Case Report

Functioning Adrenocortical Carcinoma with Superior Vena Cava and Upper Airway Obstructions

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Background: *Adrenocortical carcinoma (ACC) is one of the most aggressive endocrine malignancies with a dismal prognosis. Typically, the tumor is large and has regional invasion or distant metastasis at initial presentation.*
Objective: *To describe an unusual case of functioning ACC presenting with superior vena cava (SVC) and upper airway obstruction.*
Material and Method: *A 23-year-old man with cushingoid appearance was evaluated for a neck mass and SVC syndrome. Hormonal assessment and neck mass biopsy including immunohistochemistry study were performed.*
Results: *Cushing's syndrome was confirmed by elevated 24-hr urinary free cortisol and no suppressible cortisol level after standard low dose (2mg/day) of dexamethasone suppression test. Computerized tomography (CT) study revealed a huge left suprarenal mass and multiple mediastinal lymph nodes compressing SVC and trachea. Histopathological findings of the neck mass were compatible with metastatic ACC.*
Conclusion: *The present report describes a functioning ACC patient with an unusual metastatic site causing SVC and upper airway obstruction. His hospital course was progressively worsened due to peptic perforation and decompensated respiratory failure, which led him to expire.*

Keywords*: Adrenocortical carcinoma, Superior vena cava obstruction, Cushing's syndrome*

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Adrenocortical carcinoma (ACC) is a highly malignant endocrine tumor that grows rapidly and tends to metastasize. Its prognosis is dismal due to a significant proportion of patients having distant metastasis at the time of initial presentation[1]. ACC is classified as either functioning or nonfunctioning, depending on its hormonal production. About 60% of ACC occurring in adults are functional and Cushing syndrome is the most common presentation[2]. The authors report, herein, a rare case of a large functioning ACC with unusual metastasis presentation to the mediastinum, causing superior vena cava (SVC) obstruction and upper airway obstruction.

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Case Report

A 23-year-old Thai man presented with facial swelling, progressive dyspnea and hoarseness of voice. He was in excellent health until 3 months earlier, when he noticed his facial and neck swelling and increased abdominal girth with purplish striae. He also complained of shortness of breath while walking up the stairs and hoarseness of voice. He was a non-smoker. There was no history of any malignancy among his relatives. Temperature was 37.2°C, pulse was 92/min, and respiration was 28/min. Blood pressure was 180/90 mmHg. On physical examination, cushingoid

appearance and a right cervical mass, 3x3 cm, were found. Swelling of both arms, upper part of his trunk and neck along with superficial vein engorgement was identified. Abdominal examination revealed an ill-defined mass at the left upper quadrant. Lung auscultation was clear without inspiratory stridor. Cushing syndrome was confirmed by high urine free cortisol level of 732 mg/24 hr (0-141.75) and an insuppressible plasma cortisol (22 mg/dL) after standard low dose (2 mg) dexamethasone test, and a low plasma adrenocorticotropic hormone (ACTH) level of 4 mg/dl (0-71) suggested its adrenal origin. Other adrenal hormones were normal for plasma renin activity, serum aldosterone, serum DHEAS, serum testosterone and 24-hr urine metanephrine/normetanephrine. His laboratory tests showed hematocrit of 40.2%; white blood cell count of 14,200/mm^3 (82% polymorphonuclear cells, 10% lymphocytes, 6% monocytes, 2% eosinophils) and a platelet count of 540,000/mm^3. Fasting plasma glucose was 120 mg/dL with normal serum electrolyte especially potassium. Computerized tomography (CT) of the whole abdomen showed a large retroperitoneal soft tissue mass, 9x7 cm in size, mainly occupying the left suprarenal region with extension along the left para-aortic region (Fig. 1). CT of the chest revealed multiple enlarged matted mediastinal lymph nodes, encasing the aorta and the origins of its branches with compression of the SVC and trachea (Fig. 2).

