Yonago Acta medica 2007;50:65–68

Pigmented Neurofibroma in the Appendix Diagnosed with Colonoscopy

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Pigmented (melanotic) neurofibromas in the appendix are extremely rare. To our knowledge, this is the first case of appendiceal pigmented neurofibroma in a patient without neurofibromatosis 1, which was colonoscopically diagnosed. Histologically, the tumor cells were spindle shaped with indistinct cell borders. The tumor cells had cytoplasms with many gray-brown pigments. Immunohistochemical examinations showed that the tumor cells were strongly positive for S-100 protein, and were focally positive for Melan-A. They were also diffusely positive for Leu7 (CD57), or neuron-specific enolase (NSE). No positive expression of tumor cells was observed for α-smooth muscle actin, desmin, CD34, c-kit, HMB45. No mitotic figures were observed. The Ki-67 labeling index was less than 1%. The tumor was thus diagnosed as primary pigmented neurofibroma in the appendix. In the present case, tumor cells showed no mitotic activity and a Ki-67 index of less than 1%, suggesting a benign tumor.

Key words: appendiceal tumor; pigmented neurofibroma

Pigmented (melanotic) neurofibromas are rare (Fetsch et al., 2000). According to the Armed Forces Institute of Pathology, pigmented neurofibromas constitute less than 1% of all neurofibromas (Sharon et al., 2001). One case of diffuse neurofibroma in the appendix associated with neurofibromatosis 1 (von Recklinghausen's disease) was reported (Miettinen et al., 2001). The present article reports a colonoscopically diagnosed pigmented neurofibroma in the appendix. To our knowledge, this is the first case of appendiceal pigmented neurofibroma in a patient without neurofibromatosis 1.

Patient Report

Clinical summary

A 59-year-old Japanese man, who had stools with occasional signs of blood on occasion, underwent colonoscopic examination. A doughnut-like protruding tumor, slightly whitish in color and about 1.5 cm in diameter, was found in the appendiceal orifice (Fig. 1). However, there were no remarkable abnormalities upon physical or laboratory examinations.

Pathological findings

Histopathological evaluation of the biopsy specimen revealed pigmented neurofibroma in the

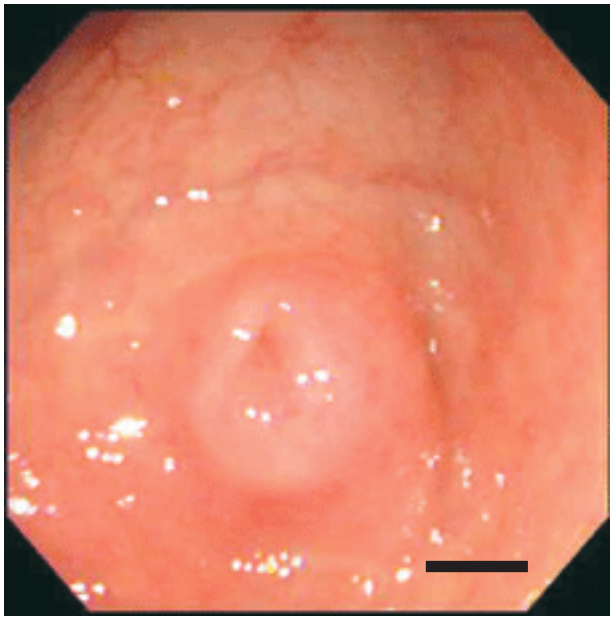

Fig. 1. Endoscopic finding. There is a doughnut-like protruding tumor at the appendiceal orifice. The tumor is slightly whitish in color and 1.5 cm at its greatest dimension. Macroscopically, the surface of the tumor is smooth. Bar = 1 cm.

appendix. Histologically, the tumor cells proliferated in the lamina muscularis mucosae and submucosal tissues (Fig. 2). The tumor was composed of spindle shaped cells with indistinct cell borders. No mitotic figures were observed (Fig. 2). Most of the tumor cells had many gray-brown pigments within cytoplasms, which stained black with Fontana-Masson stain for melanin (Fig. 3). Immunohistochemical studies of the tumor cells were performed for S-100 protein, Melan-A, Leu7 (CD57), neuron-specific enolase, α-smooth muscle actin, desmin, CD34, c-kit and HMB45. The Ki-67 labeling index was less than 1%. The results of the immunohistochemical studies are summarized in Table 1.

Discussion

Sometimes appendiceal tumors are found when the patient has symptoms in the appendix or through intussusception (Abramson et al., 1997). In our case, there were no appendix symptoms

