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CASE REPORT OPEN ACCESS

Metastatic Adrenocortical Carcinoma of the Lung In A Four Years Old Child

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Background: Studies of adrenocortical carcinoma is an aggressive rare type of endocrine tumors. It possesses a high mortality rate. This type of carcinomas occurs sporadically, while it could be part of hereditary syndromes. Only limited data is found about the recurrence of these tumors after resection and their prognosis is unclear.

Case Presentation: We present a case of a four-year-old boy who presented with virilization symptoms and was referred for further investigation of left abdominal mass. He was cushingoid upon examination. The patient was managed by left nephrectomy and chemotherapy. Upon follow up, residual mass lesion was seen on CT. Re-resection of the residual tumor was done. Adjuvant mitotane therapy and radiotherapy were started, 7 months later the patient was discovered to have left lung metastasis in which he underwent left lung wedge resection.

Keywords: Adrenocortical tumors, adrenocortical carcinoma, lung metastasis

Introduction

Adrenocortical tumors are rare in children, while adrenocortical carcinoma is even more uncommon in this age group (1). Although ACC is rare but it's one of the aggressive types of endocrine tumors (2). It has been reported by its tragic high mortality rate (3,4). The worldwide annual incidence of ACT is only 0.3 - 0.38 per million children below the age of 15 years (5,6).

Commonly adrenocortical carcinoma occurs sporadically. It could also present as part of hereditary syndromes like Li-Fraumeni syndrome and Beckwith-Wiedemann syndrome (7, 8), in children with genetic predisposition (R337H mutation) like in south Africa where its prevalence is more than three times higher than other areas (6).

The peak incidence of ACC is between the fourth and fifth decades, although it can occur in all age groups (2). Females have slight predominance (9). Lung metastasis have been reported with ACC (10).

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In this report, we present a case of a 4-year-old boy with metastatic left adrenocortical carcinoma. Lung metastasis have occurred almost 7 months after the primary tumor resection. The study was approved by Institutional Review Board At King Fahad Medical City in Riyadh, Saudi Arabia.

Case Presentation

Four years old Sudanese boy was referred for further management of left abdominal mass. Symptoms started 2 months prior to presentation, when he developed acne mainly in the forehead involving scalp, weight gain, increase in appetite, gradual increase in the abdominal girth, penile enlargement with pubic hair, change in sweat smell (adult odor), fatigability, mild on and off abdominal pain, urinary frequency and behavioral changes. There was no family history of tumors or cancers. The mother underwent thyroidectomy due to goiter with hypothyroidism. On examination, he was vitally stable with cushingoid features, rounded face with pudgy cheeks (Moon face), penile enlargement with pubic hair but no facial hair.

The abdomen was distended without any tenderness. Palpable mass was noted in the left side of the abdomen. Otherwise normal examination with clear chest. CT of abdomen showed a large circumscribed left flank heterogeneous soft tissue lesion measuring 10x9x11 cm, which caused displacement of the surrounding vascular structure with no evidence of encasement.

There was displacement of the left kidney inferiorly, with no evidence of liver, lung, or osseous metastasis, and no intra-spinal extension. Laboratory work up showed high plasma LDH level (Almost triple the normal), low plasma ACTH level, normal serum cortisol and total testosterone levels, high serum dehydro epiandrosterone sulfate levels. The case was discussed in multidisciplinary tumor board meeting and the plan was operative resection. Upfront surgical resection plus left nephrectomy 26.5.2016 was done with fragile tumor spillage intraopera-tively. Irrigation and suction was done. The tumor was involving the upper pole of the kidney and it was inseparable from the renal parenchyma (Figure-1) so the decision was to do radical nephrectomy in addition to adrenalectomy to reduce the chance of recurrence. Post-operative course was uneventful.

Pathologic examination of the primary tumor revealed multinodulated white tan mass measuring 10x8x4 cm replacing most of the kidney parenchyma and reaching to the renal sinus and perinephric fat grossly. No adrenal gland was identified grossly. Tumor was not reaching the vascular margins and no lymph nodes identified in the hilar fat.