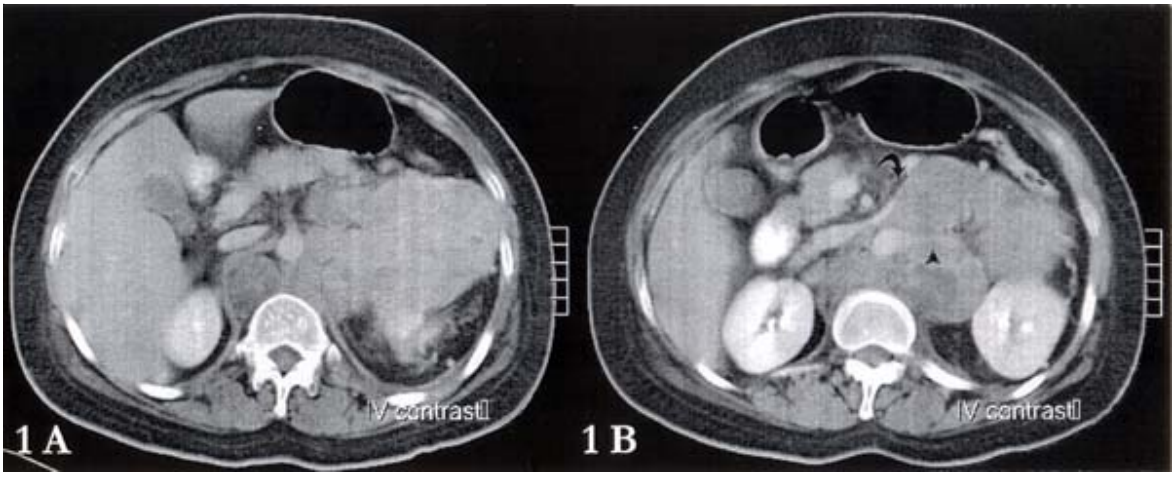

Fig. 1 **(A)** CT scan of the abdomen at the level of superior mesenteric artery origin showed a large left suprarenal mass with enlarged retrocaval and para-aortic lymph nodes. **(B)** At the level of left renal artery origin (arrowhead), the mass extended into left renal hilum encasing the left renal artery and stretching of the left renal vein (curved arrow) were noted

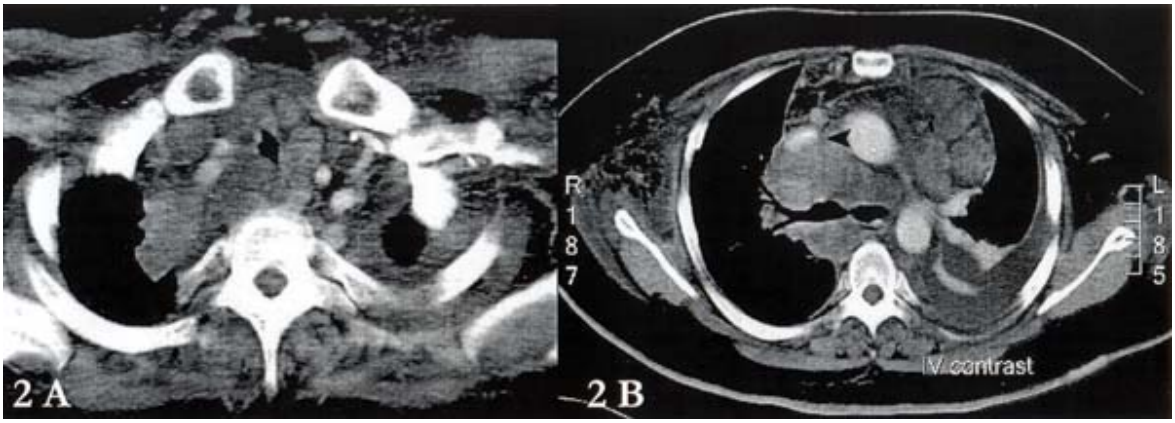

Fig. 2 **(A)** CT scan of the chest showed matted paratracheal lymph nodes causing trachea narrowing. **(B)** Enlarged mediastinal lymph nodes caused SVC compression (arrowhead)

