

Malignant Peripheral Nerve Sheath Tumor in Descending Colon

- A Case Report -

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We report a unique case of malignant peripheral nerve sheath tumor (MPNST) of colon, not associated with neurofibromatosis or parasite infection. The tumor presented as an encircling mass in descending colon causing obstruction with numerous metastatic lesions in a 43-year-old man. The tumor was largely composed of spindle cells which showed strong positivity for vimentin, S-100 protein and Leu-7. The tumor often exhibited epithelioid feature where tumor cells were weakly positive for cytokeratin.

Key Words : Nerve Sheath Tumors-Colonic Neoplasms

Although neurofibromas occasionally occur in patients with von Recklinghausens disease, schwannomas or neurilemmomas are uncommon among the spindle cell mesenchymal tumors of the gastrointestinal tract. They have occasionally been documented as primary gastrointestinal tumors. Diamaru *et al.*¹ estimated the incidence of myenteric schwannomas as being 2 to 6 percent of stromal tumors of the gastrointestinal tract. According to the largest published series, they most commonly occur in the stomach.² Among these, schwannomas arising in the colon in the absence of neurofibromatosis are even more exceedingly rare, and only a small number of cases have been reported.²⁻⁵ Recently, total of 20 colorectal schwannomas have been identified and analyzed in a review of more than 600 achieves of mesenchymal tumors of the colon and rectum.⁶ All colorectal schwannomas analyzed in this study behaved in a benign fashion with no evidence of aggressive behavior.

To the best of our knowledge, there has been only one case

reported as malignant schwannoma arising in the colon, and that case was associated with *Schistosoma Japonicum*.⁷ In this report, we describe another unique case of a malignant schwannoma or malignant peripheral nerve sheath tumor (MPNST) in descending colon, not associated with neurofibromatosis or parasitic infection.

CASE REPORT

A 43-year-old man visited the emergency room. He had an acute onset of vomiting and diarrhea, which had started about 4 days earlier. On physical examination, an ill-defined and deep-seated mass was found by palpation in the left lower quadrant of the abdomen. A delayed view of the small bowel series showed luminal narrowing and stenosis in some parts of the small bowel. Abdominal computed tomography revealed



Fig. 1. Abdominal computed tomography shows an ill-defined mass adjacent to the descending colon with cavity formation.

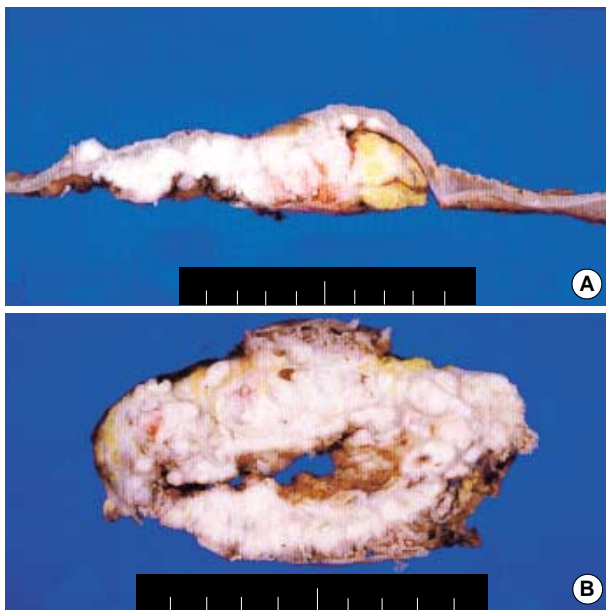


Fig. 2. (A) Longitudinally sectioned view of the lesion. The tumor is located at the submucosa without definite mucosal lesions. Multiple metastatic nodules are seen. (B) Cross section of the lesion. The tumor shows grayish white nodularity with fibrous septa, and a cavity in the center. This cavity is connected to the colonic lumen.

an approximately 12 cm-sized cavitory mass, which was suggested to be a malignant gastrointestinal tumor (Fig. 1). There were also multiple low attenuated lesions in the liver, sugges-