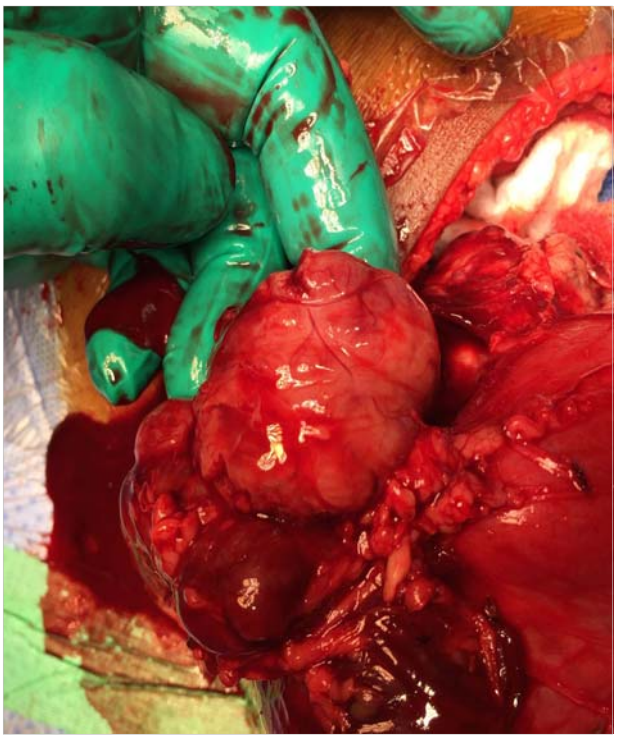

Figure-1. Intraoperative primary tumor

Under microscope, the tumor showed diffused proliferation of highly pleomorphic epithelioid cells seen as sheets and nests with highly pleomorphic and bizzar nuclei with some multinucleated cells. Cells show abundant eosi-nophilic granular cytoplasm. Clear cells change was seen in about 10% of tumor. Mitoses were brisk with many atypical mitoses no-ted (Figure-2).

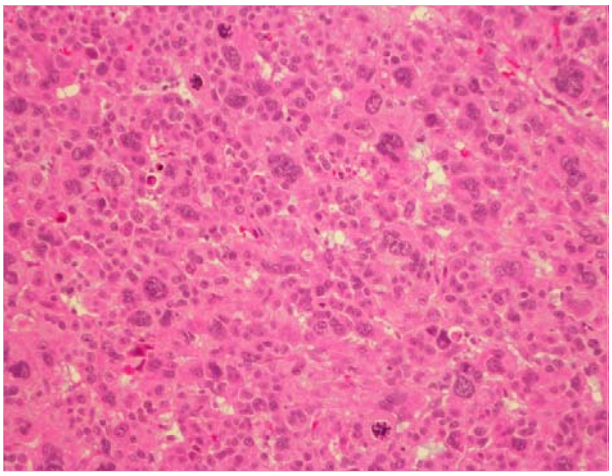

Figure-2. Atypical mitosis

Necrosis was prominent (Figure-3). Vascular invasion near the capsule was also noted. However, the renal vein and arterial vas-cular margins were clear. The tumor appeared to have pushing borders at the tumor-kidney interface and didn't show any evidence of invasion into the renal parenchyma (Figure-4).

