success in pheochromocytoma with advance vascular involvement. Adopting this approach, adrenalectomy with complete thrombus excision by inferior vena cava exploration and right atriotomy were performed successfully by a multidisciplinary team.

Key words:

Cardiopulmonary bypass;
 Hypothermia, induced;
 Multiple endocrine neoplasia type 2a;
 Pheochromocytoma;
 Vena cava, inferior

關鍵詞：

心肺分流術；
 低溫，引發性；
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 腔靜脈，下面的

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本文報告首宗成功手術個案，替患上多發性內分泌瘤II A型的病者切除向腔靜脈和右心房生長的惡性嗜鉻細胞瘤。這名21歲的女性病者，經基因確定患上多發性內分泌瘤II A型病症，並發現有惡性嗜鉻細胞瘤，腫瘤血栓伸展至腔靜脈和右心房，造成布加氏綜合徵。面對這種非常罕見的病例，外科醫生既要完全切除腫瘤，又要保護血管。參考有限的文獻後，發現有病例成功以心肺分流術和降溫停迴圈技術切除這種影響血管功能的嗜鉻細胞瘤。本例採用同樣方法，由多個部門的醫生合作施以腎上腺切除術，在下腔靜脈探查，並切開右心房，最後把腫瘤血栓完全切除。

Introduction

The majority of pheochromocytomas are sporadic in origin and roughly 10% of these tumours are malignant. Malignant transformation occurs less frequently in familial than in sporadic type.^{1,2} Primary malignant pheochromocytoma with extension into vena cava and right atrium is rare with only two reported cases in the literature.^{3,4} We report the first patient with multiple endocrine neoplasia type 2A (MEN 2A) presenting with a malignant pheochromocytoma extending into the vena cava and right atrium. Surgical resection was successfully performed using cardiopulmonary bypass and hypothermic circulatory arrest.

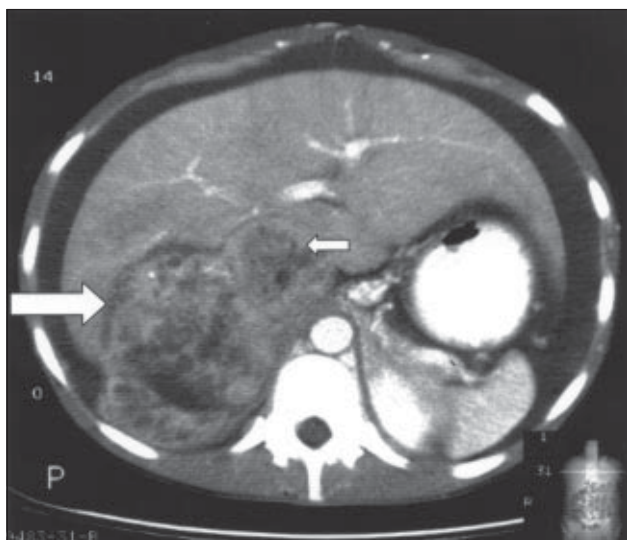


Fig 1. Contrast computed tomographic scan of the abdomen showing tumour thrombus in the inferior vena cava (short arrow) next to the large adrenal phaeochromocytoma (long arrow)

Case report

A 21-year-old female university student with a known family history of MEN 2A presented with abdominal distension for 2 months. She experienced palpitations and weight loss 6 months prior to presentation. Four of her eight maternal siblings had undergone either adrenal and/or thyroid surgery elsewhere and were confirmed to have MEN 2A from characteristic clinical syndromes or genetic testing. Her family, however, declined early genetic diagnosis and the possibility of prophylactic surgery. On examination, her blood pressure was 180/110 mm Hg with a heart rate of 105 beats per minute. The abdomen was distended with multiple dilated veins over the anterior abdominal wall forming a caput medusa. A right loin mass was felt and was associated with gross ascites. Computed tomography showed a 12-cm right adrenal mass with suspected tumour thrombus extending into the inferior vena cava and right atrium of the heart (Fig 1).

Twenty-four-hour urinary assay for fractionated catecholamines showed elevated levels of vanillyl-mandelic acid to 380 $\mu\text{mol/d}$ (reference level, $<41 \mu\text{mol/d}$), norepinephrine to 7000 nmol/d (reference level, $<440 \text{ nmol/d}$), normetanephrine to 25 000 nmol/d (reference level, $<240 \text{ nmol/d}$), epinephrine to 9650 nmol/d (reference level, $<110 \text{ nmol/d}$), metanephrine to 27 400 nmol/d (reference level, $<275 \text{ nmol/d}$), and dopamine to 2450 nmol/d (reference level, $<2570 \text{ nmol/d}$). Overnight dexamethasone suppression test was within normal range. Magnetic resonance imaging (Fig 2) and echocardiography confirmed right