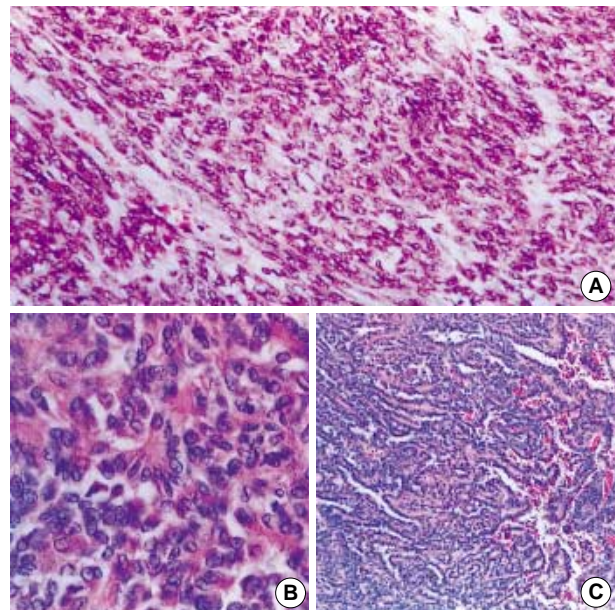


Fig. 3. (A) The tumor cells are generally spindle in shape. (B) Obvious rosette formations are frequently seen. (C) In some areas tumor cells are in papillary arrangement.

tive of metastasis. At operation, the mass was found to be encircling nearly half of the circumference of the descending colon and it was severely adhered to the adjacent small intestines. Adhesiolysis and palliative left hemicolectomy was done.

Grossly, the mass measured 15 cm in the greatest dimension, and it was totally encircling the descending colon. There were numerous nodular lesions scattered on the surrounding serosa. No mucosal lesion was seen at the lumen of the colon but there was a sinus tract from the lumen to the center of the mass. On transverse section, the mass looked as if it had originated from the wall of the colon rather than from the mucosa (Fig. 2A). The cut surface of the mass was grayish-white with focal hemorrhage and necrosis, and it was in a multinodular pattern with fibrous septa (Fig. 2B). Histological examination of the mass revealed a highly cellular, multinodular submucosal tumor, basically composed of spindle cells (Fig. 3A). Prominent lymphoid cuffing and inflammatory cell infiltrations into the fibrous septa were also seen. The tumor cells were sometimes round with abundant cytoplasm having conspicuous nucleoli, and they also showed frequent rosette formations (Fig. 3B). Interestingly, there were areas where tumor cells were arranged in papillary structures (Fig. 3C). Although atypical mitoses were sparse, all the nodular lesions on the serosal surface turned out to be metastatic nodules, and there were metastasis in 28 out of 31 regional lymphnodes.

Epithelioid leiomyosarcoma and malignant gastrointestinal

stromal tumor (GIST) were initially considered as differential diagnosis, and immunohistochemical study was performed. Smooth muscle actin (1:150, Dako, Carpinteria, CA, U.S.A.), desmin (1:150, Dako, Carpinteria, CA, U.S.A.), CD117 (c-kit, 1:50, Dako, Carpinteria, CA, U.S.A.) and CD34 (1:300,

