Paraganglioma associated with neuroblastoma: rare composite tumor in a 16-year-old girl

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Abstract

Composite pheochromocytomas are very rare and account for only 3% of both adrenal and extraadrenal pheochromocytomas. We report herein a case of 16-year-old girl with tumor of the retroperitoneal space. In her history she had episode of circulatory-respiratory collapse with pulmonary oedema during induction to general anaesthesia. Diagnosis from microscopic examination was unclear: paraganglioma in specimens obtained by core needle biopsy; neuroblastoma in material from open tumor biopsy. Preoperative imaging and scintigraphic studies as well as laboratory tests did not allowed to distinguish between paraganglioma and neuroblastoma. Preoperative studies have not shown any metastasis; the tumor size did not decrease after 4 courses of chemotherapy for neuroblastoma. After preoperative preparation with phenoxybenzamine patient underwent surgical removal of the tumor. Histopathologic study revealed paraganglioma with extensive areas of fibrosis. Patient remains disease free in 2 years follow up. In case of composite pheochromocytomas/paragangliomas an adequate preoperative diagnosis is not always possible using clinical, laboratory and imaging studies. In particular cases, even histopathologic examination of the biopsy specimen did not allow to establish firm diagnosis.

Key words: composite paraganglioma, pheochromocytoma-neuroblastoma

Introduction

Composite pheochromocytomas are very rare and account for only 3% of both adrenal and extraadrenal pheochromocytomas [1]. These tumors contain a ganglioneuroma or less frequently a ganglioneuroblastoma component. Children with composite pheochromocytomas according to the literature tended to be older than patients with classical pheochromocytoma, and the tumors were mainly functional (catecholamine secreting) [5]. Some of these cases were associated with neurofibromatosis and multiple endocrine neoplasia [1, 8]. Extraadrenal paraganglioma is rare in the pediatric po-
population and occur mostly in older children and adolescents [12]. We report herein a rare case of 16-year-old girl with a composite tumor (paraganglioma with neuroblastoma component) located in the retroperitoneal space.

**Case report**

A 16-year-old girl was referred to the Department of Oncology in Szczecin, Poland for the treatment of the retroperitoneal tumor. She had 2-year history of periodic, recurrent abdominal pain managed with spasmytic agents. She did not have any additional complaints. On physical examination she was in good general condition, antropometrically presenting short height, and slightly disturbed body proportions (long body corpse and short extremities) similar to her mother. Her blood pressure and glycemia was normal, she did not have any episodes of vomiting, hypertension, or tachycardia. On physical examination there was an ill-defined, slightly tender, non-movable mass over the left side of her abdomen. Abdominal ultrasonography revealed left paraspinal mass, with intensive vascularity and mixed echogenicity. Fine needle aspiration biopsy detected atypical cells. Contrast enhanced computed tomography of the abdomen revealed a left retroperitoneal tumor (65 mm × 46 mm × 90 mm) below the pancreatic tail, attached to aorta and reaching aortic bifurcation. The mass was well defined, good vascularized, a pressure effect on the left iliopsoas muscle and lower pole of the left kidney was seen. The tumor displaced left renal, splenic and lower mesenteric vessels. There was no extension in the vertebral foramina (Fig. 1A, Fig. 1B).

During induction to general anaesthesia, she had an episode of circulatory-respiratory collapse with pulmonary oedema. Using epidural analgesia, core needle biopsy of the tumor was performed, and the specimen was delivered for hematoxylin/eosin staining as well as for immunohistochemical studies. These studies were performed with commercially available antibodies (S-100 protein, chromogranin, synaptophysin, MIB-1, NSE and vimentin) and according to standard protocols. Pathological studies of the tumor revealed paraganglioma.

