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Peripheral Neuroblastoma of the Ulnar Nerve : Diagnosis by Fine Needle Aspiration Cytology

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= Abstract =

A 30-year-old woman who was diagnosed as peripheral neuroblastoma by fine needle aspiration of a soft mass of the right upper arm is described. She presented a slowly growing, soft mass of the right upper arm for 1 month. The right humerus revealed no abnormal finding on X-ray. Ultrasonogram of the right upper arm revealed a well demarcated, smooth marginated solid mass without invasion of adjacent structures. Fine needle aspiration was done under the impression of soft tissue tumor with undetermined biologic behavior. The aspirates were highly cellular and the tumor cells were dispersed both singly and in clusters of varying size. The clusters occasionally showed a central capillary core and rosette-like structures. The tumor cells were small in size and had a small to medium amount of cytoplasm. Some of them revealed slender cytoplasmic processes. The nuclei showed distinct nuclear membranes, finely clumped chromatin and small conspicuous nucleoli. Cellular pleomorphism or mitotic figure was not definite. These cytologic findings were interpreted as a malignant, non-lymphomatous, small round cell tumor, most likely representing peripheral neuroblastoma or Ewing's sarcoma. Final diagnosis was confirmed by simple excision as peripheral neuroblastoma.

Key words : Peripheral neuroblastoma, Ulnar nerve, Aspiration cytology

Introduction

Peripheral neuroblastoma is an uncommon malignancy arising in widely disparate anatomic sites. Although the tumor in many cases occurs in association with peripheral nerves, it may lack any discernible anatomic relationship to peripheral nerves. Histologically, peripheral neuroblastoma presents as a small round cell malignant

tumor with various appearances. It may be confused with other small round cell malignant tumors, such as embryonal rhabdomyosarcoma, extraskeletal Ewing's sarcoma, metastatic neuroblastoma, undifferentiated small cell carcinoma and malignant lymphoma[1]. Features of differential diagnostic value include formation of Homer-Wright rosettes and/or Flexner rosettes and the immunohistochemical demonstration of neuron-specific enolase (NSE) within the tumor cells and the ultrastructural demonstration of neurosecretory granules in the tumor cells.

The aspirates of peripheral neuroblastoma show small round malignant cells with occasional rosette-like structures, a central capillary core and slender cytoplasmic processes[2]. The tumor cells are so undifferentiated that differential diagnosis from other lesions with similar cytologic features was difficult. But diagnosis is possible when the rosette-like structure, the central capillary core and slender cytoplasmic processes are noted.

To the best of our knowledge, this paper reports the second case in the English literature in which the diagnosis was initially suggested by fine needle aspiration cytology on peripheral neuroblastoma.

Case Presentation

A 30-year-old woman presented a slowly growing mass of the right upper arm for 1 month. On physical examination, a soft movable mass with tenderness was noted in the anteromedial side of the right upper arm, measuring 5 cm in diameter. X-ray of the right humerus showed no abnormal finding. The ultrasonogram of the right upper arm showed a well demarcated, solid mass with smooth margin and without invasion of adjacent structures (Fig. 1). The results of other laboratory studies were within normal limits. Fine needle aspiration (FNA) of the mass revealed cytologic findings consistent with peripheral neuroblastoma. A few days later a simple excision with axillary lymph node dissection was done.

Cytologic and Histologic Findings

The aspirates from the right upper arm mass had a tendency to stick to the slide as a thick layer of cell clusters from which numerous aggregated and single tumor cells detached to fill the spaces in between. The tumor cells were seen both singly and in clusters of varying size (Fig. 2). They were round to oval in shape, small in size, and had a small to medium amount of cytoplasm (Fig.

Fig. 1. The right humerus X-ray reveals a well demarcated mass of soft tissue.

Fig. 2. The tumor cells are seen both singly and in clusters of varying size in clean background (Papanicolaou, ×40).

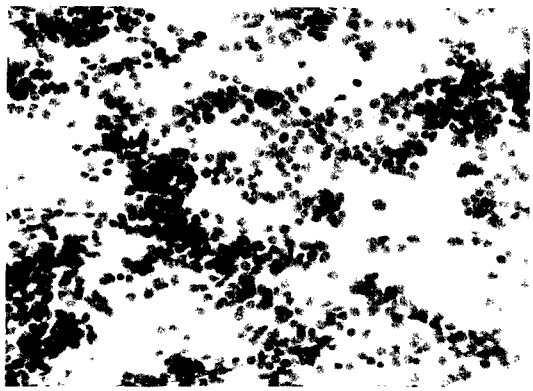

Fig. 3. The tumor cells are monotonous, round to oval in shape, small in size and have a small amount of cytoplasm (Papanicolaou, ×200).

