Pigmented Epithelioid Melanocytoma
-A Case Report-

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Heavily pigmented epithelioid melanocytic tumors are rare. They include epithelioid blue nevus with or without Carney complex, epithelioid combined nevus, and the recently described pigmented epithelioid melanocytoma. Despite histologic similarities, these lesions have varying clinical courses, ranging from benign indolent lesions to tumors that metastasize. We report a case of pigmented epithelioid melanocytoma in a six-year-old girl who had no symptoms or signs of Carney complex. No malignancy was detected by clinical evaluation. (Dermatol Sinica 24: 67-71, 2006)

Key words: Pigmented epithelioid melanocytoma, Epithelioid blue nevus, Carney complex, Equine melanoma, Combined nevus

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INTRODUCTION

Heavily pigmented epithelioid melanocytic tumors were first described by Carney in 1996 as epithelioid blue nevus in association with the Carney complex. The latter is a familial syndrome characterized by cutaneous and cardiac myxomas, lentigines, blue nevi, endocrine overactivity, and psammomatous melanotic schwannomas. Cases of similar epithelioid nevi occurring in the absence of the Carney complex have subsequently been reported. In rare cases, lymph node metastases can occur from these melanocytic lesions. The histopathology is indistinguishable from animal-type melanomas or equine melanotic disease. Therefore, a new name, pigmented epithelioid melanocytoma, was proposed to describe these low-grade melanocytic tumors with unpredictable clinical behavior and metastatic potential. We report the case of a young girl with a pigmented epithelioid melanocytoma.

CASE REPORT

A 6-year-old girl had noted an enlarging nodule on her left posterior auricular fold for one year. There was no family history of melanoma, atypical nevus, or Carney complex. On examination, there was a round, firm, black nodule with desquamation on the left posterior auricular fold (Fig. 1). The physical examination was otherwise normal. The initial clinical diagnosis was a nevus or hemangioma, and local excision was performed.

Microscopically, the sections showed a heavily pigmented, compact lesion with fairly symmetrical growth on low power field (Fig. 2A). It was composed of intensely pigmented globo-ular and dendritic cells admixed with lightly pigmented polygonal and spindle melanocytic cells in the reticular dermis, dermal papillae, and dermoepidermal junction, accompanied by marked pseudoepitheliomatous hyperplasia of the epidermis (Fig. 2B & 2C). Moderate mononuclear infiltration was noted focally at the periphery of the lesion. After bleaching, the nuclei were fairly uniformly oval and had small distinctive nucleoli without evidence of mitoses or cytologic atypia. The proliferative index on Ki-67 staining was low. HMB-45 antibody reacted with epithelioid and dendritic melanocytes with dendritic prolongations at the dermoepidermal junction. Polygonal epithelioid cells with vesicular nuclei and distinctive nucleoli were clearly seen on bleached section stained with HMB 45. (Fig. 2D) The above features suggested a pigmented epithelioid melanocytoma.
melanocytoma. A detailed physical examination was performed. No palpable lymph nodes or atypical nevi were noted. There was no sign of local recurrence after 3 months of follow up.

**DISCUSSION**

In common with our case, on scanning magnification, a compound blue nevus appears as a dome-shaped, heavily pigmented, symmetric lesion extending to the reticular dermis. Compound blue nevus was first reported by Kamino and Tam in 1990 as comprising heavily pigmented spindled and dendritic melanocytes in dermis and dermoepidermal junction without nest formation.4, 5 The overall architecture of the two lesions are similar except that compound blue nevi lack the epithelioid or polygonal melanocytes seen in our case of pigmented epithelioid melanocytoma. It is possible that the compound blue nevus is a variant of or falls within the spectrum of pigmented epithelioid melanocytoma composed of dendritic melanocytes. Because of the prominent epithelioid cells seen in our case, epithelioid blue nevus was also considered. In the series reported by Carney, one or more blue nevi could be found in 20 of the 104 patients with Carney complex and pigmented skin lesion, with epithelioid blue nevus strongly associated with the complex. These lesions were darkly pigmented, less than 1 cm in diameter, and appeared on the extremities and trunk in young patients (mean age 16.3 years). The histology consisted of an admixture of heavily pigmented globular cells and lightly pigmented polygonal cells. Recurrence and metastasis did not occur during a mean follow up of 11.1 years, and none had evidence of metastasis on 2.5 years' follow up. Groben concluded that epithelioid combined blue nevus comprises a group of benign melanocytic neoplasms.7

