Sarcomatoid Carcinoma of the Descending Colon

A Histological, Immunohistochemical and Ultrastructural Analysis

Mitsuhiko Shoji, Yoh Dobashi, Keiichi Iwabuchi, Sadahito Kuwao, Tetuo Mikami and Toru Kameya

From the Department of Pathology, Kitasato University School of Medicine, Kanagawa, Japan

Correspondence to: Dr Toru Kameya, Department of Pathology, Kitasato University School of Medicine, 1-15-1 Kitasato, Sagamihara, Kanagawa 228-8555 Japan. Tel: +81 427 78 9020. Fax: +81 427 78 8441. E-mail: kameya@med.kitasato-u.ac.jp

Acta Oncologica Vol. 37, No. 7/8, pp. 765–768, 1998

Received 18 May 1998
Accepted 18 August 1998

Sarcomatoid/anaplastic carcinomas have frequently been described in the upper respiratory tract (1), lung (2) and other organs (3, 4). Although in the digestive organs similar tumours have been reported in the oesophagus (5) and stomach (6), this type of tumour is rarely reported in the colon. This may be due to the difficulty in diagnosing these tumours because of their marked similarity to malignant mesenchymal tumours, such as leiomyosarcoma, stromal cell sarcoma (GIST) and malignant fibrous histiocytoma (MFH). Furthermore, in those rare cases reported in the literature, most of them are small-cell carcinomas or sarcomatoid carcinomas with neuroendocrine differentiation and morphological similarity to carcinoid tumours (7). We describe a case of sarcomatoid carcinoma entirely composed of spindle-, or oval-shaped cells arranged in occasional fascicular patterns. The diagnosis of sarcomatoid carcinoma was made on the basis of immunohistochemical and electron microscopic analyses, although no evident epithelial features were identified throughout the entire specimen.

Case report. A 78-year-old male was admitted to the Kitasato University Hospital because of continuous abdominal pain and bloody diarrhoea. A Barium enema demonstrated an apple-core sign in the descending colon (Fig. 1a). Colonic endoscopy revealed a 3 cm (Borrmann) type 2 tumour in the mid portion of the descending colon. None of the serum tumour marker levels, including AFP, CEA and CA19-9, was elevated. A biopsy was performed proving the diagnosis of a malignant tumour and the patient underwent a hemicolectomy. Systemic examinations showed that there was no distant visceral metastasis. The patient was given chemotherapy treatment with mitomycin C (18 mg) and his postoperative course has been uneventful for 16 months since undergoing surgery.

Pathological findings. The surgical specimen was a 27.5 cm segment of the descending colon with an attached juxtacolonic omentum on the serosal side. The tumour was a $5 \times 3 \times 2$ cm, slightly elevated lesion with a centrally located deep erosive crater. The cut surface of the tumour was grey-white and firm in appearance and the tumour extended to the subserosa (Fig. 1b, c). No swollen lymph nodes were identified.