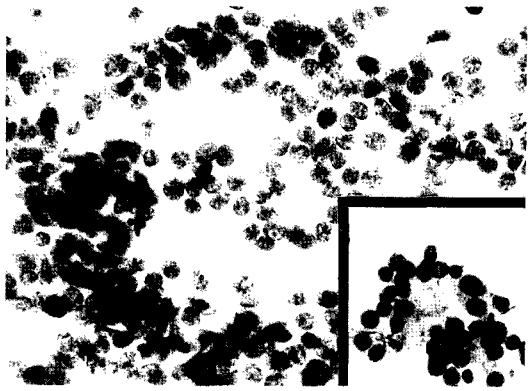

Fig. 4. The clusters of tumor cells occasionally show a central capillary core. Some of the tumor cells display slender cytoplasmic processes. Inset shows rosette-like structure, containing fibrillary material in the center (Papanicolaou, ×400).

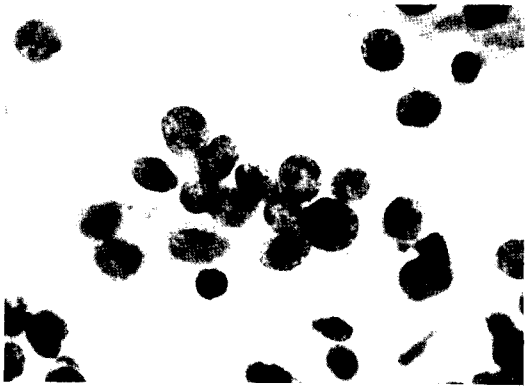

Fig. 5. High-power photomicrograph showing round to oval nuclei with finely clumped chromatin and prominent nucleoli (Papanicolaou, ×1,000).

3). The clusters occasionally showed a central capillary core and rosette-like structures. The center of these rosettes contained weakly cyanophilic fibrillary material. Some of the tumor cells displayed slender cytoplasmic processes (Fig. 4). The cytoplasm stained weakly cyanophilic with the Papanicolaou stain. The cytoplasmic borders were ill defined. The nuclei showed slight variation in size and shape and exhibited finely clumped chromatin. The nuclear membranes were distinct, and small conspicuous nucleoli were present (Fig. 5). Mitotic figure was not definite. These cytologic findings were interpreted as a malignant small cell, nonlymphomatous tumor, most likely representing Ewing's sarcoma or peripheral neuroblastoma.

The excised specimen of the arm mass included a segment of the ulnar nerve. The ulnar nerve segment measured 4.0 cm in length. The nerve trunk was deformed by a fusiform tumor, measuring 5.0 cm in length and 3.7 cm in diameter. The surface was relatively smooth. The cut sections revealed a grayish-white firm surface, homogeneous to lobulated. At the distal aspect of the fusiform mass the nerve trunk emerged. The tumor was present within the epineural sheath (Fig. 6). Microscopic examination revealed some fields which showed segments of relatively intact nerve fibers surrounded by a highly cellular primitive-appearing neoplasm (Fig. 7). Other fields consisted of sheets of closely packed small cells arranged in a lobular pattern with interspersed thin fibrovascular stroma. The tumor cells were relatively uniform and small with poorly defined borders and scanty to imperceptible cytoplasm. The nuclei of the tumor cells were round to oval and contained dense chromatin and indistinct nucleoli. There were scattered mitotic figures. The most significant diagnostic feature was the presence of numerous rosettes. The center of these rosettes contained tangled fibrillar material. These rosettes were interpreted as being distinctive of the Homer-Wright type (Fig. 8). Some of the tumor cells contained diastase-digested periodic acid-Schiff material, presumably glycogen. Immunohistochemical study for neuron-specific enolase (NSE) was weakly positive and for S-100 protein was negative. Ultrastructurally, the well preserved tumor tissue, fixed

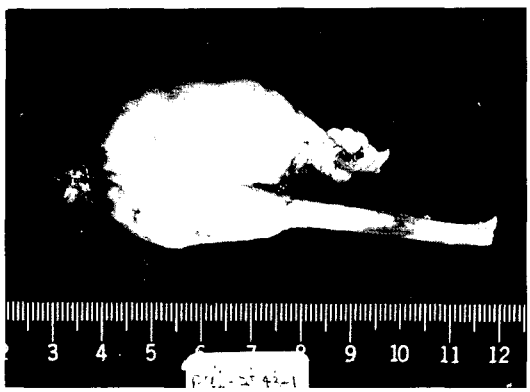

Fig. 6. The tumor includes a segment of the ulnar nerve. The nerve trunk is deformed by a fusiform tumor, measuring 5.0×3.7 cm. The surface is relatively smooth. The cut surface reveals whitish-gray, firm and homogeneous to lobulated appearance.

