Purely Epithelioid Malignant Peripheral Nerve Sheath Tumor of the Vulva

Primary malignant peripheral nerve sheath tumors(MPNST) of the vulva are extremely rare and most of them are composed of a spindle cell component. A few cases of MPNST containing partially or purely epithelioid cells have been reported. Purely epithelioid MPNST differ from the ordinary epithelioid MPNST due to the absence of a spindle cell component. We present the first case of purely epithelioid MPNST arising in the vulva reviewing in the world literature without definite evidence of von Recklinghausen's disease or nerve involvement. The patient was a 63-year-old woman with a palpable vulvar mass, 6 x 4 x 1.5cm in dimension, was not encapsulated but well-demarcated, ovoid and rubbery and showed pale yellow, homogeneous, fish-flesh appearance with focal cystic changes on cut surface. The histologic features consisted of solely epithelioid cells which were arranged in tight clusters or cords with solid growing pattern and focally scattered rosette-like structures. According to the immunohistochemical results, most of tumor cells were strongly positive for neuron specific enolase, and some of them were weakly positive for S-100 protein and vimentin. We considered that purely epithelioid MPNST would represent a certain degree of differentiation toward nerve or neuronal cells rather than Schwann cells. *(JKMS 1997; 12 : 78~81)*

Key Words : *Purely epithelioid malignant peripheral nerve sheath tumor, Vulva*

Youn Soo Lee, M.D., Yeong Jin Choi, M.D., Chang Suk Kang, M.D., Seuk Jin Kang, M.D., Byung Kee Kim, M.D., Sang In Shim, M.D.

Department of Clinical Pathology,
Catholic University Medical College

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Address for correspondence
Youn Soo Lee, M.D.,
Department of Clinical Patholgy,
Catholic University Medical College,
Kangnam St. Mary's Hospital, 505 Bonpo-dong,
Seocho-gu Seoul, 137-040, Korea
Tel : (02)590-1603, Fax : (02)592-4190

INTRODUCTION

Among primary sarcoma of the vulva, leiomyosarcoma is thought to be most common, followed by either rhabdomyosarcoma (1) or the fibrohistiocytic malignancy (2). Primary MPNSTs involving the external female genitalia are extremely rare, especially in the vulva. Three forms of epithelioid or epithelial-like tissues-glandular epithelium, neuroepithelium and epithelioid cell-may be observed in MPNST (3). The epithelioid type, reported by McCormack et al.(4), has been the least well defined and not widely appreciated. Most reported epithelioid MPNSTs possess a certain degree of a usual spindle cell component, however when the tumor is composed of solely epithelioid cells, a correct diagnosis would depend upon the proof of nerve involvement or neural differentiation by immunohistochemistry and/or electron microscopy.

In this study, we report a case of purely epithelioid MPNST of the vulva without spindle cell component, evidence of von-Recklinghausen's disease, or nerve involvement.

CASE REPORT

The patient was a 63-year-old woman with palpable subcutaneous mass of the vulva which was evident for 2 months. The patient was otherwise healthy and did not show any stigmata of von-Recklinghausen's disease by careful physical examination. The patient underwent a local excision of the mass. On the operative field, there

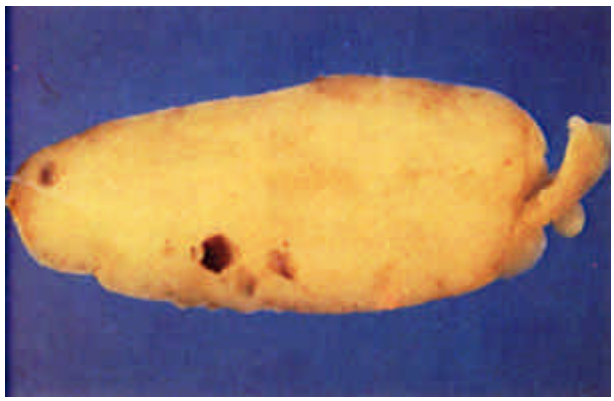

Fig. 1. The tumor was well demarcated without encapsulation and cut surface showed pale yellow and homogeneous, fish-flesh appearance with focal cystic change.