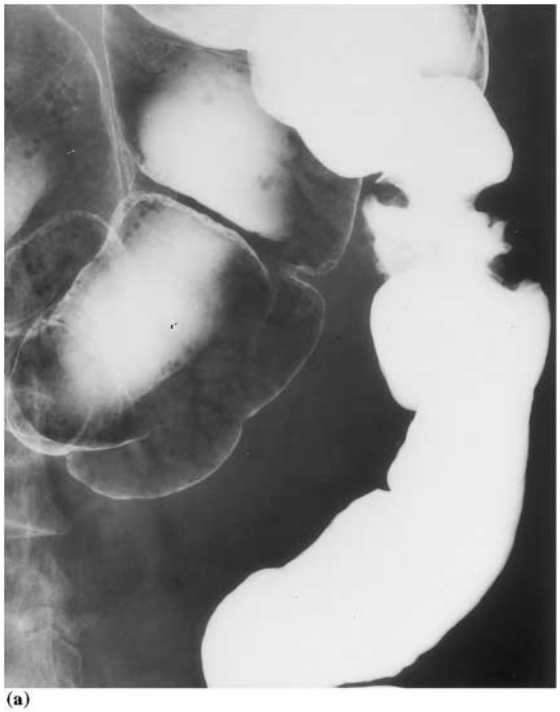
Histologically, the tumour was composed of spindle- or oval-shaped cells arranged in short fascicular or haphazard fashion without any evident morphological features, which suggests epithelial differentiation. Moreover, definitive growth patterns, such as herring-bone, storiform or palisading patterns, were not clearly identifiable. Tumour cells possessed markedly hyperchromatic nuclei with or without large prominent nucleoli and ample eosinophilic cytoplasm (Fig. 2a, b). The tumour invaded some blood vessels. Periodic-acid-Schiff (PAS) and alcian-blue for mucin were negative. Silver impregnation and Masson trichrome stains outlined a rich network of reticulin and collagenous fibres around the tumour nest.

On immunohistochemical analysis, a large proportion of the tumour cells stained positively for cytokeratin (CAM 5.2 and AE-1 for anti-epithelial cytokeratin), and occasional cells stained positively for vimentin and neuron-specific enolase (NSE) (Fig. 2c, d). Other immunohistochemical markers, including S-100 protein, desmin, EMA (epithelial membrane antigen), α-SMA (smooth muscle actin), CEA (carcinoembryonic antigen), keratin (conventional polyclonal anti-keratin antibodies), CD34, chromogranin and synaptophysin were all negative (Table I).

Intertwined tumour cells were detected by electron microscopy, and occasional primitive cellular junctional complexes, without apparent structures reminiscent of desmosomes or the assembly of tonofibrils, were identified (Fig. 3a, b). Although extremely rare, several intracytoplasmic vacuoles which were rich in glycogen granules were also noted. The nuclear density was more pronounced than is the case for MFH.

Discussion. Sarcomatoid/anaplastic carcinomas of the intestine (8, 9) have rarely been described in the literature. In particular, those of the colonic primary are extremely rare (10, 11). Anaplastic carcinoma of the colon and rectum, first reported as 'small-cell carcinoma', comprises approximately 0.2 to 0.4% of all malignancies in these regions and those anaplastic carcinomas had a neuroendocrine cell component based on the positive Grimelius and anti-NSE stainings, and specific dense-cored neurosecretory granules revealed by electron microscopy (EM) (12). These anaplastic carcinomas with neuroendocrine component grow rapidly and produce widespread metastases, resulting in a very poor prognosis (7, 12). Thus, sarcomatoid/anaplastic

 ISSN 0284-186X



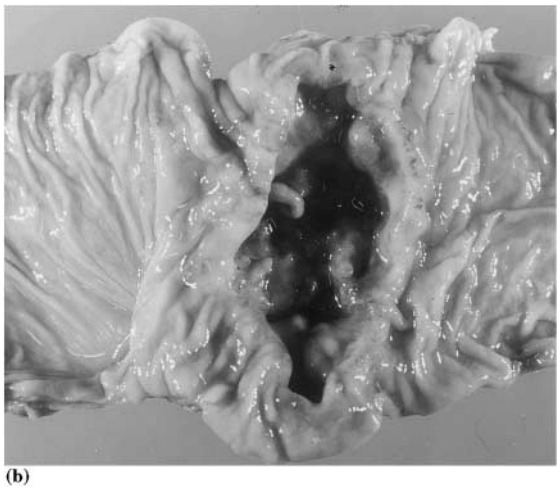


Fig. 1. a) A Barium enema showing an apple-core sign in the descending colon. b) Gross appearance of the resected specimen showing a type 2 ulcerated tumour, the surface of which was covered in necrotic debris. c) Cut surface of the tumour revealed its extension to the subserosa.