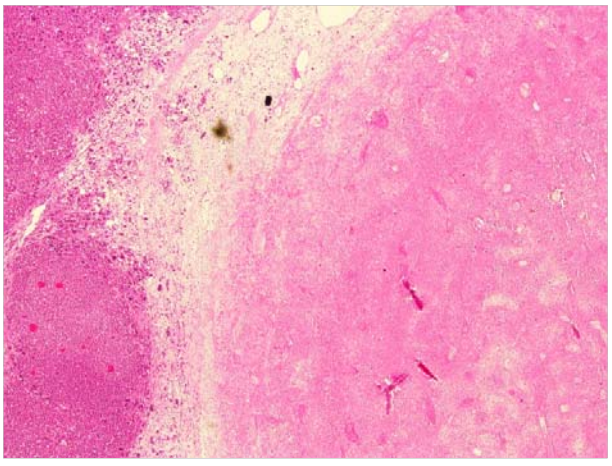

Figure-3. Areas of necrosis

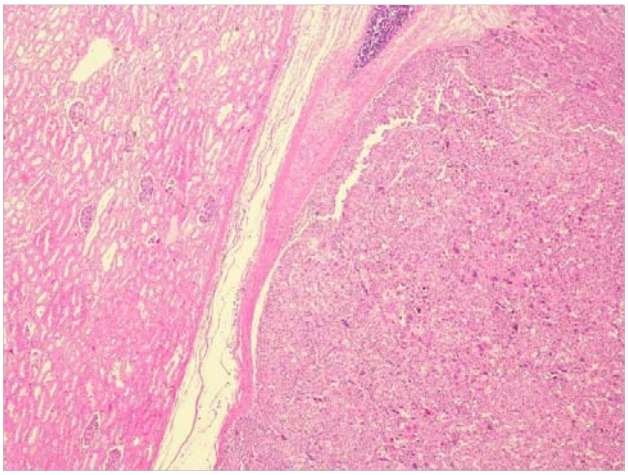

Figure-4. Kidney tumor interface shows intact kidney surface

On immunohistochemistry, the tumor was positive with Vimentin, Melanen A and Synaptophysin and was negative with Cytokeratin, EMA (Only focally positive), Inhibin, Calretinin, S100, Chromnogranin, and CD56 (which showed very focal positive). This immunoprofile was in keeping with adrenal cortical tumor. Although negative staining with both inhibin and calretinin is unusual, but it can rarely be seen in adrenal cortical neoplasma. MelanA positivity is helpful for the diagnosis. The diagnosis was agreed on by two independent pathologists.

Post-operative follow-up CT scan 10 days after surgery showed interval resection of the large left suprarenal mass and left kidney, small enhancing soft tissue seen in the left paravertebral region, could be residual tumor or peritoneal deposits. With no evidence of chest metastasis. The patient underwent chemotherapy COG (ARAR0332 protocol). He had four cycles with poor response, rather suggestive of tumor progression on chemotherapy with rising DHEA levels.

CT chest, abdomen and pelvis three months after, showed Residual well demarcated predominantly hypodense soft tissue mass lesion noted in the left renal/adrenal region measures

3.9x2.3x3 cm most likely representing local residual. In the chest satisfactory position of the left central line, no hilar lymphadenopathy. Both lungs are within normal limits with no suspicious pulmonary nodules.

Table-1. Weiss system and Modified Weiss system.

Parameters	Weiss system	Modified Weiss system
High nuclear grade (Fuhrman grade 3 / 4)	√	
Mitotic rate >5 / 50 hpf	√	√× 2
Atypical mitoses	√	√
Clear cells comprising <25% of the tumor	√	√× 2
Diffuse architecture (>one third of tumor)	√	
Necrosis	√	√
Venous invasion	√	
Sinusoidal invasion	√	
Capsular invasion	√	√
	Score < 3	Score > 3
	Risk of local recurrence / metastasis	
Weiss (1989)	0%	91%
	5 years survival	
Lucon (2002)	100%	62%