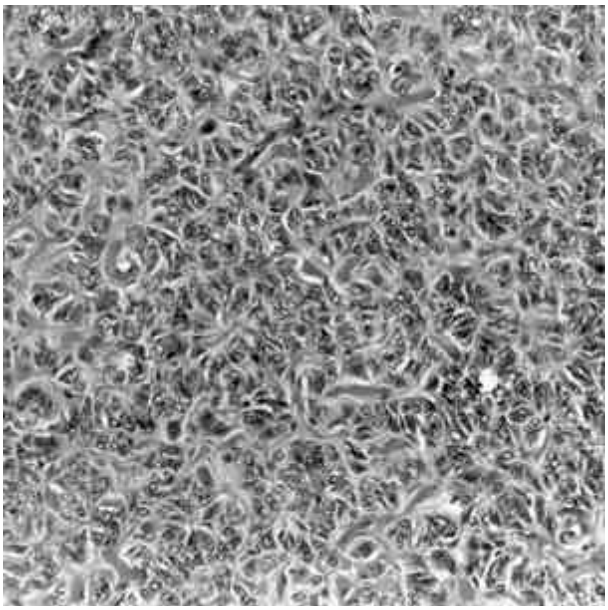

Fig. 2. The tumor cells showed solid growing pattern composed of epithelioid cells arranged in tight clusters and stringy cords.

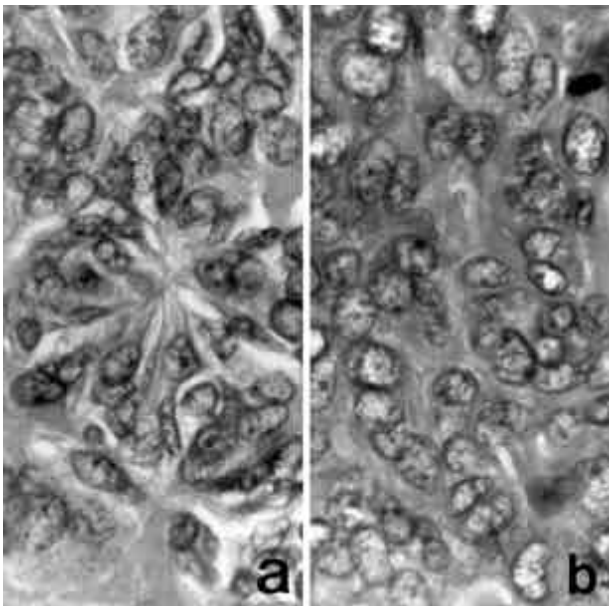

Fig. 3. a) Some of the epithelioid cells formed Homer-Wright rosette-like structures. b) The epithelioid tumor cells had round to oval nuclei with inconspicuous nucleoli and abundant eosinophilic cytoplasm with indistinct border.

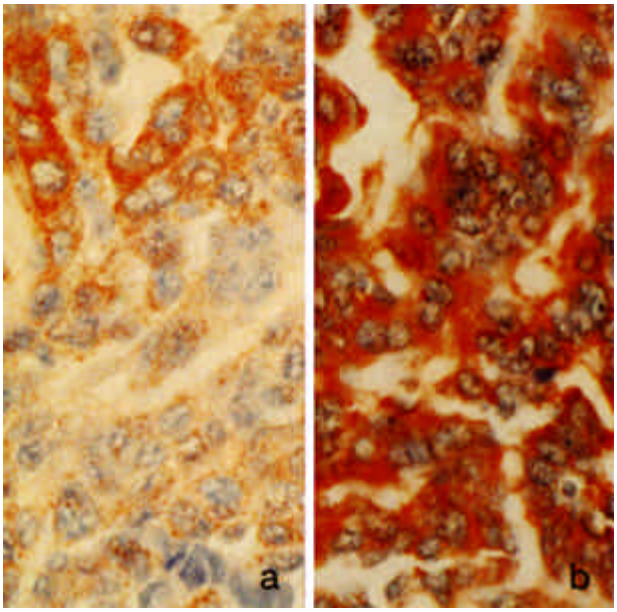

Fig. 4. a) Immunohistochemical staining for S-100 protein showed weak positive reaction. b) Immunohistochemical staining for neuron-specific enolase showed strong positive reaction

was no proof of the tumor arising from the nerve. The mass, measuring 6×4×1.5cm in dimension, was ovoid, rubbery and well-demarcated without encapsulation (Fig. 1). The cut surface showed a yellow homogeneous, fish-flesh appearance with foci of cystic changes. No hemorrhage or necrosis was observed.

Light microscopically, the tumor showed a solid growing pattern consisting of purely epithelioid cells, which were arranged in tight clusters or cords (Fig. 2) with focally scattered areas showing Homer-Wright rosette- like structures (Fig. 3a). The tumor cells had round to ovoid vesicular nuclei with inconspicuous small nucleoli and abundant eosinophilic cytoplasm (Fig. 3b). Mitotic figures were observed as many as 5 in ten high-power fields. Large amounts of collagen fibers laid down between the clusters or cords. No heterologous element such as bone, cartilage or skeletal muscle were identified. There was no melanin pigment in the cytoplasm. Both Grimelius staining for argyrophilia and Fontana-Masson method for melanin pigment were negative. The diastase-Periodic acid Schiff and alcian blue stains were also negative.

