Case Report

Composite pheochromocytoma – neuroblastoma of the adrenal gland associated with systemic lupus erythematosus; diagnosed on cytology

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ABSTRACT

Composite pheochromocytoma (CP) is a rare tumor of the adrenal medulla that refers to a pheochromocytoma that has a component resembling neuroblastoma, ganglioneuroblastoma, ganglioneuroma or even a malignant peripheral nerve sheath tumor. There are very few reported cases of CP, with majority of the cases having elements of ganglioneuroma with pheochromocytoma. We report the case of a 27-year-old female with a history of systemic lupus erythematosus, sustained hypertension, and an adrenal mass. Computed tomography guided fine needle aspiration cytology of the mass revealed CP with elements of neuroblastoma. We report this case because of its rarity.

Key words: Composite pheochromocytoma, fine needle aspiration cytology, neuroblastoma, pheochromocytoma, systemic lupus erythematosus

INTRODUCTION

Pheochromocytoma is an uncommon tumor arising from catecholamine producing cells of the adrenal medulla.[1] Extra adrenal pheochromocytoma is known as paraganglioma. Composite pheochromocytoma (CP), a rare tumor of the adrenal medulla, typically consists of a predominant pattern of pheochromocytoma combined with ganglioneuroma, ganglioneuroblastoma, neuroblastoma or rarely, other components such as malignant peripheral nerve sheath tumor and neuroendocrine carcinoma. The frequency of composite adrenal tumors has been reported as ranging from <3% of all adrenal gland neoplasms to between 1% and 9% of pheochromocytomas.[2] So far, around 70 cases have been reported in the literature, most of which were located in the adrenal glands. Occasional cases with extra-adrenal involvement have also been reported.[3]

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CASE REPORT

A 27-year-old hypertensive female with history of systemic lupus erythematosus (SLE) was referred to DKM Diagnostic Centre, Jhothwara, Jaipur, Rajasthan for computed tomography (CT) assisted fine needle aspiration cytology (FNAC) of a left sided adrenal mass. CT abdomen showed a solid space occupying lesion in the left adrenal gland. CT guided FNAC was done using 22 gauge spinal needle, which yielded blood mixed particulate material. The smears were fixed in 100% methanol and stained with hematoxylin and eosin.

Microscopic examination revealed cellular smears with a bimodal population of cells. One population of cells showed dispersed and loosely clustered arrangement, at places forming semilunar rows of cells. These cells had indistinct cell borders with abundant cytoplasm and round to oval nuclei with bland chromatin. Another cell population showed sheets of small blue round cells at places forming rosettes. These cells had scanty cytoplasm and round hyperchromatic nuclei. A provisional diagnosis

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of CP – neuroblastoma was made and the patient was subjected to further relevant investigations. A 24 h urine sample of the patient revealed raised metanephrine and vanillylmandelic acid. Rest of the parameters were within normal limits. A core biopsy was taken from the mass and sent for immunohistochemistry to confirm the diagnosis. The areas with pheochromocytoma showed positivity for chromogranin A and synaptophysin and the areas with neuroblastoma showed positivity for CD56, chromogranin A, and synaptophysin.

DISCUSSION

Pheochromocytoma, also known as paraganglioma of the adrenal medulla, is a tumor arising from the catecholamine producing cells in the adrenal medulla. Pheochromocytoma is also known as the "10% tumor." This is because around 10% of all pheochromocytomas are bilateral, 10% are extra-adrenal, 10% occur in children, and 10% are malignant. Pheochromocytoma arising in extra-adrenal sites is known as paraganglioma. Various extra-adrenal sites from where pheochromocytoma can arise include the organ of Zuckerkandl, the preaortic region in the abdomen and the wall of urinary bladder.[1]

Neuroblastoma is a type of neuroblastic tumor which in turn is a childhood embryonal tumor of the adrenal medulla. Depending on the grade of neuroblastic differentiation and the degree of schwannian stroma, neuroblastic tumors are designated as: (1) Neuroblastoma (poor schwannian stroma); (2) ganglioneuroblastoma, intermixed (rich schwannian stroma); (3) ganglioneuroblastoma, nodular (composite schwannian stroma-rich/stroma-dominant and stroma-poor) and (4) ganglioneuroma (dominant schwannian stroma). Thus neuroblastoma is the most immature among all the neuroblastic tumors.[1,4]

Composite pheochromocytoma refers to a pheochromocytoma that has a component resembling neuroblastoma, ganglioneuroblastoma, ganglioneuroma or even a malignant peripheral nerve sheath tumor.[5]

The origin of CP may be attributed to disturbance in migration or maldevelopment of the neural crest resulting in the development of composite tumors.[6]

Composite pheochromocytomas are rare with <70 reported cases so far. In the majority of the reported cases, the tumor was located in the adrenal glands, as was seen in our case. Few cases with extra-adrenal CP have also been reported.

The age range of patients in the previously reported cases was from 5 to 82 years with the majority of patients being 40–60 years in age. Males and females were found to be affected equally.[2] Our patient was a 27-year-old female which was in accordance with the age range of the previously reported cases.

Composite pheochromocytoma, very much like ordinary pheochromocytoma, is a functional tumor. Most patients with clinically active pheochromocytoma present with classical symptoms of headache, palpitation, and excessive perspiration. In addition to these, hypertension (either sustained or paroxysmal) is another cardinal feature of functional pheochromocytoma.[6] Various authors have stated that the frequency of hypertension in pheochromocytomas is 72.4%, while that of sustained hypertension is only 47.9%.[7] In the present case, the patient presented with sustained hypertension.

Among the reported cases of CP, around 71% cases had elements of ganglioneuroma mixed with pheochromocytoma. This was not in accordance with our case which showed elements of neuroblastoma with pheochromocytoma.[2]

Association of SLE with pheochromocytoma has been reported in few cases. Lin *et al*. reported a case of SLE associated with pheochromocytoma where there was resolution of SLE upon removal of the tumor.[8] Wu *et al*. in their case report concluded that pheochromocytoma can be a cause of hypertension in SLE.[9]

Fine-needle aspiration cytology of pheochromocytomas is usually contraindicated in view of the risk of precipitating a hypertensive crisis. However, this complication occurs only rarely as per the literature.[10]

CONCLUSION

Composite pheochromocytomas are rare mixed tumors of the adrenal glands with few reported cases so far. Association of SLE with CPs is still rare. The rarity of these tumors can be attributed to under-recognition or under-reporting of these tumors. Clinical features of CPs are similar to that of ordinary pheochromocytomas, but little is known about the biologic behavior, outcome or molecular genetic profile.

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