In further diagnostic evaluation Metaiodobenzyl guanidine I 131 scintigraphy (MIBG) revealed uptake only within the tumor in left mid-abdomen with no metastasis. Laboratory data included urine catecholamine metabolites revealed increased level of vanilmandelic acid (VMA) (15.2 – 16.1 mg/24 h, N: 0.41 – 3.74). Based on these findings, pheochromocytoma or neuroblastoma was suspected. Open tumor biopsy was performed and histological evaluation revealed neuroblastoma (Fig. 2A, Fig. 2B). N-myc was not amplified in the molecular study of the tumor sample. Treatment with combination chemotherapy was executed (PACE protocol for III stage neuroblastoma: 4 preoperative cycles of vincristine, doxorubicin, cyclophosphamide and cisplatin). Tumor response for oncological treatment was judged as negative. Tumor size remained unchanged; whereas significant decrease of previously elevated level of VMA in 24-hour urine collection was noted (8.6 mg/24 h vs 15.2 mg/24 h).

Patient was referred to the Department of Pediatric Surgery, Collegium Medicum in Bydgoszcz, for the surgical treatment. After 3-week preoperative preparation with phenoxybenzamine patient underwent surgery. Transperitoneal approach was used for the complete removal of the tumor. Macroscopically tumor displayed hemorrhagic areas. Histo-pathologic study revealed paraganglioma with extensive areas of fibrosis (Fig. 3A, Fig. 3B). There was no perioperative and postoperative complications. In 2 years follow up patient remains free of disease.

**Discussion**

Composite pheochromocytomas – ganglioneuro (blasto) mas are rare composite tumors of both adrenal and extra-adrenal pheochromocytomas [6]. Other non-pheochromocytomas – ganglioneuro (blasto) mas are rare composite tumors of both adrenal and extra-adrenal pheochromocytomas [6].
Cytoma components have been also reported [2,3,7,10]. Such type of pheochromocytoma is designated “composite” or “mixed”, depending whether the pheochromocytoma and non-pheochromocytoma components show the same embryonic origin [4]. Pediatric composite pheochromocytomas associated with neuroblastomatous elements are very rare [8]. According to the fact that these tumors exhibit areas of divergent differentiation, the diagnosis of can be complicated. Yoshimi et al described pathological features of composite pheochromocytoma-ganglioneuroma. Histologically, the two components of this tumor were minimally admixed with abrupt transition [13]. In other reported case, Pytel et al have described intimately admixed areas of ganglioneuroma and paraganglioma and this histomorphological finding allowed to proper diagnose composite paraganglioma [9]. One can conclude that histology of composite tumors may vary in each case. According to literature pheochromocytoma component in composite tumors is usually predominant [5]. To avoid the misdiagnosis of concomitant histological pattern in composite tumor, it is essential to adequately sample the tumor specimen. In case of composite tumors, the most challenging situation for pathologist, is when multiple histological patterns are present in the same tumor, and when there is limited amount of tissue available for evaluation (such as core needle biopsy). For these reasons authors reevaluated microscopic specimens obtained from the tumor by open biopsy (Fig. 2A, Fig. 2B). Surprisingly, one of three independent pathologists (all from reference centers) recognized in examined specimens only paraganglioma, but not with neuroblastoma components as was done by the others. This could illustrate problems in equivocal judgement of histomorphological studies in case of rare tumors when multiple histological patterns are present in the same tumor.

Further problems which are arising is that because of the rarity, adjuvant therapy standards and final outcomes for
composite pheochromocytomas / paragangliomas with neuroblastoma component yet has not been well established. Nakagawara et al suggested that the metastatic pattern is defined by the major component of tumor; one can ask the question if the tumor would not metastasize to the other organs, even if the foci of neuroblastoma are small [8]. In our case, although preoperative evaluation did not reveal any signs of metastatic disease, the suspicion of neuroblastoma really existed and chemotherapy protocol for neuroblastoma component was administered. After complete surgical resection of the tumor our patient did not demonstrate any signs of disease recurrence in 2 year follow up.

Conclusions

We can conclude, that in case of composite pheochromocytomas / paragangliomas an adequate preoperative diagnosis is not always possible using clinical, laboratory and imaging studies. In particular cases, even histopathologic examination of the biopsy specimen did not allow to establish firm diagnosis. Composite or mixed tumors in children are rare and difficult to diagnose and treat. In these cases good communication between specialists involved in diagnostics and the treatment of the patient (surgeon, oncologist, radiologist and pathologist) is required.

References