Immunohistochemically, the tumor cells were weakly positive for vimentin and S-100 protein (Fig. 4a), but strongly positive for neuron-specific enolase (Fig. 4b). They didn't show any reactivity with cytokeratin, CEA, and EMA. The patient was healthy without local recurrence or distant metastasis for sixteen months after the operation.

DISCUSSION

Primary MPNST arising from the external female genitalia are extremely rare. Table 1 summarizes the ten documented cases of MPNST arising from the external

Table 1. Malignant peripheral nerve sheath tumor of the external female genitalia

Case	Age (Yrs)	Site	Size (cm)	Histologic type	NI	Stigmata of VRN	Treatment	Recurrence	Metastasis	Prognosis (time after surgery)	Ref.
1	39	perianal	5x3	spindle	NA	-	radical excision lymphadenectomy	+	pulmonary	Alive (39 mon)	DiSaia et al., 1971
2	25	labium major	2.5x1.5	spindle	NA	+	radical excision	-	-	Alive (9 yr)	DiSaia et al., 1971
3	45	labium minor	2.5	spindle	NA	-	radical excision lymphadenectomy	-	-	Alive (18 mon)	DiSaia et al., 1971
4	44	vulva paravaginal	8x5	spindle	-	-	wide local excision	-	-	Alive (12 mon)	Lawrence and shingleton, 1978
5	40	labium major	3	spindle	-	-	local excision	+	-	Alive (24 mon)	Davos and Abett, 1976
6	NA	perineum	NA	NA	NA	NA	NA	NA	NA	NA	Vieta and Pack, 1951
7	NA	perineum	NA	NA	NA	NA	NA	NA	NA	NA	Das Gupta and Brasfield, 1970
8	NA	perineum	NA	NA	NA	NA	NA	NA	NA	NA	Das Gupta and Brasfield, 1970
9	50	labium major	5x3	spindle	-	-	wide local excision	-	-	Alive (10 yr)	Lundwell, 1961
10	19	vulva paravaginal	12x6x4	spindle	+	-	radical excision lymphadenectomy	+	pulmonary	DOD (11 mon)	Terada et al., 1988

NI : nerve involvement VRN : von-Recklinghausen's neurfibromatosis
DOD : dead of disease NA : not available

female genitalia. The age of the patients at presentation ranged from 19 to 50 years (mean age : 40 years). The size of the tumors ranged from 2.5cm to 12cm in diameter of the long axis. All of them except our case showed usual histologic features of peripheral nerve sheath tumor consisting of spindle cells (listed in Table 1). Only case 2 manifested the characteristic stigmata of von-Recklinghausen's disease. Other two cases (case 5 and 10) showed the tumors admixed with both solitary and plexiform neurofibroma, respectively. Three patient (case 1, 5 and 10) had local recurrence of the tumor and two of them (case 5 and 10) subsequently developed distant metastasis to the lung, in spite of radical excision and lymphadenectomy. Our case was alive for 16 months after local excision without recurrence or metastasis. The most common findings of cases were interlacing fascicles of slender and wavy spindle cells, which were packed closely together or arranged in a loose fashion. However, our case was composed of only epithelioid cells. The epithelioid type is an unusual form of MPNST that closely resembles carcinoma or melanoma. Distinction from metastatic carcinoma or sweat gland carcinoma is difficult, but represent frequent immunoreactivity of epithelioid MPST for S-100 protein and nonreactivity for keratin : metastatic carcinomas are frequently S-100 negative and keratin positive : sweat gland carcinomas

Table 2. Purely epithelioid malignant peripheral nerve sheath tumors

	Age (Yr)	Site	Sex	Tumor size(cm)	Nerve	Stigmata of VRN	Treatment	Recurrence	Metastasis	Prognosis (time after surgery)	Reference
1	30	ankle	M	5x3x1	peroneal	-	wide local excision lymphadenectomy	+	-	DOD(6yr)	McComack et al., 1954
2	34	popliteal fossa	M	7.5x5x3.5	sciatic	-	wide local excision	NA	NA	NA	Dicarlo et al., 1986
3	24	popliteal fossa	M	3x3x2	tibial	-	wide local excision amputation due to local recurrence	+	-	NA	Dicarlo et al., 1986
4	28	neck	M	5x3x3	vagus	-	local excision	NA	NA	NA	Kim et al., 1986

VRN : von-Recklinghausen's neurofibromatosis DOD : dead of disease
NA : not available

are invariably S-100 positive and also positive for keratin. Unlike most melanomas, epithelioid MPNSTs are non-argyrophil, nonargentaffin, and free of melanin. Enzinger and Weiss (5) estimated that the epithelioid type comprised about 5% of MPNST, but others had indicated a higher incidence of this type : White (6) found four of 15 (26%) and Tsuneyoshi and Enjoji (7) found six of 35 cases (17%).