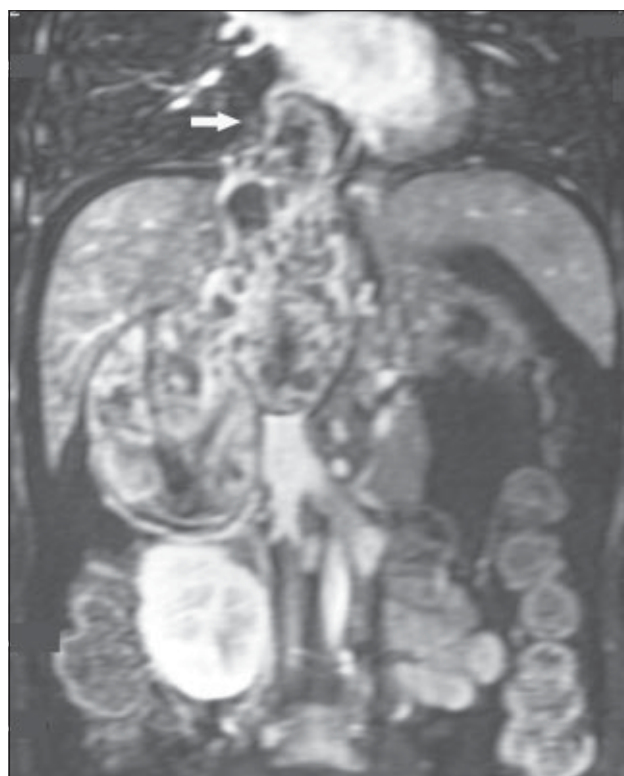


Fig 2. Magnetic resonance image of the abdomen showing right adrenal phaeochromocytoma with tumour thrombus in the inferior vena cava and right atrium (arrow)

adrenal phaeochromocytoma with tumour thrombus in right atrium. There was no evidence of distant metastasis. Alpha-blockage with phenoxybenzamine was commenced for preoperative preparation followed by beta-blocker with propranolol. Blood calcium and basal calcitonin levels were within normal limits but pentagastrin-stimulated calcitonin assay was positive with a significantly elevated level 2 minutes after pentagastrin injection. Ultrasonography of the thyroid gland showed a 1.5-mm hypoechoic lesion in the posterior aspect of the middle pole of right lobe of thyroid.

Right adrenalectomy with exploration of inferior vena cava and right atrium by cardiopulmonary bypass and hypothermic circulatory arrest was planned with a multidisciplinary team approach that included an endocrine surgeon, a cardiothoracic surgeon, a hepatobiliary surgeon, and an anaesthetist. Laparotomy was performed through a midline xiphoid to pubic symphysis incision. There was 2.9 L of straw-coloured ascitic fluid. The liver was enlarged and congested secondary to the Budd-Chiari syndrome arising from the tumour thrombus in the inferior vena cava and the right atrium. There was a large but well-circumscribed right adrenal phaeochromocytoma extending through

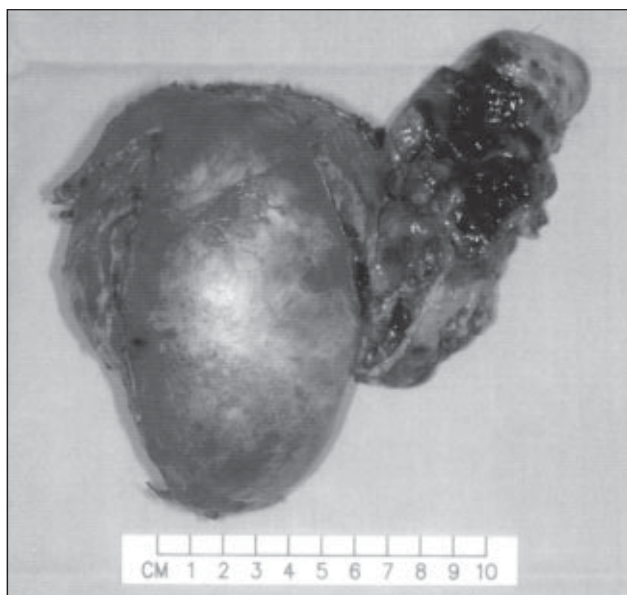


Fig 3. Resected specimen demonstrating a 12 cm x 9 cm right adrenal pheochromocytoma with a tumour thrombus extending through the adrenal vein and lateral wall of the inferior vena cava into the right atrium

