

## A Case of Non-Functioning Huge Adrenocortical Carcinoma Extending Into Inferior Vena Cava and Right Atrium

Primary adrenocortical carcinoma (ACC) is a rare tumor and its usual sites of metastasis are the lung (71%), lymph node (68%), liver (42%), and bone (26%). However, intracaval invasion extending into the right atrium is very rare and spontaneous regression of tumor burden in adrenal carcinoma is also rare. We report a case of ACC with direct invasion of the inferior vena cava and right atrium. A 34-yr-old male patient presented with progressive dyspnea, weight loss, and poor oral intake over 3 months. Non-functioning ACC with direct invasion of the inferior vena cava and right atrium was confirmed by imaging, pathologic, and hormonal study. Chemo-radiotherapy was attempted. However, tumor burden was not changed, but rather toxic hepatitis and thrombocytopenia were developed. His subjective symptoms and general conditions were improved after 1 month of conservative management and the patient was discharged. During clinical follow-up, this tumor showed spontaneous regression.

**Key Words :** Adrenocortical Carcinoma; Neoplasm Metastasis; Vena Cava, Inferior

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## INTRODUCTION

Primary tumors of the heart are rare, occurring at a frequency of 0.02% in pooled autopsy series. Secondary or metastatic cardiac tumors occur more frequently, with an at least 100 times higher, than primary cardiac tumors. Although every malignant tumor can metastasize to the heart, the common tumors with cardiac metastasis are carcinomas of the lung, the breast, and the esophagus, malignant lymphoma, leukemia, and malignant melanoma (1).

Adrenocortical carcinoma (ACC) is a rare malignant neoplasm with poor prognosis and it occurs approximately 0.5-2 out of 1 million population per year. It grows rapidly and 82% of the patients already had dissemination of the tumor. Usual metastatic sites are the lung (71%), lymph node (68%), liver (42%), and bone (26%) (2-4). However, intracaval invasion extending into the right atrium is very rare and only several cases were reported (5-14).

Spontaneous regression of tumor is an interesting phenomenon and well documented in some types of tumor, but occurs infrequently. Although spontaneous regression of cancer has been reported in almost every type of cancer, the largest numbers of cases are reported in a few types of cancer such

as neuroblastoma, renal cell carcinoma, and leukemias/lymphomas (15-18).

We report a case of non-functioning huge ACC extending into the inferior vena cava and right atrium in a young man which showed a tendency of spontaneous regression.

## CASE REPORT

A 34-yr-old male patient presented with progressive dyspnea, weight loss, and poor oral intake over 3 months. Physical examination revealed increased jugular venous pulsation and decreased breathing sounds on right lower lung fields, and palpable 10 cm sized non-tender mass on right upper quadrant of abdomen.

Laboratory findings revealed no significant abnormal findings except for mild leukocytosis (12,000/ $\mu$ L). Chest radiograph revealed moderate amounts of right pleural effusion. Abdominal sonography revealed a huge lobulated mass in right adrenal gland. Abdominal and chest computed tomography (CT) revealed 17  $\times$  10 cm sized huge lobulated mass arising from right adrenal gland, tumor thrombi in the inferior vena cava (IVC), and right atrium (RA) (Fig. 1). Transtho-