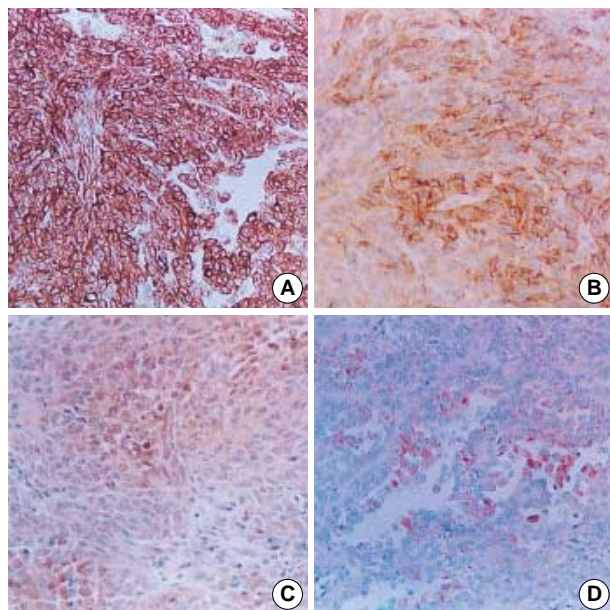


Fig. 4. Immunohistochemical study for (A) vimentin, (B) S-100 protein, (C) Leu-7, and (D) cytokeratin. It reveals that tumor cells are diffusely reactive for vimentin, S-100, and Leu-7, and weakly reactive for cytokeratin only in papillary structures.

Immunotech, Miami, FL, U.S.A.) were consistently negative in the tumor cells. S-100 (1:1,200, Dako, Carpinteria, CA, U.S.A.) and CD57 (Leu-7, 1:50, Becton-Dickinson, Franklin Lakes, NJ, U.S.A.) were strongly positive in both the papillary and spindle cell areas. Vimentin (1:100, Dako, Carpinteria, CA, U.S.A.), CD56 (1:200, Zymed, South San Francisco, CA, U.S.A.) and neuron specific enolase (1:300, Dako, Carpinteria, CA, U.S.A.) were diffusely positive and pancytokeratin (1:100, Dako, Carpinteria, CA, U.S.A.) was focally positive only in the papillary area (Fig. 4).

Since the ultrastructural examination was performed from the tumor of a formalin fixed tissue, the intracellular structures were not clearly discernable. However, it was obvious that the tumor cells were generally spindle in shape with asymmetrical tapered ends. These tumor cells were coated by basal lamina, and intercellular junctions were frequently seen (Fig. 5).

Based on these findings, a diagnosis of epithelioid MPNST of the descending colon was made.

DISCUSSION

The mesenchymal tumors of the gastrointestinal tract form a heterogeneous group that consists of several different entities with distinctive clinicopathological profiles. The main entities include leiomyomas, schwannomas, and GIST.⁸ Among these,