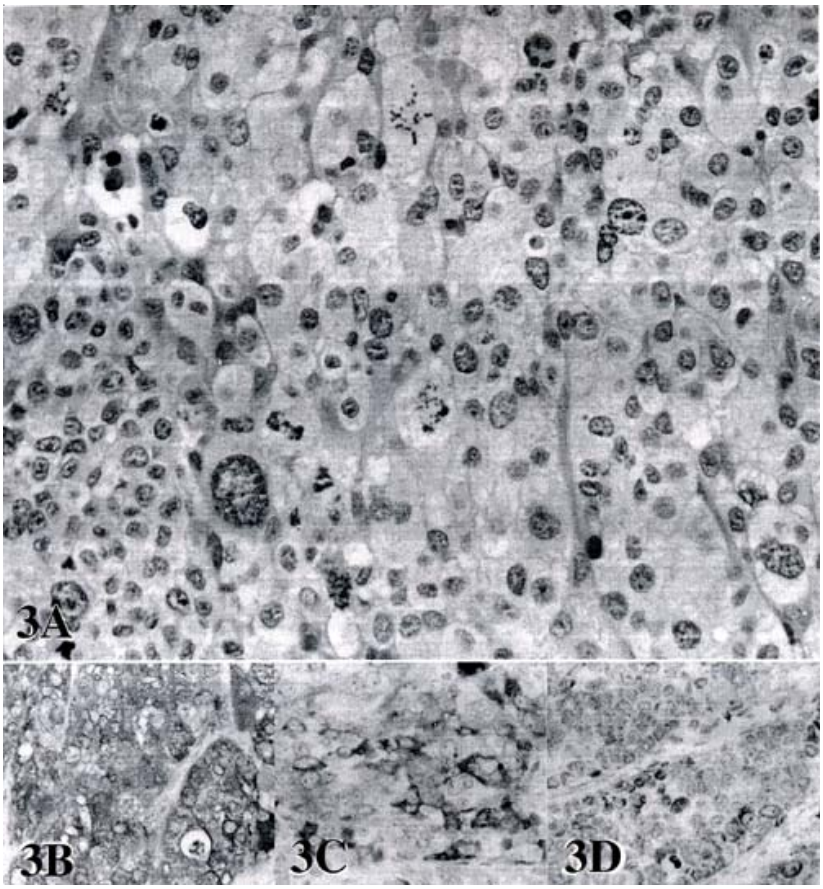

Fig. 3 Histopathology of the neck mass. Hematoxylin-and eosin-stained section **(A)** showed tumor cells with pleomorphic nuclei and foamy cytoplasm. They formed sheets, intervened by delicate fibrovascular septa. Note mitotic figures. Expression of synaptophysin **(B)**, inhibin alpha-subunit **(C)** and melan-A **(D)** was demonstrated by immunohistochemical studies

Biopsy of the neck mass (Fig. 3) disclosed sheets of pleomorphic neoplastic cells with foamy cytoplasm, intervened by delicate fibrovascular septa. Multiple foci of necrosis were detected, and mitoses were frequently encountered. Immunohistochemical studies showed that the tumor cells expressed synaptophysin, S-100 protein, inhibin alpha subunit and melan-A. They were non-reactive with pancytokeratin, chromogranin A and ACTH. The pathological diagnosis of metastatic ACC was, then, rendered. His hospital course was complicated with peptic perforation and decompensated respiratory failure, which led him to expire.

Discussion

ACC is a rare malignant tumor with an annual incidence of approximately 0.5 to 2 cases per million[3]. There is a bimodal occurrence by age, with the first peak occurring before 5 years of age and the second peak between the fourth to fifth decades of life[1,2]. Most series show a slight female preponderance especially functioning ACC[1,2,4]. The clinical presentation of ACC depends on whether or not the tumor is hyperfunctioning. The tumor is typically large with regional invasion or distant metastasis commonly encountered at initial presentation[1]. The kidney and inferior vena cava (IVC) are the frequent sites of local extension, with an incidence of vena cava involvement up to 30% of patients[5]. The vena cava obstruction may be asymptomatic or manifest as ascites, nephrotic syndrome, hepatomegaly, acute tricuspid regurgitation or Budd-Chiari syndrome. Right-sided tumors are more prone to venous involvement, presumably due to direct extension via the short right adrenal vein. Although external compression of the vessel or direct vascular wall invasion has been reported, the majority of these tumors

spread intraluminally to supradiaphragmatic part of the vena cava or right atrium[6]. Common metastatic sites are liver, lung and bone. They have also been reported in the pancreas, brain, diaphragm, small intestine and thyroid[2].