Nearly all case of the individually described and illustrated epithelioid MPNST have areas of spindle cells resembling the conventional MPNST. When MPNST is composed of only epithelioid cell component, the usual criteria for conclusive diagnosis of MPNST are confirmation of nerve involvement or association with von-Recklinghausen's disease (8~10). However in cases that do not fulfill the above criteria, one should confirm a proof of neural origin by immunohistochemical method and/or electron microscopy. The ultrastructural features of epithelioid MPNST are variable depending on the degree of differentiation. It is possible to identify interlocking cell process invested with basal laminar and displaying cell junctions, but these features are not invariablly present (5). Our case was a purely epithelioid MPNST arising from the vulva without evidence of von-Recklinghausen's disease or demonstration of nerve involvement. Only four cases of purely epithelioid MPNST were reported in the literature : Table 2 summarizes the documented four cases of purely epithelioid MPNST. The age of the patients at presentation ranged from 24 to 34 years (mean age : 29 years). All of them occurred in men and had peripheral nerve involvement. The size of the tumors ranged from 3cm to 7.5cm in diameter of the long axis. All patients did not reveal any stigmata of von-Recklinghausen's disease. Two patients (cases 1 and 3 in Table 2) had local recurrence after wide local excision of tumor. Our patient had no recurrence or metastasis. The majority of purely epithelioid MPNST followed a less aggressive course than epithelioid MPNST or conventional MPNST (3). In MPNST, most cells are positive for S-100 protein, which suggest of Schwann cell differentiation, intermingled with these cells are neuron specific enolase or neurofilament - positive cells which suggest nerve cell differentiation. Epithelioid MPNST are thought to be composed of dedifferentiated Schwann cells that had somewhat lost their capacity to synthesize S-100 protein. Neuron specific enolase-positive epithelioid cells are considered to show a certain degree of nerve cell differentiation. In our case, most tumor cells were strongly positive for neuron specific enolase, and a few tumor cells were weakly positive for S-100 protein. We considered that our case is the first case of purely epithelioid MPNST involving female genital tract in the world.

REFERENCES

1. DiSaia PJ, Rutledge P, Smith JP. *Sarcoma of the vulva : Report of 12 patients. Obstet Gynecol 1971 ; 38 : 180-4.*
2. Davos I, Abett MR. *Soft tissue sarcomas of the vulva. Gynecol Oncol 1976 ; 4 : 70-86.*
3. Dicarlo EF, Wooduff JM, Bansal M, Erlandson RA. *The purely epithelioid malignant peripheral nerve sheath tumor. Am J Surg Pathol 1986 ; 10 : 478-90.*
4. McComack LJ, Hazard JB, Dickson JA. *Malignant epithelioid schwannoma. Cancer 1954 ; 7 : 725-8.*
5. Enzinger FM, Weiss SW. *Soft tissue tumors. St. louis : CV Mosby, 1983 ; 719-815.*
6. White HR, Jr. *Survival in malignant schwannoma ; An 18-year study. Cancer 1971 ; 27 : 720-9.*
7. Tsuneyoshi J, Enjoji M. *Primary malignant peripheral nerve tumors (malignant schwannoma) : A clinicopathologic and electron microscopic study. Acta Pathol Jpn 1979 ; 29 : 363-75.*
8. D'Agostino AN, Soule EH, Miller RH. *Primary malignant neoplasms of nerves (malignant neurilemomas) in patients without manifestations of multiple neurofibromatosis (von Recklinghausen's disease). Cancer 1963a ; 16 : 1003-14.*
9. D'Agostino AN, Soule EH, Miller RH. *Sarcomas of the peripheral nerves and somatic soft tissues associated with multiple neurofibromatosis (von Recklinghausen's disease). Cancer 1963b ; 16 : 1015-27.*
10. Ghosh BC, Ghosh L, Huvos AG, Fortner JG. *Malignant schwannoma : A clinicopathologic study. Cancer 1973 ; 31 : 184-90.*