carcinoma should be carefully examined and distinguished from malignant mesenchymal tumours, because of its close resemblance to MFH, leiomyosarcoma and others like GIST (8, 9). In the present case, histology of the entire tumour revealed the proliferation of bizarre spindle-shaped tumour cells without areas of glandular differentiation. However, we prefer the diagnosis of sarcomatoid/anaplastic carcinoma for the following reasons. First, the gross appearance of the tumour was typical for advanced colonic adenocarcinoma. Second, immunohistochemical analysis of the tumour cells disclosed a diffuse positive reaction for cytokeratin, AE-1 and CAM 5.2. Third, the EM findings were consistent with the epithelial nature of the tumour. Possible differential diagnoses still remaining are leiomyosarcoma, GIST and MFH. Leiomyosarcoma was ruled out since immunohistochemistry and EM did not provide evidence to support this diagnosis. The possibility of MFH is less likely because of the EM picture, but histological profiles of the tumour in the present case were similar to some cases of MFH and, in fact, several cases of MFH of an epithelial nature have been described; immunohistochemical positivity for cytokeratin or EMA (13, 14) and occasional primitive junctional complexes between the tumour cells (13). However, the gross appearance of the tumour in the present case, and the lack of typical cellular pleomorphism and storiform pattern made us cautious regarding a diagnosis of MFH. The exact differential diagnosis between MFH with epithelial nature and anaplastic carcinoma is still open to us and requires further investigation including analysis of the histogenesis of these tumours and their aberrant differentiation during the process of tumour progression. GISTs, stromal tumours can be considered, but the nuclear features, lack of collagen, EM and immunohistochemistry do not support that particular tumour form.

Table I

Sources of the antibodies for immunohistochemical staining and results

Antibody	Source	Dilution	Results
AE1	ICN	1:200	+(diffuse)
CAM5.2	Becton-Dickinson	1:300	+(diffuse)
EMA	DAKO	1:2 000	–
CEA	DAKO	1:500	–
Vimentin	Amersham	1:200	+(focal)
α-SMA	DAKO	1:1 000	–
CD34	Becton-Dickinson	1:100	–
Desmin	Lipshaw	1:300	–
S-100 prot.	DAKO	1:3 000	–
NSE	DAKO	1:1 000	+(focal)
Chromogranin A	DAKO	1:1 000	–
Synaptophysin	DAKO	1:50	–
PGP-9.5	ULTRACLONE	1:3 000	–
Leu-7	Becton-Dickinson	1:500	–

Abbreviations: EMA = epithelial membrane antigen, CEA = carcinoembryonic antigen, α-SMA = α-smooth muscle actin, NSE = neuron-specific enolase, PGP-9.5 = protein gene product 9.5