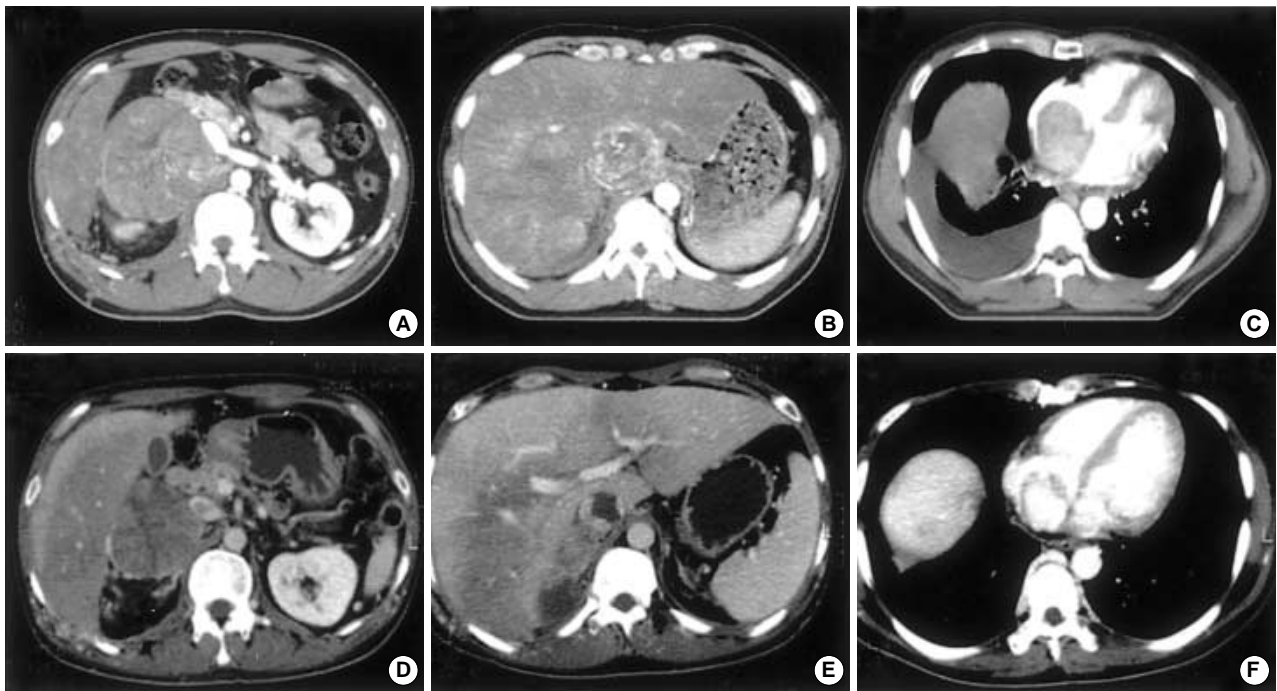


Fig. 1. Computed tomography (CT) at initial diagnosis (upper panel) reveals 17.5 × 10 cm sized huge lobulated mass arising from the right adrenal gland (A), heterogeneously enhanced tumor thrombi in inferior vena cava (IVC) (B), and filling defect caused by tumor which occupied nearly entire space of right atrium (RA) (C). Follow-up CT scan (lower panel) reveals marked reduction of tumor size (about 9.5 × 5.5 cm in size) in the right adrenal gland (D), decreased filling defect in IVC, and markedly reduced filling defect in RA (F).

