Solitary Malignant Gastrointestinal Stromal Tumor Associated with a Neurofibromatosis Type I

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Gastrointestinal stromal tumors are usually late manifestations of neurofibromatosis (von Recklinghausen’s disease) and most become clinically apparent in middle-aged patients as multiple benign tumors. To our review of the literature, solitary malignant stromal tumor of gastrointestinal tract is exceptionally rare in von Recklinghausen’s disease. We herein present a case of solitary jejunal stromal tumor in a 50-year-old woman with NF1, which histopathologically showed a malignant change and combined smooth muscle-neural type.

Key Words: Neurofibromatosis Type I, Gastrointestinal Stromal Tumor

Neurofibromatosis are cancer-prone hamartomatoses that involve a variety of tissues and cell types. Gastrointestinal stromal tumors are frequently associated with this condition, and are usually multiple benign tumors showing diverse histopathological features. Malignant stromal tumors of gastrointestinal tract are rarely associated with von Recklinghausen’s disease. We herein present a case of solitary malignant jejunal stromal tumor in a 50-year-old woman with NF1.

CASE REPORT

A 50-year-old Korean woman with a history of intermittent abdominal pain of two years’ duration consulted for her skin lesions. Her entire body was covered with multiple, discrete, variable sized freckles and several café au lait spots (Fig. 1A). Physical examinations revealed multiple freckles on the whole body including axillary and inguinal regions with no subcutaneous nodules of skin (Fig. 1B). Her brother and her son had the same appearance in addition to multiple neurofibromas. She was diagnosed to have neurofibromatosis type I. Esophagography and gastroscopy revealed no polyps. Pelvic MRI revealed intestinal mass (Fig. 2). At exploratory laparotomy, a jejunal segment with an attached mass on the serosal surface was resected. The mass, 12.0 × 7.0 × 6.0 cm and 250g, is roughly ovoid and firm, with a smooth brown external surface. On sectioning the mass showed firm, pale brown whorled cut surfaces with foci of hemorrhage. Histologic examinations of the lesions revealed involvement of serosal surface. The tumor consisted of multiple interweaving bundles of spindle cells with indistinct cell borders. The nuclei were, for the most part, oval with blunted ends (Fig. 3A). In some areas, the nuclei were more pleomorphic, becoming larger and more rectangular, but mitotic figures were rarely observed (Fig. 3B). Multiple foci of necrosis were observed. Immunohistochemical stains for actin, desmin, S-100 protein, neuron-specific enolase (NSE), neurofilament, and synaptophysin were performed. The lesion

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was strong positive for NSE, focally positive for actin, and had scattered S-100 protein-positive cells, but negative for desmin, neurofilament, synaptophysin.

**DISCUSSION**

Neurofibromatosis are a heterogenous set of genetic disorders that involve a variety of tissues and cell types. The most frequent form of neurofibromatosis is type 1 (NF1), also known as von Recklinghausen’s disease, the gene of which is located at 17q11.2.

The diagnostic criteria of the National Institute of Health for NF1 are met in an individual if two or more of the following are found: six or more café-au-lait macules; multiple freckles in the axillary or inguinal regions; optic glioma; two or more Lisch nodules; a distinct osseous lesion, such as sphenoid dysplasia or thinning of the bone cortex with or without pseudoarthrosis; or a first degree relative (parent, sibling, or offspring) who meets these criteria for NF1. Our patient meets this criteria in that she shows ten café-au-lait macules and multiple freckles in the axillary and inguinal regions, and her brother and her son meet the diagnostic criteria.

Gastrointestinal manifestations of NF1 were reviewed by Fuller and Williams. The most common gastrointestinal finding is a stromal tumor with varying degrees of neural or smooth muscle differentiation; such a tumor occurs in middle-aged patients as multiple benign tumors. A minority of such tumors show convincing evidence of neural or muscle differentiation either on electronmicroscopy or on immunohistochemistry but many defy classification and can only be designated as gastrointestinal “stromal” tumors. The small number of stromal tumors from NF1 patients studied by Fuller and Williams showed focal strong S-100
positivity, but no other unequivocal evidence of neural origin. Our case was similar to leiomyoma with hematoxylin-eosin stain but was negative for desmin, focally positive for actin, strong positive with NSE, and had scattered S-100 protein-positive cells. We finally diagnosed this tumor as combined smooth muscle-neural tumor. Neoplasms resembling leiomyomas in the gastrointestinal tract of patients with neurofibromatosis were first reported by Lukash. While some might argue that such cases represent the coincidental occurrence of leiomyomas in the gastrointestinal tract of patients with neurofibromatosis, the relative rarity of both gastrointestinal leiomyomas and neurofibromatosis, plus the presence of gastrointestinal involvement in as many as one fourth of patients with neurofibromatosis, would argue against this.

Malignant stromal tumors of gastrointestinal tract is exceptionally rare in von Recklinghausen’s disease. Few reported cases have led to metastatic spread and most have been regarded as malignant on the basis of conventional criteria of malignancy, namely tumor size and mitotic activity. Although scant mitotic figures, our case could be regarded as malignancy due to multiple foci of necrosis, large tumor size, and moderate cellular pleomorphism.

The risk of developing malignant tumors and early death is increased in patients with neurofibromatosis. These risks need to consider gastrointestinal tumors when gastrointestinal symptoms develop in NFI patients although clinical surveys of symptomatic gut tumors in NFI patients are much less and affect less than 5% of patients. Also, we should know that von Recklinghausen’s neurofibromatosis denotes more than the dermatologic curiosity of café au lait spots.

REFERENCES