]Iranian Journal of Pathology (2012)7 (2), 130 - 134

Case Report

Nonfunctional Adrenocortical Carcinoma with Foci of Osseous Metaplasia in a Young Girl

Srilatha Parampalli Srinivas[1], Alfred Roy[2], Vijay kumar[3]

1. Dept. of Pathology, Melaka Manipal Medical College, Manipal University, Manipal, India
2. Dept. of Pathology, KMC International Centre, Manipal University, Manipal, India
3. Dept. of Paediatric Surgery, Kasturba Medical College and Hospital, Manipal University, Manipal, India

ABSTRACT

Nonfunctional adrenocortical carcinoma is an extremely rare malignant tumor in children. Unlike the functional tumor which is detected early due to its hormonal presentation, nonfunctional tumor is detected at a later stage. Here we report a case of a 10 year old girl who presented with abdominal mass and symptoms of short duration. No hypertension and cushingoid features were seen. Serum alpha-fetoprotein, urine vanillyl mandelic acid and homovanillic acid levels were not elevated. CT scan showed multiple pulmonary nodules suggestive of metastatic deposits. With gross and light microscopic findings differential diagnoses of hepatoblastoma, paraganglioma, renal cell carcinoma, adrenal cortical and medullary tumours were made. An array of immunohistochemical markers was done and the final diagnosis given was nonfunctional adrenocortical carcinoma with foci of osseous metaplasia.

Keywords: Adrenocortical Carcinomas, Bone, Metaplasia

Introduction

Adrenocortical carcinoma (ACC) is a rare malignancy with incidence of 2 per million population per year. In children, it accounts for 0.002% of all malignancies in this age. Due to rarity of nonfunctional adrenocortical tumors in the pediatric age group, there is very few case reports of them compared to their functional counterpart (1). Unlike the functional ACC, there are no hormonal manifestations. They usually present with abdominal complaints only and hence they present in the advanced stages of the disease. Patients with early diagnosis and surgical resection have better prognosis (2, 3). The differential diagnosis of ACC includes adrenal adenoma, phaeochromocy-

Received: 2 July 2011
Accepted: 9 October 2011
Address communications to: Dr Srilatha Parampalli Srinivas, Depatment of Pathology, Melaka Manipal Medical College, Manipal University, Manipal, India
Email: drsrilatha2003@hotmail.com

tomas /paragangliomas, renal cell and hepatocellular carcinomas. Immunohistochemistry plays an important role in differentiating these tumours.

We present a case of a 10 year old girl with abdominal mass and symptoms with no hormonal manifestations. Abdominal tumor was resected and diagnosed as nonfunctional adrenocortical carcinoma with foci of osseous metaplasia and lung metastases. In ACC, osseous metaplasia is an extremely uncommon finding and the rarity of a nonfunctional ACC in a child prompted us to make this case report.

Case Report

A 10 year old girl presented with complaints of fever, vomiting and loose stools of two days duration. She also had abdominal fullness since ten days. On physical examination an abdominal mass was palpable in the right hypochondrium extending 6 cm below costal margin and moved with respiration. No hypertension or Cushingoid features seen. Serum alpha-fetoprotein, urine vanillyl mandelic acid and homovanillic acid levels were not elevated. Liver function tests were normal.

A CT scan showed a large heterogenously enhancing mass with calcification and central necrosis. The mass is seen displacing the inferior vena cava and right kidney and abutting the right lobe of liver with loss of fat planes, suggesting infiltration. Multiple bilateral pulmonary nodules were also visualized. FNAC done was reported as germ cell tumor / anaplastic lymphoma. Patient was operated and the mass was removed.

Grossly, the mass was 16 x 15 x 08 cm, weighing 1000g, encapsulated with central areas of necrosis bordered by hard gritty areas (Fig.1). Light microscopic examination of the mass showed tumor with cells arranged in trabecular, organoid and sinusoidal pattern (Fig. 2). The cells had granular eosinophilic cytoplasm, large nuclei with prominent nucleoli and 4 to 5 mitotic figures per 50 HPF. Focus of capsular invasion, large areas of necrosis, foci of calcification and osseous metaplasia (Fig. 3) noted. A differential diagnosis of hepatoblastoma, paraganglioma, renal cell carcinoma, adrenal cortical and medullary tumors were made.

