Peripheral Primitive Neuroectodermal Tumor with Neuronal and Glial Differentiation : Report of a Case Arising in Suprarenal Region

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Abstract

It is well known that embryonal neuroectodermal tumors of the central nervous system (CNS) not infrequently display varying amount of neoplastic cells acquiring glial differentiation. In contrast, glial differentiation rarely occurs in primitive neuroectodermal tumors outside the CNS being documented in less than ten cases. The author presents herein a case of peripheral primitive neuroectodermal tumor with prominent glial differentiation identified by the presence of glial fibrillary acidic protein (GFAP) arising in the right suprarenal region of a 32-year-old man, histologically indistinguishable from an ordinary neuroblastoma.

Key word : Primitive Neuroectodermal Tumor, Neuroglial Differentiation, Suprarenal Region

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Embryonal neuroectodermal tumor or primitive neuroectodermal tumor (PNET), a collective term for small cell poorly differentiated neoplasms thought to arise from primitive neuroepithelium can occur in or outside the CNS. In the CNS, the classification issued by WHO encompassed a broad spectrum of tumors displaying variation in type and degree of differentiation[1]. Glial differentiation is not uncommon. It was reported to be approximately 30 to 60 per cent in studies mainly based on medulloblastomas[2-4], present in 9 of 10 supratentorial PNETs in one study[5], and documented in a variety of embryonal neuroectodermal brain tumors[6-8] and some rare non-categorized neoplasms[9-11]. Glial differentiation in CNS Embryonal neuroectodermal tumor is particularly interesting among the other lines of diffentiation because it was shown to be a potentially significant prognostic parameter[2]. In contrast, a collection of primitive neuroectodermal tumors outside the CNS including neuroblastoma, peripheral primitive neuroectodermal tumor (PPNET) or malignant

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peripheral neuroectodermal tumors, and Ewing's sarcoma display glial diferentiation in very rare instances, to the best of my knowledge, being documented in only 9 cases[12,13-17] and even less if cases with very focal GFAP positivity are excluded. The author presents herein a case of peripheral primitive neuroectodermal tumor with prominent glial differentiation identified by the presence of glial fibrillary acidic protein (GFAP) arising in the right suprarenal region of a 32-year-old man, histologically indistinguishable from an ordinary neuroblastoma.

CASE REPORT

A 32-year-old man experienced right upper quadrant abdominal discomfort for 5 months. Computerized topographic scan revealed an hypodensity mass in right upper quadrant with attachment to the sixth segment of liver, right adrenal gland and inferior venacava with compression to upper half of the right kidney. En-bloc hepatic segmentectomy and right nephrectomy with tumor removal were performed.

Pathologic examination

The mass, measuring 15 x 13 x 10 cm is encapsulated and located anterior to and compresses the upper half of the right kidney. A portion of liver tissue is attached to the mass. Both the liver tissue and the right kidney can be separated from the mass without any invasion by the tumor. Adrenal gland tissue is not seen around the tumor. Sections of the tumor show variegated whitish yellow, grayish and dark reddish soft friable cut surfaces. Microscopically (Fig. 1A), there is dense aggregation of small round cells, mingled with irregular areas of fibrillary matrix and occasional Holmer-Wright pseudorosettes. The tumor cells possess hyperchromatic nuclei and ill-defined scanty cytoplasm. High mitotic rate and frequent patchy necrosis are observed. Immunohistochemical study (Fig. 1B-D) reveals strong GFAP positivity in scattered isolated tumor cells and more frequently in the tumor cells around fibrovascular stroma. Neurofilament is expressed in rare tumor cells, whereas, synaptophysin is diffusely expressed.

DISCUSSION

The current small round blue cell tumor was histologically similar to neuroblastomas in that it showed fibrillary matrix of varying size and Holmer-Wright pseudoresettes. However, the rosette-like structure was observed in PPNET, exceptional case of Ewing's sarcoma and variety of non-neuroepithelial related small round cell tumors[18]. The current tumor was not regarded as extraskeletal Ewing's sarcoma because it showed significant degree of neuronal and glial differentiation. Although a neuroblastoma, a tumor of primitive neuroblasts of sympathetic ganglia and adrenal medulla can occur in adult life[19], the presence of prominent GFAP positivity, which identifies glial differentiation in addition to neuronal differentiation precludes the diagnosis of adult neuroblastoma. Therefore, peripheral primitive neuroectodermal tumor with neuroglial differentiation was the most appropriate diagnosis.