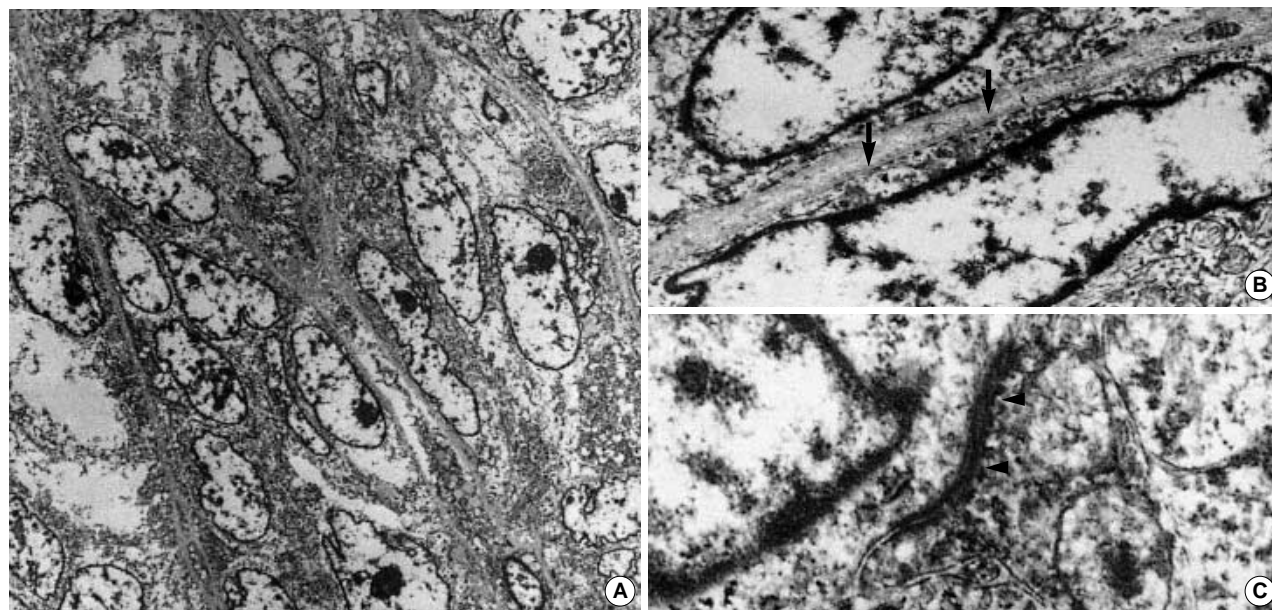


Fig. 5. Ultrastructurally, tumor cells have asymmetrically tapered spindle shape (A, $\times 2,000$). The tumor cells are outlined by basal lamina, (B, $\times 8,000$), and intercellular junctions (C, $\times 17,000$) are readily seen.

GIST constitutes the most common mesenchymal tumors of the stomach and intestine, whereas typical leiomyomas are more common in the esophagus.⁹ The case in this report is an obvious malignant gastrointestinal mesenchymal tumor arising in the colon, and since there has been only one reported case of malignant schwannoma, we considered leiomyosarcoma and malignant GIST as differential diagnosis. In a relatively large scale study, most GISTs in colons were positive for c-kit (76%) and CD34 (59%) but none of them showed positive staining on desmin or S-100 protein. According to that study, leiomyosarcomas in colons were all negative for CD34 and c-kit but most of them showed positive staining on smooth muscle actin, desmin or both.¹⁰ These tumors also differ in histological patterns. In schwannoma, prominent lymphoid cuff, diffuse lymphoid infiltration, and microtrabecular architectural patterns are commonly seen, whereas these features are not usually seen in GIST or leiomyosarcoma.^{11,12} In our case, we observed strong positivity for S-100 protein and Leu-7 and negativity for smooth muscle markers, c-kit and CD34. These immunohistochemical findings are in contrast to the findings expected in the true smooth muscle tumors or the specific GIST.

Another important differential diagnosis was malignant melanoma. Malignant melanoma is another S-100 protein positive tumor that can occur from the bowel and form a polypoid mucosal lesion or a larger transmural mass. To rule out that possibility, immunohistochemistry for HMB-45 was done, and the results were negative. Primary melanomas of the anus and anal canal may extend into the lower rectum but the primary melanoma of the rectum is rare and that of colon is even rarer. There have been only a few reports on primary colonic melanoma.¹³ The diagnosis of primary melanoma of the gastrointestinal tract is usually based on the lack of known primary lesions elsewhere. On the other hand, melanoma of the skin often metastasizes to the gut, particularly to the small intestine.¹⁴ Malignant melanoma, whether a primary lesion in the esophagus or anal region or a metastasis to any region of the gastrointestinal tract, is immunoreactive with vimentin, S-100 protein, and HMB-45,¹⁵ and negative with keratin and leukocyte common antigen. The positive immunoreactive antibodies are individually sensitive but not highly specific. Therefore, application of all three antibodies is strongly recommended, and positive reactions with all three provide the greatest likelihood of correctly identifying the tumor as a malignant melanoma.¹⁶

Schwannoma in the colon is an extremely rare entity. According to a recent study with over 600 mesenchymal tumors of the colon and rectum, the relative frequency of schwannomas in the

colon (18 cases) was approximately half of that of GISTs in the colon (37 cases). The most common location of colonic schwannomas was the cecum, and most of them were presented as intraluminal polypoid mass with mucosal ulcerations.¹⁰ But none of the cases were histologically or clinically malignant and there has been only one malignant case reported in a patient infected with *Schistosoma Japonicum*.⁷ Abundant epithelioid features in our case enables us to subclassify this case as epithelioid MPNST. This may explain the strong S-100 protein positivity of this tumor, since about 80% of the epithelioid MPNST are strong and diffusely positive for S-100 protein whereas its positivity usually decreases in conventional MPNST.¹⁷

In summary, we describe the clinical, pathologic, and immunohistochemical features of an extremely rare entity, MPNST in the colon with epithelioid features. As far as we know, this is the first case without any association with neurofibromatosis or parasitic infection.