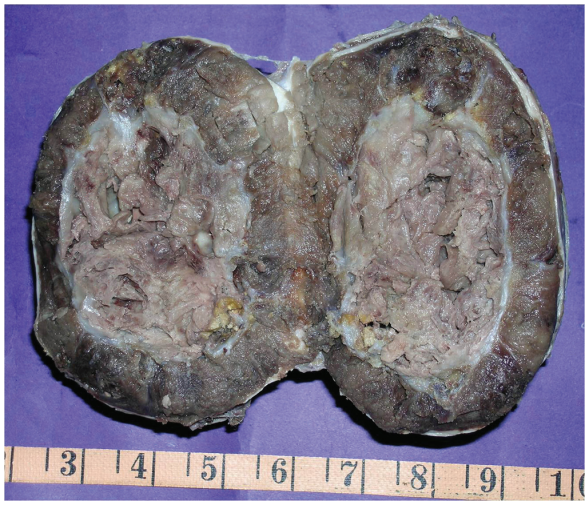

Fig.1- Gross picture of the ACC with encapsulation and central areas of necrosis bordered by hard gritty areas

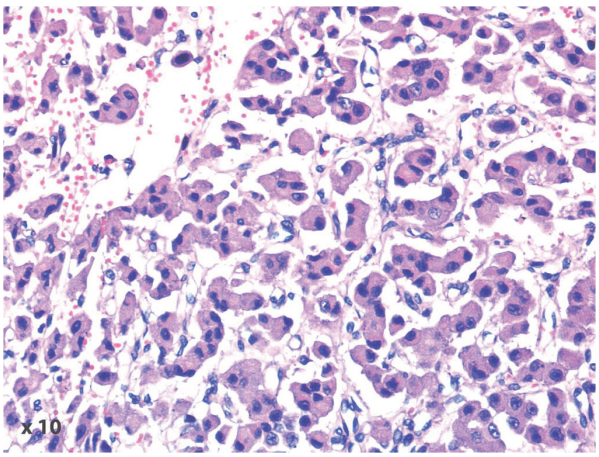

Fig.2- Histomorphology of ACC showing trabecular arrangement of large tumor cells with granular eosinophilic cytoplasm and large nucleus with prominent nucleoli (H&E staining ×400)

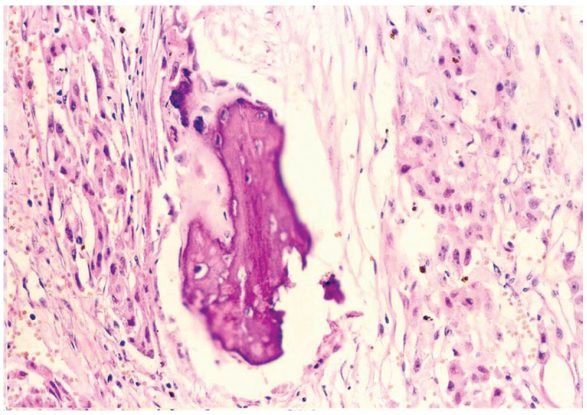

Fig.3- Microscopic view of the tumor showing osseous metaplasia (H&E staining ×400)

Immunohistochemical markers were done. Cytokeratin 7 and hepar-1 were negative. Non-specific enolase, synaptophysin and inhibin were positive. Weak cytoplasmic positivity was noted for calretinin.

Considering the clinical, biochemical, gross, light microscopy and the immunohistochemical findings, a final diagnosis of non-functional adrenocortical carcinoma with foci of osseous metaplasia was given. The patient was taken to an oncology centre for further treatment and hence was lost for follow up.

Discussion

According to the clinical presentation of ACC, it can be classified as functional and nonfunctional tumors. Functional tumors are associated with clinical syndromes like adrenogenital syndrome, Cushing's syndrome, or Corin's syndrome (2). Functional tumors produce hormones and have recognizable endocrine signs and symptoms which make them detectable early. Nonfunctional tumors do not have any hormonal manifestations and they present with clinical features related to the tumor growth like abdominal pain, palpable abdominal mass or as adrenal incidentalomas during imaging performed for unrelated reasons. Due to their silent nature, they are detected at an advanced stage with metastatic disease (1, 3). Patel VV *et al.* has described a case report of a small girl who had vague abdominal complaints like our patient and was diagnosed to have giant nonfunctional ACC lung metastases and had palliative chemotherapy due to advanced stage of presentation. The girl died after two months of diagnosis.

ACC can be associated with congenital and hereditary conditions such as Li-Fraumeni syndrome, hemihypertrophy, Beckwith- Wiedemann and MEN1 syndrome (4, 5).

Alpha-inhibin, calretinin and melan A antibodies are the most sensitive markers for ACC, although they are not highly specific. Positivity in ACC for neuroendocrine markers is restricted to NSE, and synaptophysin, whereas chromogranin A is negative, a feature which helps in the differential diagnosis with phaeochromocytoma/ paraganglioma. Adrenal tumors are usually negative or only focally positive for different types of cytokeratins and epithelial membrane antigen (EMA). Renal cell and hepatocellular carcinomas are positive for cytokeratin and EMA. Negative staining for CD10 and anti-hepatocyte antigen rules out a renal and liver neoplasm, respectively (6).