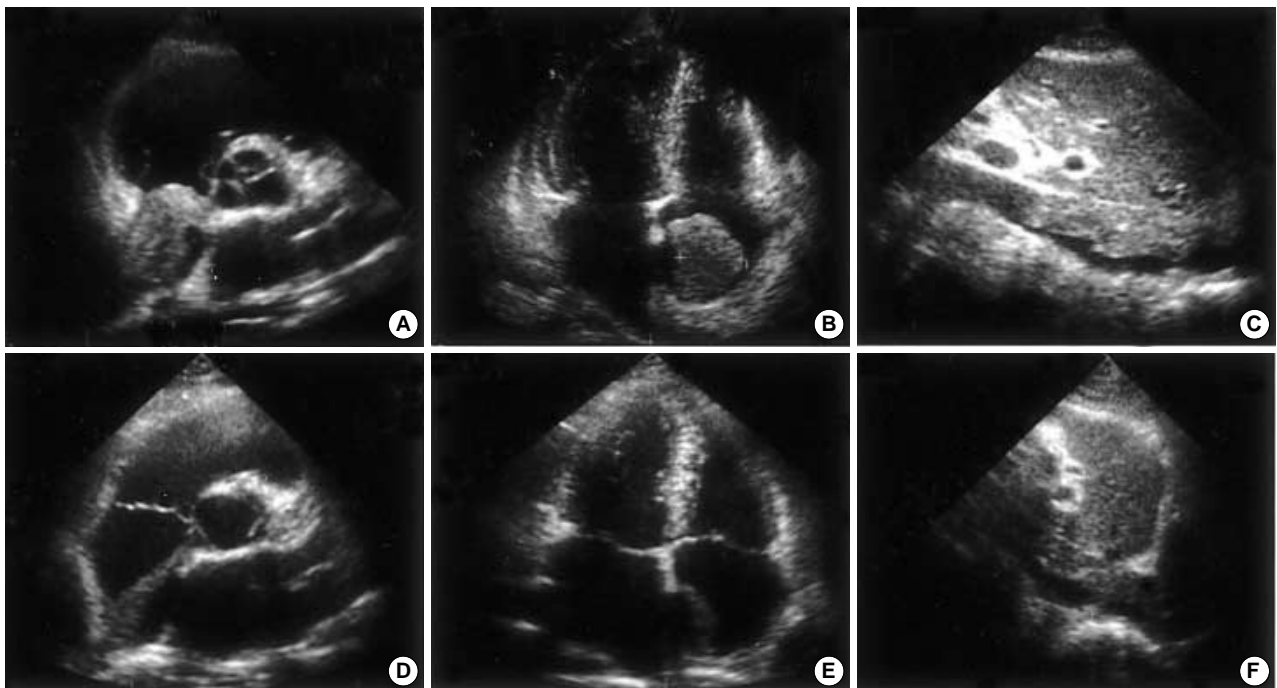


Fig. 2. Trans-thoracic echocardiography (TTE) at the time of initial diagnosis (upper panel) shows large right atrial mass which occupied nearly entire space of the right atrium (RA) on parasternal short axis view (A) and apical four chamber view (B). On subcostal view, RA mass connected continuously into the inferior vena cava (IVC) (C). Follow-up TTE (lower panel) reveals marked reduction in the size of right atrial mass on parasternal short axis view (D) and apical four chamber view (E). Tumor thrombi in IVC also shows reduction in size on subcostal view (F).

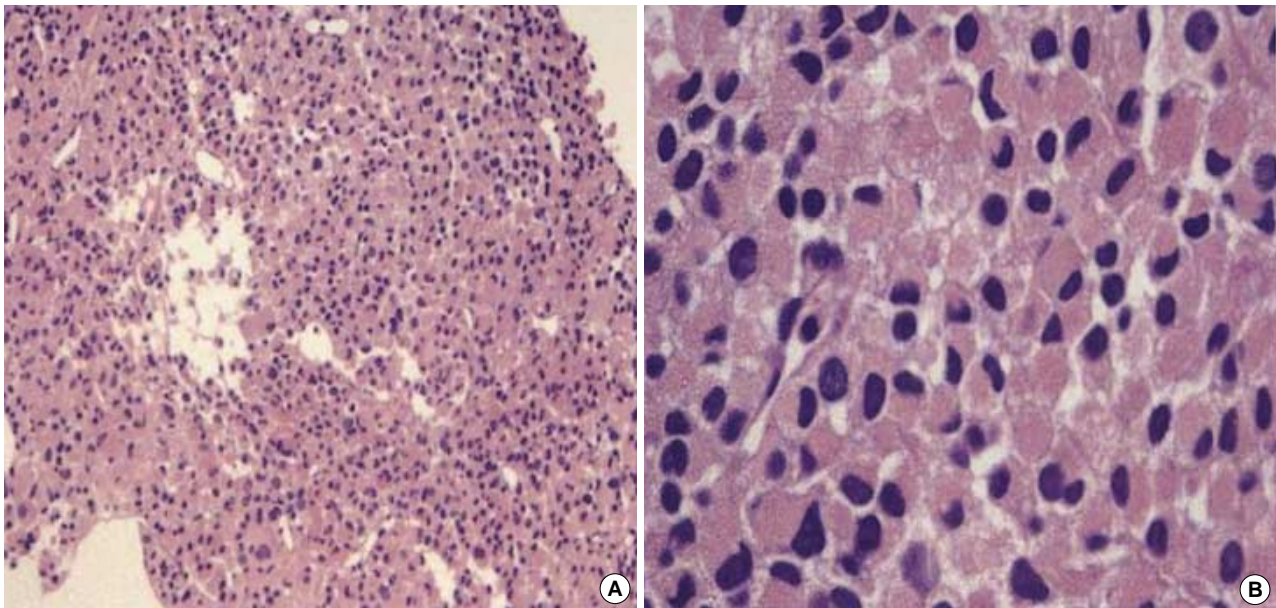


Fig. 3. Gun biopsy of the adrenal mass reveals cellular pleomorphism with large nuclei, abundant cytoplasm, and numerous small vascular channels which was compatible findings of endocrine tumor by Hematoxylin-Eosin stain (A:  $\times 40$ , B:  $\times 200$ ).