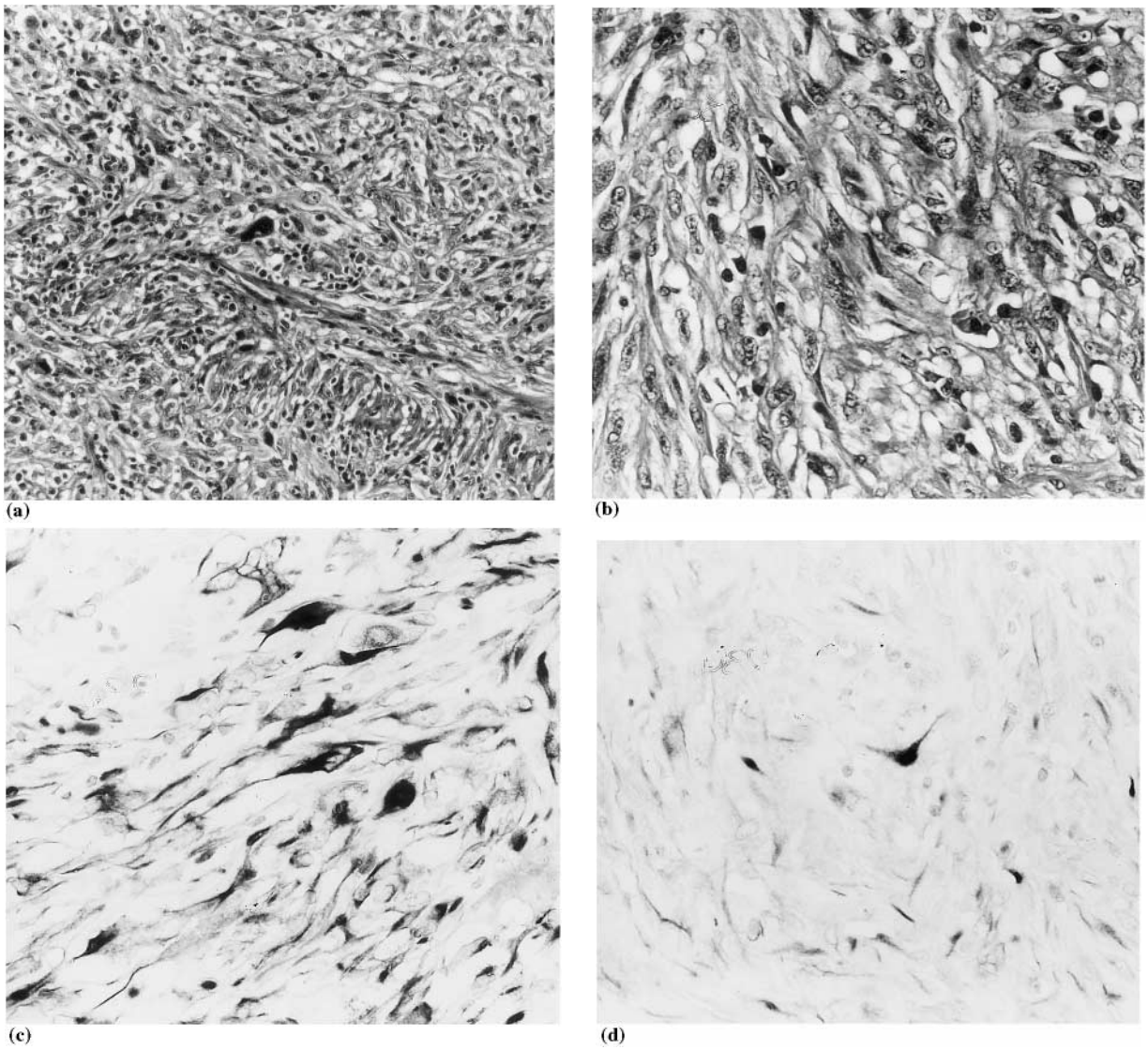


Fig. 2. a) and b) The tumour cells were arranged in short fascicular, or haphazard fashion without morphological features, suggesting epithelial differentiation (original magnification, a; × 20, b; × 40). c) and d) Tumour cells, revealed by immunohistochemical analysis, showing diffuse positivity for cytokeratin (AE1) (c; × 40) and a focal positive reaction for vimentin (d; × 40).

Various terminologies have been used to describe the cases of 'anaplastic carcinoma of the colon' reported in the literature; carcinosarcoma (15, 16), spindle-cell carcinoma (16), pleomorphic anaplastic carcinoma (8) and small-cell carcinoma (17). 'Carcinosarcoma' is a loosely defined term but the consensus is 'a malignant tumour having an admixture of carcinoma and sarcoma-like feature' (15, 16). Spindle-cell carcinoma is defined as 'a variant of squamous cell carcinoma with a biphasic appearance identifiable as a squamous cell carcinoma and a spindle-cell component derived from it' (16). Pleomorphic anaplastic carcinoma is composed mostly of MFH-like pleomorphic malignant cells with occasional foci of definitive carcinoma (8). Lastly, small-cell carcinoma is characterized by uniform small- to medium-sized cells with neuroendocrine features, which are almost identical to those of the lung (17). None of the features of these tumours fit those of our tumour.