Fig. 7. A segment of relatively intact nerve fiber surrounded by a highly cellular primitive-appearing neoplasm with a scanty stroma (H&E, ×40).

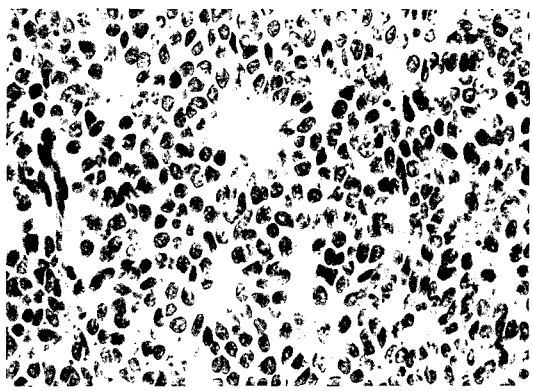

Fig. 8. Typical Homer-Wright rosettes with central fibrillary tangles are evident (H&E, ×400).

in glutaraldehyde solution, showed long cytoplasmic projections, forming complex interdigitations with neighboring cells and small membrane bound electron dense granules, measuring 150-250 nm, in the periphery of the cells and in cytoplasmic extensions.

Discussion

Peripheral neuroblastoma (malignant neuroepithelioma) is a rare soft tissue neoplasm. In 1918, Stout[3] first described a primitive neuroectodermal tumor with rosettes arising in association with the ulnar nerve. Peripheral neuroblastoma arises from a peripheral nerve, but this relationship cannot always be established. Most cases occur in the second and third decades of life and have no gender predisposition. The lower extremities are most commonly involved. The presence of a mass is the most common clinical complaint and is associated with pain in approximately one half of the cases. The tumor does not arise from the sympathetic nervous system. There is no increased tendency for these tumors to occur in patients with von Recklinghausen's disease. With rare exceptions peripheral neuroblastomas have not been associated with an elevated catecholamine level[4].

Microscopically, peripheral neuroblastoma belongs to the group of small round cell malignant tumors that include embryonal or alveolar rhabdomyosarcoma, extraskeletal Ewing's sarcoma, metastatic lesion of classical neuroblastoma, undifferentiated small cell carcinoma, malignant lymphoma, and granulocytic sarcoma. In children younger than the age of five years, the tumor must be differentiated from a metastatic neuroblastoma by thorough clinical examination. In adolescent and adults the tumor must be distinguished from other small round cell malignant tumors[1]. Careful analysis of the morphologic features indicating differentiation of the tumor cells at the light microscopy level allows a precise classification in a considerable number of small round cell malignant tumors except metastatic neuroblastoma and Ewing's sarcoma. The FNA cytologic features of peripheral neuroblastoma was first described by Neuhold et al in 1989[2]. In peripheral neuroblastoma the aspirates show occasional rosette-like structure, a central capillary core and slender cytoplasmic processes[2, 5]. In embryonal or alveolar rhabdomyosarcoma the tumor cells are less uniform and show eccentric irregular hyperchromatic nuclei and dense cytoplasm with distinct round contours of rhabdomyoblasts[5]. In small cell carcinoma the nuclei of tumor cells are more variable in size, contour and configuration. Nuclear molding, coarsely textured chromatin, irregular nuclear margins and pyknosis are usually present. The cytoplasm is disintegrated. In malignant lymphoma, there is considerable variation of cell morphology within each subclassification. But generally the nuclei have a more central position in the cell with irregular nuclear membrane and the cytoplasm is more scanty and round in contour. The cells are singly dissociated and never form aggregates. Molding or necrosis is not seen. In granulocytic sarcoma, the blastic cells shed cytoplasmic fragments in both acute myeloblastic and lymphoblastic leukemia, but the clinical picture is decisive[6]. However, in some aspirates of these tumors no specific diagnosis of the tumor type is possible because no traces of differentiation at the light microscopy level are visible. Morphologically, the tumor cannot be distinguished from a classic neuroblastoma and Ewing's sarcoma. In such cases, final classification of

the tumor must wait until surgical biopsy provides more material for histopathologic examination, including special stains.

