Recurrent Dermatofibrosarcoma Protuberans of the Scalp Followed by Brain Metastasis
-A Case Report with Literature Review

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Dermatofibrosarcoma protuberans (DFSP) is a fibrohistiocytic tumor of intermediate malignancy. It is characterized by a locally aggressive growth and a high rate of local recurrence. Metastases are very rare and the most common sites of metastasis are the lungs and lymph nodes. We report a 53-year-old female patient with a DFSP on the scalp. She developed local recurrence of DFSP 4 years after simple excision and right frontal lobe metastasis in the sixth year. The pathological examinations revealed dedifferentiation from low-grade DFSP to higher grade fibrosarcomatous features in the recurrent and metastatic lesions. Immunohistochemical studies showed diffuse CD34 expression in recurrent tumor and focal loss of CD34 expression associated with fibrosarcomatous change in the brain metastatic tumor. DFSP is not only locally invasive but also has a definite metastatic potential. The importance of complete local excision with close surveillance, especially for the patients with poor prognostic factors, should be emphasized. (Dermatol Sinica 25: 159-164, 2007)

Key words: Dermatofibrosarcoma protuberans, Brain metastasis, CD34, Fibrosarcoma
INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is generally regarded as a dermal/subcutaneous neoplasm with intermediate malignancy. Typically it appears during the third or fourth decade of life. DFSP has an incidence of only 0.8 cases per million persons per year. The most common site of origin is the skin of the trunk (50% to 60%) followed by the proximal extremities (20% to 30%) and the head/neck (10% to 15%). It is locally invasive with low potential of distant metastasis. Metastases are very unusual and occur most commonly to the lungs and lymph nodes. Few reported cases have central nerve system involvement by direct invasion or hematogenous metastasis.

Here we present a rare case of recurrent scalp DFSP followed by metastasis to brain parenchyma. The histopathological features of the metastatic tumor revealed dedifferentiation from low grade DFSP to higher grade fibrosarcomatous change morphologically with focal loss of CD34 expression immunohistochemically. To our knowledge, there were only two autopsy cases of DFSPs with brain metastasis reported in the English literature.

CASE REPORT

A 53-year-old Taiwanese lady had an asymptomatic elastic-hard tumor at vertex initially noted in 1997. One year later, she received surgical excision and reconstruction with skin graft in a local hospital. Pathologically, the tumor was composed of densely packed, monomorphous, plump spindle cells arranged in a storiform pattern, whereas at the periphery there was diffuse infiltration into the subcutis. The diagnosis of dermatofibrosarcoma protuberans was made by the pathologist. Although the doctor has informed the histological diagnosis was a malignant skin tumor without appropriated surgical margin, she did not pay much attention to it.

Four years after excision, she was referred to our hospital for evaluation of a recurrent flesh-colored skin tumor (3 cm x 3.5 cm) on the margin of previous surgical flap (Fig. 1A). We performed incisional skin biopsy and pathological examination showed dense, uniform array of cells with spindle-shaped nuclei arranged into irregular, interwoven fascicles forming a storiform pattern with infiltration to subcutaneous fat. Dermatofibrosarcoma protuberans was diagnosed. The laboratory findings were all within normal limit and physical examination was unremarkable. Subsequently, the tumor was excised with Mohs micrographic surgery. The pathological examination showed in the central areas of tumor nodules densely packed, monomorphous, plump spindle cells arranged in a storiform pattern, whereas at the periphery of them there is diffuse infiltration of the spindle cells within the dermal stroma, extending into the subcutis and producing a characteristic honeycomb pattern (Fig. 2A). Immunohistochemical stains revealed that the spindle cells were mostly positive for CD34 and vimentin, and negative for smooth muscle actin (SMA), epithelial membrane antigen (EMA) and S100. Final diagnosis of dermatofibrosarcoma protuberans was established. The post-operative course was uneventful for the following months.

About one year after Mohs micrographic surgery, she suffered from dizziness and headache. She was brought to our neurosurgery outpatient department and brain computed tomography was arranged. An ill-defined globu-
lar mass (4.7 cm x 4.6 cm) with central low density over right frontal region was seen on computed tomography (Fig. 3). She underwent craniotomy and a right frontal lobe tumor with extension to the superior sagital sinus was removed. Pathologically, the brain tumor showed dense spindle cells in a storiform pattern. In some foci, there were straight fascicles of spindle cells creating the so-called herringbone pattern (Fig. 2B). The immunohistochemical study showed positive for vimentin, and negative for SMA, S100, and EMA. However, the reactivity for anti-CD34 antibody varied with different histological pattern. The area composed of typical spindle cells in the storiform pattern expressed CD34 strongly while the hypercellular areas with fibrosarcomatous change lacked CD34 expression entirely. Radiotherapy was subsequently arranged after the brain metastatic tumor was removed. Two months after operation and radiation therapy, bone scan and brain computed tomography did not reveal other residual lesion or metastatic foci.