In conclusion, the tumour described here is a sarcomatoid and/or anaplastic carcinoma of the colon without an evident focus of adenocarcinoma. Since this type of carcinoma appears to lack epithelial features either partially or completely, we should consider the possibility of the occurrence of this type of carcinoma even in the colon. Extensive examinations, including immunohistochemical and ultrastructural analyses, are required to distinguish this type of tumour from a variety of sarcomas.

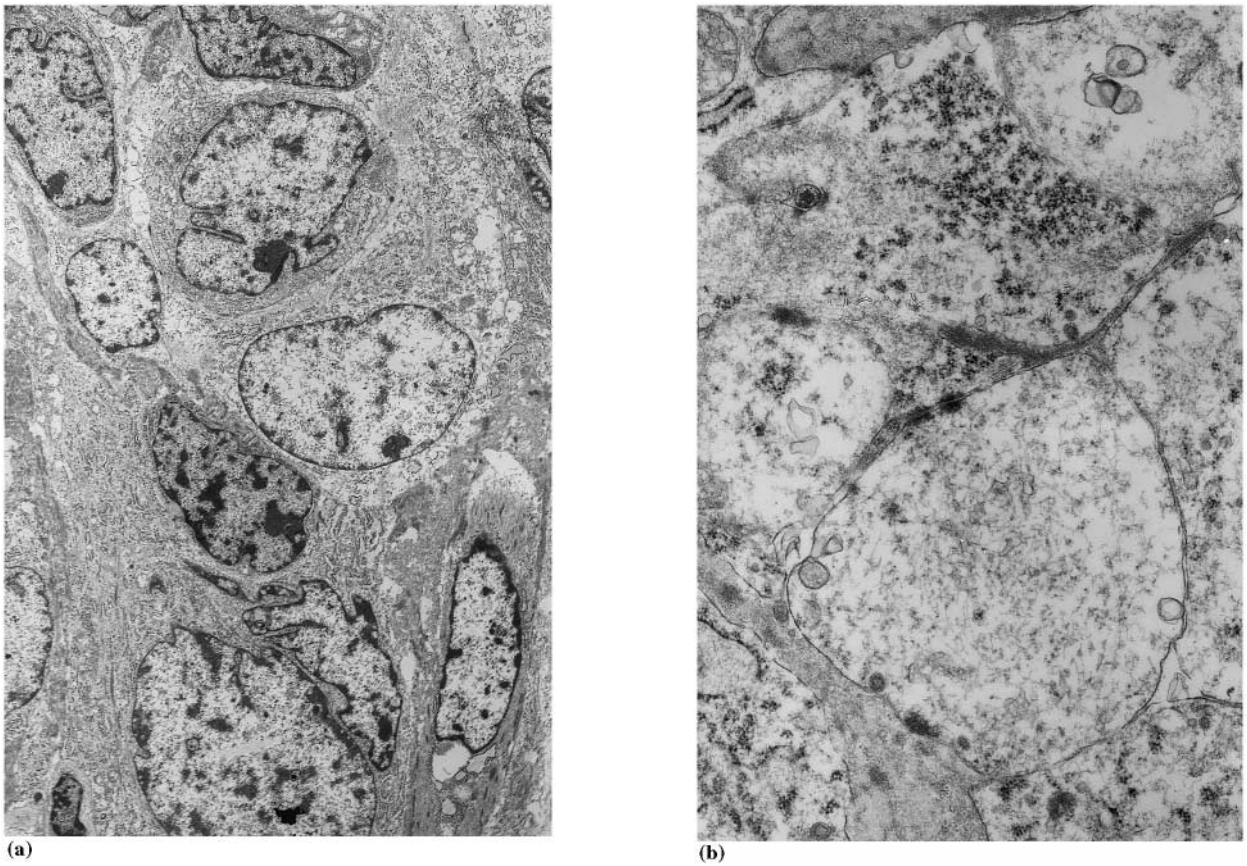


Fig. 3. a) Intertwined tumour cells of varying sizes and abundant intracytoplasmic organelles observed by electron microscope (× 3000). b) Occasional primitive junctional complexes were identifiable between the tumour cells (× 20000).