Macroscopically, tumor weight of more than 500gms, lobulated cut surface, intratumoral hemorrhage, areas of necrosis and calcification has been used to predict malignancy (3). Weiss listed the following nine microscopic criteria as suggestive of malignancy in an adrenocortical tumor: high nuclear grade, mitotic rate greater than 5/50 per high power field, atypical mitotic figures, eosinophilic cytoplasm (in greater than 75% of tumor cells) and paucity of clear cells (less than or equal to 25%), diffuse architecture present in 33% or greater of the tumor, necrosis, invasion of venous structures, invasion of sinusoidal structures and capsular invasion. Tumors

with 4 or more features are considered as malignant (3, 7).

Features that ruled out a diagnosis of adrenocortical adenoma in our patient were,

Weight of the tumor- 1000g

Mitoses- 4 to 5 / 50 HPF

Large areas of necrosis

Predominance of eosinophilic cells and paucity of clear cells

Capsular invasion

Metastatic deposits in the lungs

Osseous metaplasia in ACC is a very rare finding which we have observed in our case. There are reports of phyllodes tumour of breast, renal cell carcinoma, colonic adenomas and carcinomas, gall bladder and endometrium showing osseous metaplasia in the literature. Only Poiana *et al.* has reported osseous metaplasia in their study of 2 cases- an adrenal adenoma and adrenocortical carcinoma (8).

Common sites of metastasis of ACC include liver, lung, lymph nodes and bone. Metastatic deposits in diaphragm, small intestine thyroid, pancreas and brain also have been reported. Local invasion can occur into the kidneys and inferior vena cava (3).

Surgery is the main treatment for ACC. Chemotherapy is administered to those tumors which are resectable, cannot be completely resected or with metastasis. Mitotane alone or in combination with etoposide and cisplatin can be used. Radiotherapy is given as a palliation in patients with bone metastasis (3, 5).

Prognosis is better in children compared to adults. It also depends on the stage at diagnosis. Surgery done in early stage has a better survival rate. Based on a study conducted by Linda ng and Libertino, average survival for patients with unresectable tumor was 3 to 9 months and after complete surgical removal was 13 to 28 months (3).

Conclusion

Nonfunctional ACC is less common in children and it presents at a late stage as our patient presented with lung metastases. Prognosis is better with early diagnosis and surgical resection. Immunohistochemical markers are a great help in its differential diagnosis from phaeochromocytoma, paraganglioma, hepatocellular and renal cell carcinoma and Weiss histological criteria provides the basis for distinction between benign and malignant adrenal tumors.

Acknowledgements

We thank Prof. Pathmanathan, Head of Department of Pathology, School of Medicine and Health Sciences, Monash University, Sunway campus, Malaysia for doing the immunohistochemical marker study for our case. The authors declare that there is no conflict of interests.

References

1. Patel VV, Shah DS, Raychaudhari CR, Patel KB. Giant non-functioning adrenocortical carcinoma: A rare childhood tumor. Indian J Med Paediatr Oncol 2010;31(2):65-8.

2. Lele SM, Mittal BV, Vora IM, Kulkarni HS. Nonfunctioning adrenocortical carcinoma. J Postgrad Med 1992;38(3):145-7.

3. Ng L, Libertino JM. Adrenocortical carcinoma: diagnosis, evaluation and treatment. J Urol 2003;169(1):5-11.

4. Mayer SK, Oligny LL, Deal C, Yazbeck S, Gagne N, Blanchard H. Childhood adrenocortical tumors: case series and reevaluation of prognosis--a 24-year experience. J Pediatr Surg 1997;32(6):911-5.

5. Budhwani K, Ghritlaharey R, Debbarma M. Adrenal cortex tumor in a six year girl- A case

report and review of literature. Indian J Med Paediatr Oncol 2004;(25):71-5.
6. Volante M, Buttigliero C, Greco E, Berruti A, Papotti M. Pathological and molecular features of adrenocortical carcinoma: an update. J Clin Pathol 2008;61(7):787-93.
7. Jain M, Kapoor S, Mishra A, Gupta S, Agarwal A. Weiss criteria in large adrenocortical tumors: a validation study. Indian J Pathol Microbiol 2010;53(2):222-6.
8. Poian C, Carsote M, Baloescu R, Stanescu B, Petrescu R, Corneci C, *et al.* The adrenalectomy in rare endocrine tumors – 2 cases report. Jurnalul de Chirurgie, Iasi 201;6(1):47-53.