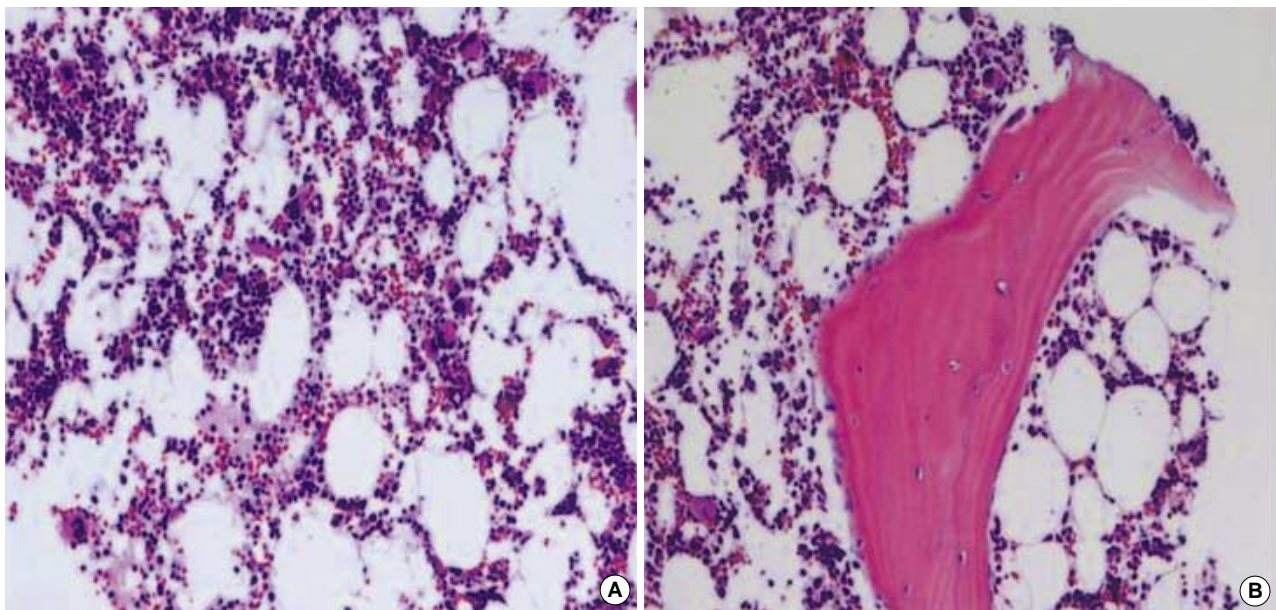


Fig. 4. Hematoxylin-Eosin stain of bone marrow biopsy reveals increased number of megakaryocytes without abnormal cells suggesting immune thrombocytopenic purpura (ITP) after the chemotherapy (A:  $\times 40$ , B:  $\times 100$ ).

raphic echocardiography (TTE) revealed large right atrial mass which occupied nearly entire space of RA. On subcostal view, the RA mass connected continuously into IVC (Fig. 2).

Hormonal study of adrenal gland was normal. Gun biopsy of the mass revealed cellular pleomorphism with large nuclei, abundant cytoplasm, and numerous small vascular channels which was compatible findings of endocrine tumor (Fig. 3). After pathological diagnosis of non-functioning ACC, 5-fluorouracil, adriamycin, and carboplatin based chemotherapy

and radiotherapy were done. However, tumor burden was not changed and toxic hepatitis and thrombocytopenia were developed. Platelet count was lowered to  $15,000/\mu\text{L}$ . Liver enzymes and bilirubin were elevated. Bone marrow biopsy revealed increased number of megakaryocytes without abnormal cells suggesting immune thrombocytopenic purpura (Fig. 4). Steroid therapy was started. Platelet count was normalized 1 month later from the initiation of steroid therapy and liver function tests were also normalized. His subjective

symptoms and general conditions were improved and the patient was discharged.

During out-patient clinic follow-up, abdominal CT and TTE, rechecked 3 months after discharge, revealed marked reduction of adrenal and RA tumor burden (Fig. 1, 2). Surgical removal of primary tumor including carvoatrial mass using cardiopulmonary by-pass is recommended, but the patient refused surgery. Thus, we manage the patient conservatively in out-patient clinic. The patient showed good general health status and had no subjective symptoms during 8-month clinical follow-up.