When difficulty is encountered in distinguishing between neuroblastoma and PPNET, ancillary methods can be useful. Cytogenetic evidences show that PNET and Ewing's sarcoma share (11; 22)(q24; q12) chromosomal translocation whereas neuroblastomas do not but instead usually possess characteristic 1p deletion. In addition, the expression of MIC-2 gene product as detected immunohistochemically by antibody O13 (HBA71, CD99) has been identified as a relatively specific marker of Ewing's sarcoma and PPNET but not of classic neuroblastoma[18].

PPNET with glial differentiation is very rare. The available documented sites included uterus [14], soft tissue of the neck[15] and skin[16]. More rarely, it may occur in association with malignant mesenchymal tumor[13]. The paravertebral location of the current tumor has not been previously described and is the typical location of neuroblastoma. In practice, due to the rarity of glial differentiation in PNETs outside the CNS, GFAP immunostaining is frequently omitted when small round blue cell tumors are suspected for PPNET and neuroblastoma are encountered. Therefore, some cases of PPNET with glial differentiation could have been missed, especially for those occurring in the paravertebral region. The current case reveals that prominent glial differentiation can take place even in a tumor without any clue towards glial differentiation.

The author presented the suprarenal region as the location of the tumor not to commit whether the tumor originated in the adrenal gland or not, since no adrenal gland tissue was found on gross examination. In regard to the cell of origin, the tumor