A few recent studies have shown that small round cell malignant tumors may be diagnosed effectively when the aspirated material from these tumors is studied by both light microscopy and electron microscopy[7, 8]. However, the ultrastructural observations in that case helped only to exclude other small round cell malignant tumors ; it failed to reveal the neuroectodermal derivation of the tumor since neither microtubules nor neurosecretory granules were detected. This may be due to the relatively small amount of aspirated material available for ultrastructural studies.

It has been shown that the accuracy of cytologic diagnosis can be increased by using immunocytochemistry as an adjunct to routine cytologic procedures. In particular, the use of NSE and antibodies to intermediate filaments has been reported to provide diagnostically meaningful information that can improve the accuracy of the differential diagnosis of small round cell malignant tumors[9~12]. Like classical neuroblastomas, they are positive for NSE which helps in differentiating them from Ewing's sarcoma[10~12]. The presence of vimentin in the tumor cells distinguishes peripheral neuroblastoma from classic neuroblastoma, which is negative for vimentin[11]. Other small round cell malignant tumors can be ruled out by the negative staining for desmin (poorly differentiated rhabdomyosarcoma) and the absence of labeling of the tumor cells with Leu-5 antibody (metastases of small cell anaplastic carcinoma and Merkel cell tumor 2).

Thus the accuracy and sensitivity of the FNA diagnosis of small round cell malignant tumors can be enhanced by a combined light microscopy, electron microscopy and immunocytochemical study of the aspirate. The value of an immediate microscopic assessment of FNA is emphasized, whereby it is possible to select the cases that require the use of additional diagnostic techniques.

Clinically, the tumor is a highly aggressive neoplasm and generally refractory to therapy and lethal within 6 months to 5 years of diagnosis[13]. Metastases are not usually present at the time of diagnosis, but the tumor rapidly gives rise to metastatic lesions in the lung, lymph nodes, central nervous system, liver, and bone[13, 14]. Radiation therapy alone has shown poor responses[14, 15]. The use of chemotherapy alone or in conjunction with radiation therapy has been more efficacious, but in all cases the tumor has recurred. Surgical excision plus systemic chemotherapy constitutes a rational clinical approach to tumors of this kind[13].

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= 국문초록 =

척골신경에 발생한 말초성 신경아세포종

-세침흡인 세포검사로 진단된 1 례 보고-

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주 영 채 · 김 준 미

말초성 신경아세포종은 예후가 나쁘고 희귀한 종양으로 이 종양의 세침흡인 세포학적 소견에 관한 보고는 세계 문헌상 1988년 Neuhold에 의해 처음 기술된 1 례가 있을 따름이다.

최근 저자들은 30세 여자의 우측 상박의 연부조직 종괴로 부터 세침흡인 세포검사를 시행하여 진단된 말초성 신경아세포종을 경험하여 그 세침흡인 세포학적 소견을 기술하는 바이다. 환자는 1 개월전 부터 우측 상박에 서서히 자라는 종괴를 주소로 내원하였다. 우측 상박 X-선 및 초음파 촬영술에서 주위와 잘 경계지어진 방추형의 연부조직 종괴가 관찰되었고 주변조직으로 침윤하는 소견은 관찰할 수 없었으며 상완골은 정상이었다. 종괴의 세침흡인 도말은 세포밀도가 매우 높았고 작고 둥근 세포들이 뭉쳐있거나 산재되어 있었다. 세포간의 크기나 모양의 차이는 아주 미약하였고 유사분열은 거의 관찰되지 않았다. 종양세포들의 집단은 간혹 모세혈관을 중심으로 뭉치거나, 로제트 형태를 보이며 그 세포질은 가늘고 긴 돌기를 보였다. 핵은 뚜렷한 핵막과 미세하게 뭉친 염색질 및 작고 뚜렷한 핵소체를 갖고 있었다. 이상의 소견은 작고 둥근 세포로 된 악성 종양 중 말초성 신경아세포종에 매우 합당하였으나 골외 Ewing 육종과의 감별은 불가능하였다. 단순 절제술이 시행되었고 종양은 조직학적으로 말초성 신경아세포종임이 확인되었다.