## DISCUSSION

Metastases to the heart are much more common than primary cardiac tumors. Metastatic tumors may reach the heart usually via lymphatic or hematogenous route, or by direct invasion. Transvenous extension of tumors along the IVC into the right atrium, however, is a rare condition. Some types of tumors such as hepatocellular carcinoma, renal cell carcinoma, or leiomyoma of the uterus can metastasize in such fashion (1). ACC is a rare malignant neoplasm and usually metastasize to the lung, lymph node, liver, and bone. ACC may also extend to adjacent vasculatures such as renal veins and IVC, usually accompanied by a thrombus (2-4). However, intracaval invasion extending into the right atrium is very rare and several cases were reported (5-14). Including the case of Rosen et al. (14), most of the described cases of ACC extending to RA were originated from right adrenal gland and also had tumor thrombi in IVC. This finding suggest that ACC invade directly to IVC and RA. Hedican and Marshall reported 3 cases and reviewed 26 previously reported cases of ACC (11). According to their report, about half of cases showed direct invasion of IVC and RA. As described above, our case also revealed direct invasion of right ACC to IVC and RA. To the best of our knowledge, this is the first case of ACC with direct invasion of the IVC and RA in Korea.

Approximately 60% of ACC cases presents with symptoms and signs of adrenal steroid hormone excess. However, the hormonal study was normal in our patient. Patients with a nonfunctioning ACC, just as our case, usually present with symptoms related to local mass effect like abdominal fullness, pain, indigestion, poor oral intake, nausea and vomiting.

Because chemotherapy has limited value in the treatment of ACC, complete surgical resection is the treatment of choice (1, 23). Our patient had advanced ACC with IVC and RA invasion. Several reports suggested that complete surgical removal of primary tumor with carvoatrial mass using cardiopulmonary bypass is the treatment of choice (6-8, 12, 14). However, our patient refused surgery. In patients with advanced local or metastatic disease, not amenable to surgical resection, cytotoxic chemotherapy may be attempted. Several cytotoxic agents has been used as single drug or in combina-

tion to treat advanced ACC including cisplatin, doxorubicin, etoposide, vincristine, and 5-fluorouracil (FU) (1, 23). Our patient received chemotherapy using 5-FU, adriamycin, and carboplatin, but tumor size were not changed but toxic hepatitis and thrombocytopenia developed. Thus, the patient was managed conservatively.

Spontaneous regression of tumor is an interesting phenomenon and well documented in some types of tumor, but occurs infrequently. Spontaneous regression of neoplasms occurs when the malignant tumor mass partially or completely disappears without any treatment or as a result of a therapy considered inadequate to influence systemic neoplastic disease. Although spontaneous regression of cancer has been reported in almost every type of cancer, the largest number of cases are reported in a few types of cancer such as neuroblastoma, renal cell carcinoma, and leukemias/lymphomas (15-17). In Korea, Seo et al. reported a case of spontaneous regression of liver metastasis in stage IV-S neuroblastoma after adrenalectomy (18). However, spontaneous regression in the case of ACC is very rare (19-22). Saracco et al. reported a case of spontaneously regressing ACC in a newborn (19). Kasat et al. reported a case of cortisol-producing ACC in an infant which showed complete spontaneous regression (22). In our case, the patient received chemo-radiotherapy, but the size of tumor was not changed for at least 3 months. Three months after the discharge, however, the size of adrenal mass as well as RA mass showed marked reduction despite of conservative management. The exact mechanism of spontaneous tumor regression is not established, but immune-mediated process, hormonal factors, inhibition of tumor growth by growth factors or cytokines, elimination of carcinogens, angiogenesis, tumor necrosis, apoptosis, or genetic factors would be involved (15, 16).

In summary, we report a case of 34-yr-old male patient who had non-functioning huge adrenal carcinoma extending into inferior vena cava and right atrium. This tumor showed spontaneous regression.

## REFERENCES

1. Reynen K, Kockeritz U, Strasser RH. *Metastases to the heart. Ann Oncol* 2004; 15: 375-81.
2. McClellan BL. *Staging and follow-up of renal and adrenal carcinoma. Cancer* 1991; 67: 1199-208.
3. Norton JA, Le HN. *Adrenal tumors. In: DeVita VT, editor. Cancer, 6th ed. Philadelphia: Lippincott Williams & Wilkins 2001: 1770-85.*
4. Stojadinovic A, Ghossein RA, Hoos A, Nissan A, Marshall D, Dudas M, Cordon-Cardo C, Jaques DP, Brennan MF. *Adrenocortical carcinoma: Clinical, morphologic, and molecular characterization. J Clin Oncol* 2002; 20: 941-50.
5. Schramek P, Dunser E, Bhargabha A, Hurby W, Umek H. *Adrenal cortical carcinoma: preoperative demonstration of right atrial extension by sonography and computerized tomography. J Urol* 1985; 133:

- 260-2.
6. Okazumi S, Asano T, Ryu M, Nagashima T, Odaka M, Isono K, Nishizawa T. *Surgical resection of adrenal carcinoma extending into vena cava, right atrium and ventricle: Case report and review of the literature. Nippon Geka Gekka Zasshi* 1987; 88: 231-8.
  7. Shahian DM, Nieh PT, Libertino JA. *Resection of atriocaval adrenal carcinoma using hypothermic circulatory arrest. Ann Thorac Surg* 1989; 48: 421-2.
  8. Galli R, Parlapiano M, Pace Napoleone C, Pierangeli A. *Neoplastic caval and intracardiac thrombosis secondary to reno-adrenal tumors. One-stage surgical treatment in deep hypothermia and circulatory arrest. Minerva Urol Nefrol* 1994; 46: 105-11.
  9. Bilge A, Pierard LA, Kulbertus HE. *Isolated cardiac metastasis of adrenal carcinoma: Transesophageal echocardiographic features. Am Heart J* 1996; 132: 1066-8.
  10. Yamana D, Yanagi T, Nanbu I, Tanaka K, Hirabayashi S, Tohyama J, Mizutani H, Ohba S, Katoh N, Ono Y. *Intracaval invasion of left adrenal cortical carcinoma extending into the right atrium. Radiat Med* 1997; 15: 327-30.
  11. Hedican SP, Marshall FF. *Adrenocortical carcinoma with intracaval extension. J Urol* 1997; 158: 2056-61.
  12. Salinas Sanchez AS, Segura Martin M, Lorenzo Romero JG, Hernandez-Millan I, Albertos Salvador J, Virseda Rodriguez JA. *Adrenal cortex carcinoma with right atrium involvement. Surgery with cardiopulmonary bypass. Actas Urol Esp* 2000; 24: 590-3.
  13. Chesson JP, Theodorescu D. *Adrenal tumor with caval extension. Scan J Urol Nephrol* 2002; 36: 71-3.
  14. Rosen B, Rozenman Y, Harpaz D. *Extension of adrenocortical carcinoma into the right atrium-echocardiographic diagnosis: A case report. Cardiovasc Ultrasound* 2003; 1: 5.
  15. Kaiser HE, Bodey B Jr, Siegel SE, Groger AM, Bodey B. *Spontaneous neoplastic regression: the significance of apoptosis. In Vivo* 2000; 14: 773-88.
  16. Cui Z, Willingham MC, Hicks AM, Alexander-Miller MA, Howard TD, Hawkins GA, Miller MS, Weir HM, Du W, DeLong CJ. *Spontaneous regression of advanced cancer: Identification of a unique genetically determined, age-dependent trait in mice. Proc Natl Acad Sci USA* 2003; 100: 6682-7.
  17. Chang KC, Chan KL, Lam CW. *Spontaneous regression of renal cell metastases. Hong Kong Med J* 1999; 5: 72-5.
  18. Seo HJ, Jung JH, Song YT. *Spontaneous regression of liver metastasis in stage IV-S neuroblastoma after adrenalectomy: one case report. J Korean Assoc Pediatr Surg* 2001; 7: 68-72.
  19. Saracco S, Abramowsky C, Taylor S, Silverman RA, Berman BW. *Spontaneously regressing adrenocortical carcinoma in a newborn. A case report with DNA ploidy analysis. Cancer* 1988; 62: 507-11.
  20. Gohji K, Kizaki T, Fujii A. *Spontaneous regression of pulmonary metastasis from nonfunctioning adrenocortical carcinoma after removal of the primary lesion: a case report. J Urol* 1995; 154: 1854-5.
  21. Holgersen LO, Subramanian S, Kirpekar M, Mootabar H, Marcus JR. *Spontaneous resolution of antenatally diagnosed adrenal masses. J Pediatr Surg* 1996; 31: 153-5.
  22. Kasat LS, Borwankar SS, Naregal A, Jain M. *Complete spontaneous regression of a functioning adrenocortical carcinoma in an infant. Pediatr Surg Int* 2001; 17: 230-1.
  23. Alolio B, Hahner S, Weismann D, Fassnacht M. *Management of adrenocortical carcinoma. Clin Endocrinol (Oxf)* 2004; 60: 273-87.