The SVC syndrome is a clinical syndrome of SVC obstruction due to compression, invasion or thrombus formation. Bronchogenic carcinoma, lymphoma and breast cancer are the major causes of SVC syndrome[7]. The prognosis of the patients with SVC obstruction is much more affected by the histology of the tumor than the SVC syndrome itself, which rarely leads to life-threatening complications, such as laryngeal or cerebral edema[8]. To the authors' knowledge, the present report represents the first case of ACC that caused obstruction of the SVC and trachea.

Pathological diagnosis of metastatic ACC requires a high index of suspicion. The presence of delicate vascular network was a clue towards an endocrine lesion in our case. Cushing syndrome and the morphological similarities of the tumor cells with normal adrenocortical cells prompted us to evaluate the tissue with various immunohistochemical staining. Expression of synaptophysin confirmed the endocrine feature of the tumor. Inhibin alpha-subunit and melan-A immunoreactivities, which have been recently found in adrenocortical neoplasms, provided the definite diagnosis of metastatic ACC[9,10].

The prognosis of ACC is rather poor; more than half of the patients die within 2 years[3]. Survival was significantly lower in old age and distant metastatic lesions at the time of diagnosis. Complete surgical removal of the primary tumor and any local or distant metastases is the mainstay of treatment and cardiac bypass techniques can be used in cases of vena cava involvement. Mitotane has been reported to be useful for residual or recurrent tumor while the role of radiotherapy is only for pain relief[1,11]. In conclusion, the authors describe a young man with a rare presentation of functioning ACC causing SVC and upper airway obstruction.

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ผู้ป่วยชายไทยที่มีอาการอุดตันของเส้นเลือดดำซุพพีเรีย วีนา คาวา และทางเดินหายใจส่วนต้นเนื่องจากมะเร็งของต่อมหมวกไตชั้นนอกในระยะกระจาย

สฐาปกร ศิริวงศ์, ชนพ ช่วงโชติ, สุธี สฤษฏ์ศิริ, พัชราจิรี ภาคอรรถ, วีรพันธุ์ โชวิฑูรกิจ, ธิติ สนับบุญ

ผู้ป่วยชายไทยอายุ 23 ปี รับไว้ในโรงพยาบาลจุฬาลงกรณ์ เนื่องจากอาการหอบเหนื่อยและบวมบริเวณใบหน้า ตรวจร่างกายพบลักษณะของกลุ่มอาการคุชชิ่ง ก้อนบริเวณคอ และกลุ่มอาการเส้นเลือดดำซุพพีเรีย วีนา คาวา อุดตัน ผลตรวจทางฮอร์โมนเข้าได้กับกลุ่มอาการคุชชิ่งที่มีสาเหตุมาจากต่อมหมวกไต การตรวจทางรังสีพบก้อนในบริเวณช่องท้องส่วนบนด้านซ้ายขนาดใหญ่ ก้อนและต่อมน้ำเหลืองบริเวณช่องอกซึ่งกดเส้นเลือดดำซุพพีเรีย วีนา คาวา และทางเดินหายใจส่วนต้นของผู้ป่วย และผลทางพยาธิวิทยาของก้อนดังกล่าวพบเป็นมะเร็งของต่อมหมวกไตชั้นนอก การดำเนินโรคของผู้ป่วยในโรงพยาบาลอาการของผู้ป่วยเลวลงเนื่องจากมีอาการแทรกซ้อนจากแผลในกระเพาะอาหารทะลุส่งผลให้การทำงานของระบบทางเดินหายใจล้มเหลว และเสียชีวิตในที่สุด