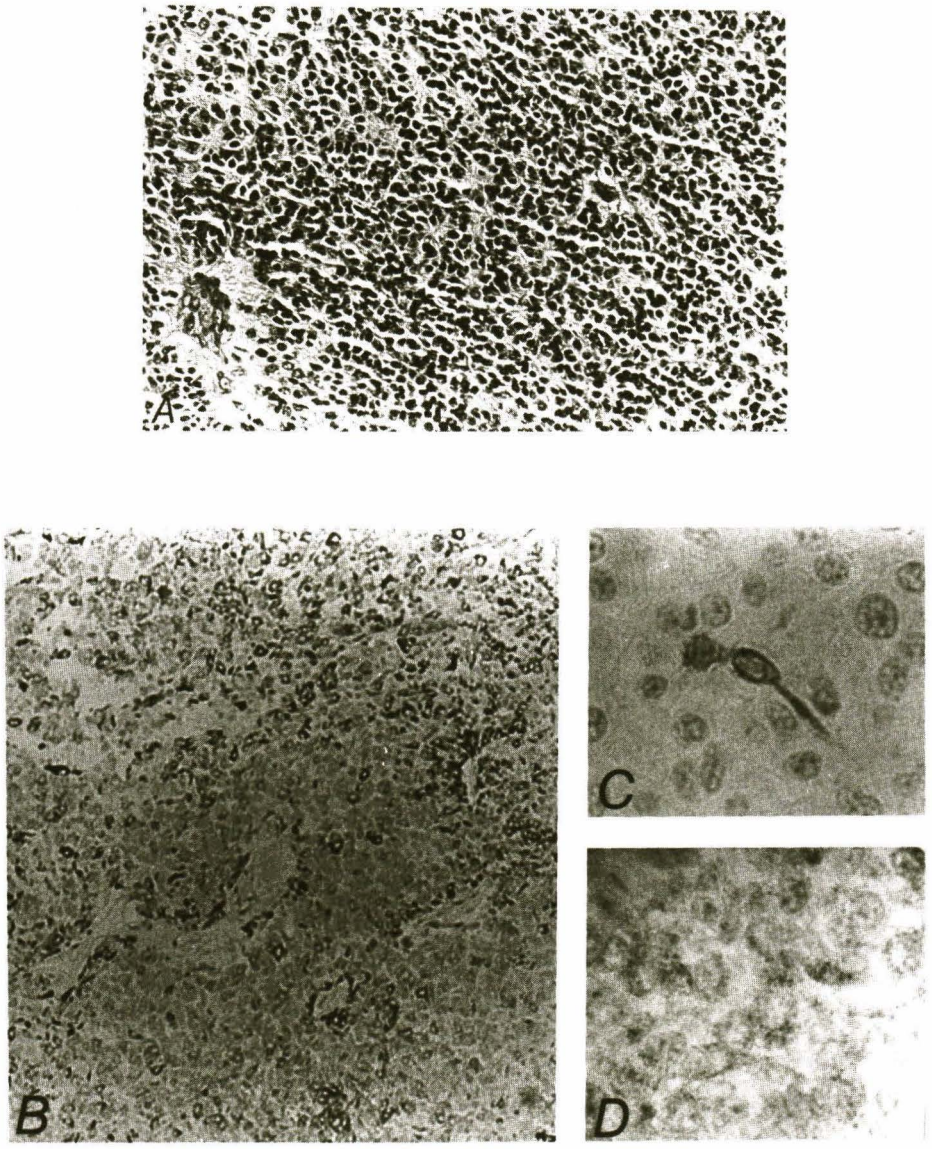

Fig. 1. **A: Dense aggregation of small round cells, mingled with irregular zone of fibrillary matrix and occasional Holmer-Wright pseudorosettes, B: Strong GFAP positivity in scattered isolated tumor cells with predilection for the tumor cells around fibrovascular stroma, C: Neurofilament positivity in rare tumor cells, D: Synaptophysin positivity in diffuse granular pattern.**

was suspected to have originated from neural crest derivatives in suprarenal region, including adrenal medulla, extraadrenal paraganglion system and aortico-sympathetic autonomic system situated along side the abdominal aorta. The occurrence of glial differentiation is explained by the fact that neural crest cells are derived from primitive neuroepithelium, which has the capability to differentiate into a variety of cell types, including glial cell. However, the basis of why glial differentiation in peripheral PNET is much less frequent than CNS PNET is not known. This could be attributed to the difference in differentiation potential between neural crest cells and neural tube cells in that, during

embryonic development, the neural crest cells do not give rise to glial cells like the neural tube cells do[20].

Finally, whether PPNET with neuroglial differentiation behaves differently from a neuroblastoma and PPNET with only neuronal differentiation or not at present is unknown. If we are aware of this type of neoplasm, more cases will be collected, and the issue may become clearer in the future.

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มะเร็งชนิด พริมิทิฟ นิวโรเอกโตเดอมัล นอกระบบประสาทส่วนกลาง มีพัฒนาการของเซลล์ ทางเซลล์ประสาทและเซลล์เกลีย : รายงานผู้ป่วย 1 ราย เกิดบริเวณเหนือไต

*ชวิษฐ์ จันทรานุวัฒน์, พ.บ.**

เป็นที่ทราบกันดีว่า มะเร็งชนิดเอมบริโอนัล นิวโรเอกโตเดอมัล ของระบบประสาทส่วนกลาง จำนวนไม่น้อยมีพัฒนาการของเซลล์ไปทางเซลล์ประสาทและเซลล์เกลีย อย่างไรก็ดี สำหรับมะเร็งชนิด พริมิทิฟ นิวโรเอกโตเดอมัล นอกระบบประสาทส่วนกลาง พบว่ามีพัฒนาการของเซลล์ไปทางเซลล์เกลียน้อยรายมาก มีรายงานปรากฏอยู่น้อยกว่า 10 ราย ผู้รายงาน ได้นำเสนอผู้ป่วยมะเร็งชนิด พริมิทิฟ นิวโรเอกโตเดอมัล นอกระบบประสาทส่วนกลาง เกิดบริเวณเหนือไตข้างขวาของผู้ป่วยชาย อายุ 32 ปี มีพัฒนาการของเซลล์ไปทางเซลล์ประสาทและเซลล์เกลีย จากการพบเกลียฟริบริลลารี แอซิดิก โปรตีน โดยมีพยาธิสภาพทางกล้องจุลทรรศน์ที่ไม่สามารถแยกได้จาก มะเร็งชนิด นิวโรบลาสโตมา

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