REFERENCES

1. Zarbo RJ, Crissman JD, Hema V, Mark A. Spindle cell carcinoma of the upper aerodigestive tract mucosa: an immunohistologic and ultrastructural study of 18 biphasic tumors and comparison with seven monophasic spindle cell tumors. Am J Surg Pathol 1986; 10: 741–53.
2. Humphrey PA, Scroggs MW, Roggli VL, Shelburne JD. Pulmonary carcinoma with a sarcomatous element: an immunohistochemical and ultrastructural analysis. Hum Pathol 1988; 19: 155–65.
3. Shindo ML, Staley RB Jr, Kiyabu MT. Carcinosarcoma of the nasal cavity and paranasal sinuses. Head & Neck 1990; 12: 516–8.
4. Raptis S, Haber G, Ferenczy A. Vaginal squamous cell carcinoma with sarcomatoid spindle cell features. Gynecol Oncol 1993; 49: 100–9.
5. Gal AA, Martin SE, Kernen JA, Patterson MJ. Esophageal carcinoma with prominent spindle cells. Cancer 1987; 60: 2244–50.
6. Hanada M, Nakano K, Takami M. Carcinosarcoma of the stomach: a case report with light microscopic, immunohistochemical and electron microscopic study. Acta Pathol Jpn 1985; 35: 951–9.
7. Gaffey MJ, Miles SE, Lack EE. Neuroendocrine carcinoma of the colon and rectum: a clinicopathologic, ultrastructural, and immunohistochemical study of 24 cases. Am J Surg Pathol 1990; 14: 1010–23.
8. Robey-Cafferty SS, Silva EG, Cleary KR. Anaplastic and sarcomatoid carcinoma of the small intestine: a clinicopathologic study. Hum Pathol 1989; 20: 858–63.
9. Jones EA, Flejou JF, Molas G, Potet F. Pleomorphic carcinoma of the small bowel: the limitations of immunohistochemical specificity. Pathol Res Pract 1991; 187: 235–40.
10. Paajanen H, Heikkinen M, Tarvainen R, Vornanen M, Paakkonen M. Anaplastic colon carcinoma associated with necrotizing vasculitis. J Clin Gastroenterol 1995; 21: 168–9.
11. Onishi R, Sano T, Nakamura Y, et al. Ectopic adrenocorticotropin syndrome associated with undifferentiated carcinoma of the colon showing multidirectional neuroendocrine, exocrine, and squamous differentiation. Virchows Arch 1996; 427: 537–41.
12. Gould VE, Chejfec G. Neuroendocrine carcinoma of the colon. Am J Surg Pathol 1978; 2: 31–8.
13. Andrew ER, John XO, et al. Expression of epithelial markers in malignant fibrous histiocytoma of the musculoskeletal system. Hum Pathol 1993; 24: 284–93.
14. Miettinen M, Soini Y. Malignant fibrous histiocytoma: heterogeneous patterns of intermediate filament proteins by immunohistochemistry. Arch Pathol Lab Med 1989; 113: 1363–6.
15. Noel W, Patricia Z. Carcinosarcoma of the colon: Report of a unique case with light and immunohistochemical studies. Cancer 1986; 58: 1126–30.
16. The World Health Organization histological typing of lung tumors. Ed 2. Am J Clin Pathol 1982; 77: 123.
17. Clery AP, Dockerty MB, Waugh JM. Small cell carcinoma of the colon and rectum. Arch Surg 1961; 83: 164–72.