Interestingly, melanoma occurring in animals may have a similar histology, appearing as a heavily pigmented dermal melanocytic tumor with an admixture of epithelioid cells and spindles cell.8 Nuclear atypia is commonly observed, but mitosis is seldom seen. Therefore, melanocytic lesions with similar histological findings and an unpredictable clinical course in humans have been described as equine- or animal-type melanoma.9 The histopathologic features of equine melanoma are indistinguishable from human epithelioid blue nevi, including our case, as are the immunohistochemical staining patterns, including s-100, HMEB-45, PCNA, and Ki-67.8

In 2004, Zembowicz, Carney and Mihm proposed a new entity called pigmented epithelioid melanocytoma to describe pigmented epithelioid melanocytic tumors histologically indistinguishable from epithelioid blue nevus and animal-type melanoma but that possess metastatic potential. They reported 41 lesions in 40 patients,10 whose median age was 27 years. The extremities were most commonly involved. In the 24 cases with known lymph node status, lymph node metastases were present in 11. The histology of these heavily pigmented dermal melanocytic tumors may be symmetrical and characterized by benign-looking epithelioid and spindled melanocytes. Some lesions may have infiltrated borders. Dendritic melanocytes at the dermoepidermal junction with epidermal hyperplasia can be seen, as was true in our case. Mitoses are infrequent and the number of atypical epithelioid cells varies. The authors found no correlation between lymph node metastasis
and ulceration, mitosis, or cytologic atypia. Even after rigorous comparison, they could not find reliable criteria to distinguish metastatic from benign epithelioid blue nevi associated with Carney complex. Therefore, they considered pigmented epithelioid melanocytoma to be a borderline melanocytic tumor or lower-grade melanoma with the frequently metastasized. They provisionally included both animal-type melanoma and epithelioid blue nevus in the same histologic group. They recommended sentinel lymph node sampling in cases of pigmented epithelioid melanocytomas because of its unpredictable behavior. Because they saw these patients in a referral center, they acknowledged that the incidence of lymph node metastasis may have been higher in their series than normal. In our case, there is no palpable lymph node or ulceration, and no sign of metastasis during follow-up. We believe it's more like the epithelioid blue nevus in the spectrum of pigmented epithelioid melanocytoma and suggest long-term follow up instead of sentinel lymph node biopsy.

Other possible differential diagnoses include malignant blue nevus, cellular blue nevus and heavily pigmented melanoma. Malignant blue nevus is defined by the presence of malignant melanoma on a preexisting or at the site of an excised blue nevus. The diagnostic features include cellular atypia, atypical mitoses, spontaneous necrosis and invasiveness in a lesion with a characteristic blue nevus pattern. In contrast to the indolent course in pigmented epithelioid melanocytoma, 80% of patients have metastases at the time of diagnosis of malignant blue nevus, and the 5-year mortality is high. Because of the aggressive behavior of malignant blue nevus, it should be included in the differential diagnosis and inquiry about changes in the site of previous blue nevus is important.

Lymph node metastasis has also been reported in cellular blue nevi. The features differentiating this lesion from malignant melanoma include the cytology and location of the cells inside the lymph node. Whereas malignant metastases with frequent mitoses usually involve the lymph node sinuses, capsules and parenchyma, relatively benign metastases are often found in marginal sinuses or capsules. Although some benign metastasizing cellular blue nevus may be similar to pigmented epithelioid melanocytoma, the lymph node metastases reported in the latter are located in the subcapsular space or lymph node parenchyma, not in the capsule or perinodal locations.

Pigmented epithelioid melanocytoma must be distinguished from pigmented primary and metastatic melanoma. Unlike primary melanoma, there is no upward pagetoid extension into the epidermis seen in pigmented epithelioid melanocytoma. Metastatic melanoma has more nuclear hyperchromasia, cytologic atypia, a higher mitotic rate, and more peripheral inflammatory infiltrates. However, distinguishing between blue nevus-like melanoma metastases and pigmented epithelioid melanocytoma may still be difficult. A clinical history of previous melanoma is important and a workup for another primary melanoma should be considered.

In summary, pigmented epithelioid melanocytomas manifest diverse, overlapping clinical and histological findings. Metastases have been reported to arise in lesions with bland cytologic features and no mitoses. It is important to recognize this tumor. If it is present, the patient should be examined thoroughly for the presence of lymph node metastases or the Carney complex and should be followed carefully thereafter.

REFERENCES
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