Macroscopic re-resection of the residual tumor was done 4 months after the primary resection, where the mass was identified, separated from medial aspect of IVC and was dissected with no evidence of tumor residual. Pathologic examination showed residual viable tumor, positive regional lymph node, no chemotherapy changes and invasion of fibro-fatty soft tissue (stage 3). Clinically he was doing fine with no virilization symptoms. 11 days post re-resection abdomen/pelvis CT showed, the previously seen left paraspinal left tissue residual mass lesion has been surgically resected. A focal area of enhancing soft tissue is seen in the tumor bed. There is another focal hypodense mass lesion measures 15x21 mm seen in the left prevertebral compartment abutting the posterior wall of the splenic artery. Adjuvant oral mitotane therapy and local radiotherapy were initiated. Follow up CT, 3 months after, revealed subtle reduction in size of the residual mass. The residual soft tissue seen in the left adrenal gland bed is demonstrated showing more enhancing component, it roughly measures 12x10 cm as compared to 22x12 mm done 3 months back. CT chest showed interval development of a lung nodule seen in the lingual measuring 5.6x5.3 mm. No major airspace consolidation or collapse. No pleural effusion or pneumothorax. The major tracheobronchial tree is patent. No size significant axillary, mediastinal or hilar lymph nodes. There's evidence of a small enhancing nodule close to the posterior left 11th rib measuring 12x6 mm suggestive of another metastatic nodule.

The patient hadmetastatic adrenocortical carcinoma to the left lung, underwent left lung wedge resection. Pathology showed residual microscopic focus of metastatic adrenocarcinoma 5%, Resection margin negative for tumor, he was started on radiotherapy to the left lung surgical bed.

Whole body PET scan, FDG avid left paraaortic nodules as well as left chest well solitary nodule measuring 1.1x1 cm. The rest of the body showed no suspicious FDG uptake. A week after, MRI chest on showed enhanced lesion in 11th intercostal space seen in the post contrast coronal T1- weighted image measures 1.2x0.7 cm. The lesion shows high signal intensity in coronal STIR weighted image and isointensity in coronal T1-weighted image.

Discussion

Adrenocortical carcinoma is known by its rarity since it represents only 0.2% of all childhood

cancers(7). The diagnosis of adrenocortical neoplasm in children is usually made as a result of symptoms caused by hormonal production by the cancer cells (11). In this case, the cushingoid features and sexual precocity drove the discovery of the mass, which was investigated and the tumor was found subsequently. Left sided ACC are generally more common than right side, as in our case (12). Carcinoma can't be distinguished from an adenoma from patient presentation, even in the presence of laboratory findings and imaging studies. Although large tumor size in imaging and heterogeneity can predict carcinomas (13). Categorization of carcinoma from adenoma in adrenocortical pathology is challenging. In 1989 the introduction of Weiss criteria was adopted to differentiate carcinoma from adenoma. This has been modified in 2002 as 'modified Weiss system' and is now the preferred modality to be used (14). In this case we used the modified Weiss system (Table-1). Presence of atypical mitoses, clear cells comprising around 10 % of the tumor and necrosis would put our patient in 62% 5 years survival rate. Larger tumor size, high percent necrosis and high mitotic rate are associated with poor outcome (15). Margin status of the tumor, extension of tumor outside the adrenal gland, presence of metastasis and age were associated with worst survival (16, 17). Using TNM staging system (Table-2) (18) prior the re-resection our patient was thought to be stage 2. Afterward, he was discovered to have stage 3 cancer. Post-radical resection of ACC, adjuvant mitotane could lengthen recurrence free survival period (19). In addition, radiotherapy is recommended in cases with high risk of local recurrence (2). Therefore, adjuvant mitotane therapy and local radiotherapy were initiated. Whereas, the 13 institutions study concluded that there's no association between adjuvant mitotane after resection and improvement of recurrence-free survival or overall survival (20).

Our patient developed lung metastasis while on mitotane therapy. In a series study done in Turkey, out of 20 ACC patients, 3 had lung metastasis at presentation in which one of them had concurrence liver metastasis. Furthermore, during mitotane therapy within 2 years' time, 3 patients developed lung and liver metastasis, while another 2 patients developed lung and bone metastasis. They have stated that (frequent imaging studies and endocrine evaluation was of utmost importance to detect recurrence in long-term follow-up of patients)(10).

Conclusion

Adrenocortical carcinoma is a rare neoplasm in children, it has a high mortality rate. Lung metastasis could occur after tumor resection even after initiation of mitotane and local radiotherapy.

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