REFERENCES

1. Daimaru Y, Kido H, Hashimoto H, Enjoji M. Benign schwannoma of the gastrointestinal tract: a clinicopathologic and immunohistochemical study. *Hum Pathol* 1988; 19: 257-64.
2. Prevot S, Bienvenu L, Vaillant JC, de Saint-Maur PP. Benign schwannoma of the digestive tract: a clinicopathologic and immunohistochemical study of five cases, including a case of esophageal tumor. *Am J Surg Pathol* 1999; 23: 431-6.
3. Hirose T, Scheithauer BW, Sanot T. Giant plexiform schwannoma: a report of two cases with soft tissue and visceral involvement. *Mod Pathol* 1997; 10: 1075-81.
4. Sasatomi T, Tsuji Y, Tanaka S, et al. Schwannoma of the sigmoid colon: report of a case. *Kurume Med J* 2000; 47: 165-8.
5. Skopelitou AS, Mylonakis EP, Charchanti AV, Kappas AM. Cellular neurilemoma (schwannoma) of the descending colon mimicking carcinoma: report of a case. *Dis Colon Rectum* 1998; 41: 1193-6.
6. Miettinen M, Kris MS, Sobin LH. Schwannomas in the colon and rectum: a clinicopathologic and immunohistochemical study of 20 cases. *Am J Surg Pathol* 2001; 25: 846-55.
7. Schwartz DA. Malignant schwannoma occurring with *Schistosoma Japonicum*: a case report. *Southeast Asian J Trop Med Public Health* 1982; 13: 601-5.
8. Miettinen M, Virolainen M, Maarit-Sarlomo-Rikala. Gastrointestinal stromal tumors value of CD34 antigen in their identification and separation from true leiomyomas and schwannomas *Am J*

- Surg Pathol 1995; 19: 207-16.
9. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. *Hum Pathol* 1999; 30: 1213-20.
 10. Miettinen M, Sarlomo-Rikala M, Sobin LH, Lasota J. Gastrointestinal stromal tumors and leiomyosarcomas in the colon: a clinicopathologic, immunohistochemical, and molecular genetic study of 44 cases. *Am J Surg Pathol* 2000; 24: 1339-52.
 11. Kindblom LG, Meis-Kindblom JM, Havel G, Busch C. Benign epithelioid schwannoma. *Am J Surg Pathol* 1998; 22: 762-70.
 12. Miettinen M, Lasota J. Gastrointestinal stromal tumors. *Virchows Arch* 2001; 438: 1-12.
 13. Poggi SH, Madison JF, Hwu WJ, Bayar S, Salem RR. Colonic melanoma, primary or regressed primary. *J Clin Gastroenterol* 2000; 30: 441-4.
 14. Ming SC. Malignant epithelial tumors of the intestines. Chapter 34 in Ming SC, Goldman H, eds. *Pathology of the gastrointestinal tract*. Baltimore: Williams & Wilkins, 1998; 886.
 15. Duray PH, Palazzo J, Gown AM, Ohuchi N. Melanoma cell heterogeneity. A study of two monoclonal antibodies compared with S-100 protein in paraffin section. *Cancer* 1988; 61: 2460-8.
 16. Sheahan DG, Crissman JD. Immunohistology and cytometry of the gastrointestinal tract. Chapter 5 in Ming SC, Goldman H, eds. *Pathology of the gastrointestinal tract*. Baltimore: Williams & Wilkins, 1998; 80.
 17. Sharon WW, Goldblum JR. Malignant tumors of the peripheral nerves. Chapter 31 in Enzingers and Weiss soft tissue tumors. 4th ed. Philadelphia: Mosby, Inc., 2001; 1209.