Six months after brain surgery, a firm subcutaneous nodule beneath right upper eyelid was noted (Fig. 1B). She returned to our outpatient department for further evaluation. Orbital magnetic resonance imaging (MRI) demonstrated an irregular hypointensity soft tissue mass on right eyelid with septum invasion and focal bony destruction (Fig. 4). On the basis of clinical and radiological investigation, metastatic dermatofibrosarcoma protuberans was suspected and skin biopsy was consequently performed for further pathological evaluation. Pathological

Fig. 2
Histopathology of the lesions from (A) Scalp: Densely packed, monomorphous, plump spindle cells arranged in a storiform pattern with infiltration of the dermal stroma, extending into the subcutis and producing a characteristic honeycomb pattern. (H&E, x20) (B) Right frontal lobe: Straight fascicles of spindle cells creating a so-called herringbone pattern. (H&E, x40) (C) Right upper eyelid: Composed of pleomorphic spindle cells bearing large vesicular nuclei and pinkish cytoplasm. (H&E, x100) (D) Right upper eyelid: Multinucleated cells with distinct nucleoli and cellular atypia were frequently seen. (H&E, x400).

Fig. 3
An ill-defined globular mass (4.7 cm x 4.6 cm) with central low density over right frontal lobe.

Fig. 4
Irregular hypointensity soft tissue mass on right upper eyelid with septum invasion and focal bony destruction.
and immunohistochemical examinations of the past surgical specimens were also reevaluated carefully by a single pathologist. Pathological examination of the right upper eyelid tumor revealed fragments of tumor beneath the dermis, subcutis and skeletal muscle. The tumor was composed of pleomorphic spindle cells bearing large vesicular nuclei and pinkish cytoplasm. Distinct nucleoli with frequent mitosis were also noted (Fig. 2C and 2D). However, neoplastic cells gave negative reactions with CD34, anti-cytokeratin, S-100, HMB45, Factor VIII and EMA but they were positive for vimentin, and smooth muscle actin. After clinicopathological correlation, the final diagnosis is sarcoma, consistent with metastatic dermatofibrosarcoma protuberans. The patient was referred to plastic surgery department for further tumor excision and reconstruction.

**DISCUSSION**

DFSP is a slow-growing neoplasm of intermediate malignancy. DFSP is made up of spindle-shaped tumor cells with a strong tendency toward infiltrative growth, resulting in a high rate of local recurrences. The rate of local recurrence after wide excision of DFSP is approximately 20% and most recurrences have been seen within the first 3 years after surgery. In adult patients, 40-50% of DFSP arise on the trunk. Involvement of the scalp is observed in less than 5% of patients with DFSP. As compared among body sites, DFSP on the head and neck has the highest recurrence rate after excision, ranging from 50% to 75%, possibly because of the difficulty in achieving wide excision margins. The scalp is a rare but significant anatomic site for this tumor because of the possibility of direct invasion into the skull and brain. DFSP metastasizes in only 5% of cases, the most common sites of spread being the regional lymph nodes and the lungs and metastases often preceded by multiple recurrences. It has been proposed that any manipulation in the form of inadequate excision, which cuts through tumor and simultaneously opens vascular channels, may be essential for metastases to develop. In each recurrence the tumor may show histological signs of progression as being more cellular, having higher mitotic index and dedifferentiation from low-grade DFSP to higher grade fibrosarcomatous morphology. The fibrosarcomatous component in our case was not present in the recurrent scalp lesion, but appeared in the metastatic tumor in right frontal lobe. In a retrospective study by McPeak et al., an autopsy case of DFSP showed brain metastases in addition to the lung and bone metastases. Onoda et al. also described another autopsy case of DFSP with skin, lung and brain metastases during a 9-year clinical course. Compared with our patient, she experienced recurrence once only and brain metastasis developed within a shorter clinical course of 6 years.

Histologically, DFSP is characterized by dense, uniform array of spindle-shaped tumor cells with slender nuclei. Tumor cells are typically arranged in a storiform or cartwheel pattern. Invariably there was local infiltration of subcutaneous tissues, mostly with a honeycomb pattern. The mitotic rate is usually low (median < 4 mitoses per 10 high-power fields). Immunohistochemically, DFSP is characterized by positive staining for vimentin and CD34.