the adrenal vein and lateral wall of inferior vena cava into the right atrium. The right lobe of liver was mobilised anteriorly, and the tumour was dissected from the kidney, liver, and retroperitoneum until it was only attached to the lateral wall of the vena cava at the area of tumour invasion. Median sternotomy was made by the cardiac surgeon. The right femoral vein, inferior mesenteric vein, superior vena cava, and the aorta were cannulated in turn for establishment of cardiopulmonary bypass after systemic heparinisation. The patient was cooled to 23°C before the aorta was cross-clamped, and cold cardioplegia was infused into aortic root to achieve cardiac arrest. The pheochromocytoma together with its tumour thrombus at the right atrium was then resected en bloc with a cuff of lateral wall of the vena cava (Fig 3), and the resection was facilitated by opening up the right atrium. The right atriotomy was closed and the abdominal vena cava was then repaired with the pericardial flap as patch graft. The patient was weaned off from cardiopulmonary bypass after full re-warming. Aortic occlusion time was 33 minutes and duration of bypass was 123 minutes. The blood pressure remained stable without any episode of hypertensive crisis. The operating time was 11.5 hours with blood loss of approximately 1000 mL. The resected specimen weighed 545 g and histology examination confirmed a diagnosis of pheochromocytoma with inferior vena cava invasion.

The patient was extubated on day 2 and had an

uneventful recovery. She was discharged home 9 days postoperatively. The postoperative 24-hour urinary catecholamines returned back to normal. Genetic study confirmed a germline mutation at codon 634 (Cys to Tyr) of exon 11 of the *RET* proto-oncogene. She remained asymptomatic with normal blood pressure 5 months postoperatively and total thyroidectomy was planned.

Discussion

It was previously estimated that approximately 10% to 15% of pheochromocytomas are due to hereditary cause, including MEN 2A.¹ The Euromen Study Group only registered 274 cases of MEN 2A patients with pheochromocytoma in eight European countries between 1969 and 1992.² Malignant transformation is less likely in patients with MEN 2A than those with sporadic pheochromocytoma. There are a very limited number of case reports on malignant pheochromocytoma with extension into the right atrium in the literature. Hartgrink et al⁴ reviewed 20 reported cases of pheochromocytoma extending into the vena cava and presented one of his own. All were sporadic cases and there were only two primary pheochromocytomas extending up into the right atrium through the vena cava.^{3,4} This present report is believed to be the first case of a malignant pheochromocytoma extending into the right atrium in a MEN 2A patient.

Surgical excision is the treatment of choice for pheochromocytoma. Depending on the level of involvement of the vena cava or the right atrium, different techniques of vascular control have been adopted in order to obtain complete removal of tumour, minimise blood loss, and prevent tumour embolism.⁵ For tumour thrombus extending below the right atrium level, besides cardiopulmonary bypass with hypothermic circulatory arrest, vascular control by clamping of the inferior vena cava with or without venovenous bypass has also been successful.⁶⁻⁹ For tumour extending into the right atrium, however, radical surgery with the use of cardiopulmonary bypass with hypothermic circulatory arrest is recommended based upon the success of surgery with such vascular involvement in renal cell carcinoma. Renal cell carcinoma is the most common retroperitoneal tumour with potential involvement of the vena cava or right atrium. Cardiopulmonary bypass with hypothermia and circulatory arrest has been employed in patients with renal cell carcinoma extending up the vena cava into the right atrium since 1984.¹⁰ This technique allows a bloodless operative field for atriotomy and venotomy

to assure a complete tumour removal, and to avoid excessive blood loss and distal tumour thrombus embolisation.³

Dunn et al¹¹ reviewed 12 cases of phaeochromocytoma with extension into the inferior vena cava in 1992. They were also the first to use cardiopulmonary bypass with hypothermia and circulatory arrest for patients with this condition. Angermeier et al³ reported the first case of primary phaeochromocytoma involving the right atrium with successful surgical excision using the same technique in 1990. On the other hand, Hartgrink et al⁴ reported massive blood loss during the dissection of the tumour from the liver capsule, and cardiopulmonary bypass with hypothermia and circulatory arrest was abundant. The clearance of tumour thrombus inside vena cava and right atrium was carried out by venotomy after cross-clamping of the vena cava below and the right atrium obliquely from above. Although the patient survived with a blood loss of more than 200 L, a residue tumour was found just caudal to the liver after 2 months and lung metastasis was detected 1 year postoperatively.⁴

Malignant phaeochromocytoma extending into the right atrium is extremely rare but can be the initial presentation of patients with MEN 2A. It might be deemed unresectable and was considered to be associated with insurmountable operative risk in the past. With the advancement of surgical techniques and perioperative care, aggressive surgical treatment seems to be justified and supported with a promising outcome. A multidisciplinary team approach with the adoption of cardiopulmonary bypass and hypothermic circulatory arrest is recommended with an aim

of complete tumour resection in a relatively bloodless field.

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