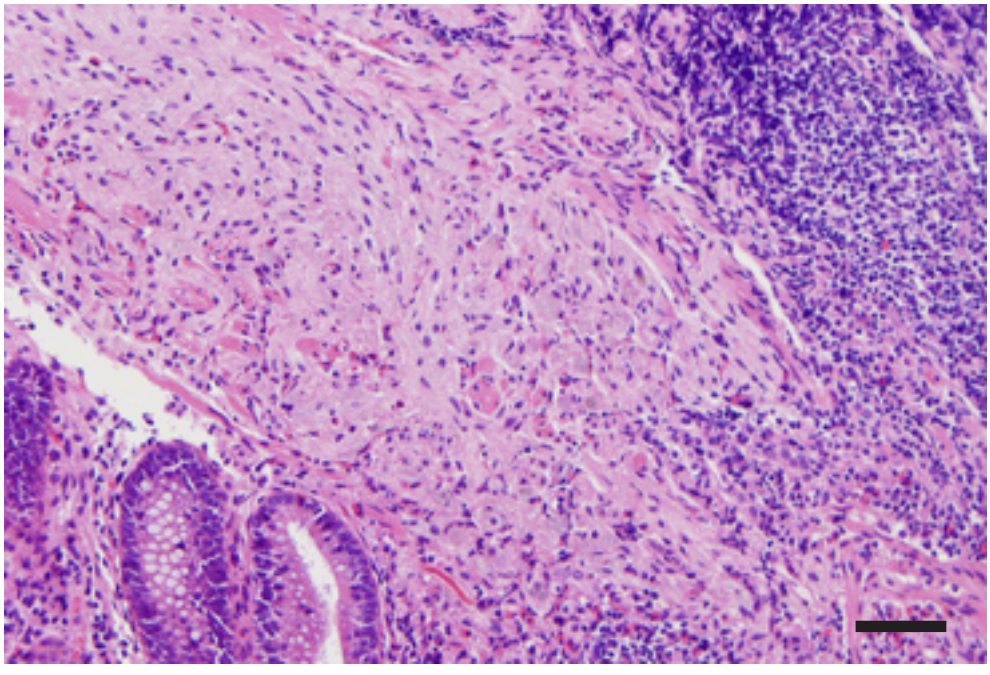

Fig. 2. Tumor cells proliferate in the lamina muscularis mucosa. The tumor is composed of spindle-shaped cells and round cells with indistinct cell borders. The cells have clear eosinophilic cytoplasms. The nuclei of the tumor cells are characteristically elongated and wavy (hematoxylin and eosin stain). Bar = 20 μm.

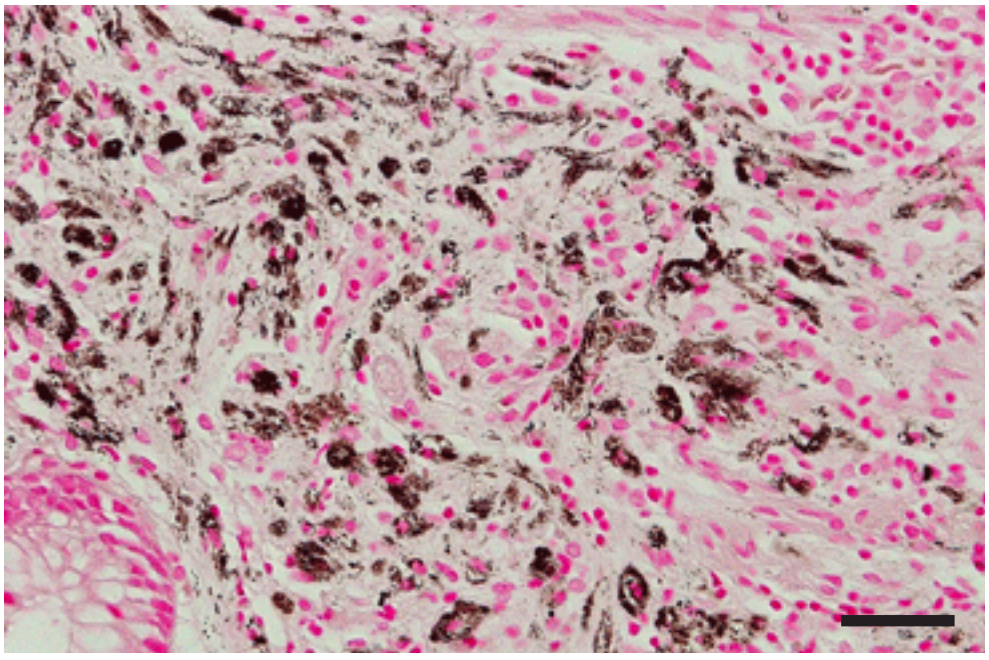

Fig. 3. Many tumor cells have intracytoplasmic melanin pigments (Fontana-Masson stain). Bar = 50 μm.

but the patient had bloody stools. Results from the histopathological examinations were consistent for pigmented neurofibroma, and excluded the possibility of leiomyoma, gastrointestinal stromal tumor and melanoma. According to Lin et al. (1997) who examined 14 neurofibromas with atypia, the Ki-67 index was less than 5% in 13 of the 14, and 10% in the rest: the factors of low cellularity and low mitotic activity were associated with good prognosis. In the present case, the tumor cells showed no mitotic activity and the Ki-67 index was less than 1%. Therefore, a benign tumor was suspected. A follow up for the patient has been carefully done for about 10 months with no signs of recurrence.

Table 1. Immunohistochemical results of the tumor cells

Antibody to	Clone	Dilution	Source	Staining result
S-100 protein	Polyclonal	Prediluted	Nichirei, Tokyo, Japan	+
CD57 (Leu7)	Polyclonal	Prediluted	Becton-Dickinson, San Jose, CA	+
NSE	Polyclonal	Prediluted	Nichirei, Tokyo, Japan	+
Melan-A	M2-7C10	Prediluted	Nichirei, Tokyo, Japan	+ (focal)
HMB45	HMB45	Prediluted	DakoCytomation, Glostrup, Denmark	–
α-SMA	1A4	1:50	DakoCytomation, Glostrup, Denmark	–
Desmin	D33	Prediluted	Nichirei, Tokyo, Japan	–
CD34	NU-4A1	1:100	Nichirei, Tokyo, Japan	–
c-kit	104D2	1:200	DakoCytomation, Glostrup, Denmark	–
Ki-67	MIB-5	1:25	DakoCytomation, Glostrup, Denmark	< 1 %

NSE, neuron-spesific enolase; α-SMA, α-smooth muscle actin.
+, positive; –, negative.

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Received July 18, 2007; accepted August 20, 2007

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