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**Fig. 5**

Immunohistochemistry of the lesions from: (A) Scalp: diffuse and strong cytoplasmic expression of CD34 (CD34 stain, x20). (B) Brain: strong (right) and moderate (left) CD34 expression (CD34 stain, x40). (C) Brain: complete loss of CD34 immunoactivity in some foci (CD34 stain, x100). (D) Eyelid: negative of CD34 expression (CD34 stain, x100).
CD34 immunoreactivity is particularly useful for the differential diagnosis of DFSP from fibrohistiocytic lesions, which CD34 expression is usually absent. The percentages of CD34-positive DFSPs have been reported to range from 20% to 100%, with an average of 90%. However, it is notable that not all DFSPs express CD34. Especially in fibrosarcomatous area of DFSP, the dedifferentiated tumor cells may lose CD34 immunoreactivity gradually and less than 50% cases of fibrosarcomatous DFSP (FS-DFSP) were positive for CD34. FS-DFSP represents a form of tumor progression and is associated with a significantly more aggressive clinical course than ordinary DFSP. It implies a possible need for treatment intensification in such cases of FS-DFSP. FS-DFSP shows a tendency to lose CD34 immunopositivity, perhaps associated with tumor progression to CD34 negative fibrosarcoma. Many of the metastatic lesions show either a fibrosarcomatous component or, much more rarely, a malignant fibrous histiocytoma-like appearance. In our case, focal loss of CD34 expression in the brain metastatic lesion with fibrosarcomatous change implied the process of dedifferentiation. The immunohistochemical stains of CD34 in the serial surgical specimens (scalp, brain and eyelid) showed the gradual change of immunoactivity (Fig. 4). Since the right upper eyelid tumor cells have completely lost the CD34 expression and lacked striking storiform pattern, it is doubtful whether the right eyelid tumor is a metastatic DFSP with fibrosarcomatous transformation or another primary sarcoma. Further detail investigations at the cytogenetic level could perhaps determine the similarity of the tumors of scalp, brain, and eyelid. Except for distant metastasis, DFSP could spread both laterally and deeply, with invasion of the subcutaneous fat, fascia, muscle, and sometimes bone. There have been three reported cases of direct brain invasion of scalp DFSPs in the literature. DFSP on the scalp is a well-known clinical entity due to the difficulty of wide surgical margin and the potential of brain involvement, either hematogenously or by direct deep invasion. Excision of scalp DFSP with clear margin is still a challenging work.

In a clinicopathologic analysis of 159 patients with DFSP, some unfavorable prognostic factors have been proposed, which were patient age older than 50 years, very close (< 1 mm) to resection margins, the FS-DFSP variant, high mitotic rate and increased cellularity. Patients with recurrent classic DFSP without evidence of adverse prognostic features may benefit from conservative management, especially in the setting of potentially unresectable disease. Since our patient had the aforementioned poor prognostic factors, more aggressive treatment and close surveillance in the postoperative period were mandatory.

Dermatofibrosarcoma protuberans has high recurrence rate after surgical excision. Gloster, et al. reviewed 317 cases of DFSP with undefined or conservative surgical margins and found total recurrence rate was 44%. They also reviewed another collection of 489 patients of DFSP with excisional margins as wide as 2 cm or more and found total recurrence rate was 20%. Parker and Zitelli measured the extension of subclinical tumor with the Mohs technique and determined that a 2.5 cm surgical margin through the deep fascia (nonscalp) or periosteum (scalp) cleared all of the tumors in 20 cases. However, Ratner D, et al. mentioned standard wide excision with a width of 1 cm around the primary tumor would have left microscopic residual tumor in 70.7%; a width of 2 cm, 39.7%; 3 cm, 15.5%; and 5 cm, 5.2%. Even an excision width of 10 cm would not have cleared the microscopic extent of some tumors. In a review of 136 patients (from 1978-2002, including 29 current cases and 107 cases in the literature review) with DFSP underwent MMS with > 5 years of follow-up, The local recurrence rate was 6.6% (9/136). Hence we believe that Mohs micrographic surgery probably represents the treatment of choice in sites in which maximum conservation of normal tissue is required.

In summary, our patient as well as the reviewed cases in the literature delineate that
DFSP has a definite metastatic potential and may involve vital organ in a short clinical course. A successful treatment depends on the achievement of local control and the prevention of cosmetic and functional deficit. Every attempt should be made for complete excision with negative margins.

REFERENCES