Multifocal Sarcomatoid Carcinoma of the Small Intestine

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Sarcomatoid carcinomas (SCs) or carcinosarcomas are rare, biphasic tumors, with poor prognosis, only rarely located in the small and large intestine. The first treatment option of these tumors is surgical approach, adjuvant therapy showing no important role in the treatment protocol. We present the case of a 63 years old male patient, hospitalized in the Surgical Department II of the County Emergency Clinical Hospital Tîrgu Mureş with the diagnosis of small intestine tumor with jejunal localization. Microscopically, in hematoxylin-eosin (HE) staining, the tumor was consisting of two components, an epithelial and a mesenchymal one. From immunohistochemical point of view, tumor cells were strongly positive for cytokeratin AE1/AE3 as well as for vimentin. They were negative for epithelial membrane antigen (EMA), CD117, CD34, S100, chromogranin-A and synaptophisin. Based on the macroscopic and microscopic appearance, respectively the immunohistochemical feature of the tumor, the patient was diagnosed with multifocal sarcomatoid carcinoma of the small intestine.

Keywords: sarcomatoid carcinoma, small intestine, immunohistochemistry

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Introduction

Sarcomatoid carcinoma or carcinosarcoma is a rare, biphasic tumor, with poor prognosis [1]. For description, literature uses a various terminology like: sarcomatoid carcinoma, carcinosarcoma, spindle cell carcinoma, pleomorphic carcinoma or anaplastic carcinoma [2]. These tumors develop in different anatomic sites such as female genital tract (malignant, mixed Mullerian tumors), respiratory tract, salivary and thyroid glands, breast, skin and other sites [3–6]. Gastrointestinal SCs are unusual tumors that occur most frequently in the esophagus, stomach and gallbladder. Those located in the small and large intestine are rarely described [7,8]. First case of SC localized in the small intestine was described by Dikman and Toke in 1973 [9] as an enteroblastoma. Surgical approach of these tumors represents the first treatment option, while adjuvant therapy has no important role in the treatment protocol [1].

Case presentation

We present the case of a 63 years old male patient, hospitalized in the Surgical Department II of the County Emergency Clinical Hospital Tîrgu Mureş with the diagnosis of small intestine tumor with jejunal localization. The surgical sample, processed at the Pathology Department, was represented by a small intestine fragment of 120×35 mm, with two tumors, one of 30×25×18 mm and one of 35×20×9 mm. Their gross feature was identical, tumors showing a solid character, with increased consistency and vaguely defined edges. Tissue samples obtained from the tumor fragments were stained with HE and alcian blue-PAS. On some of the sections were performed immunohistochemical reactions using the following antibodies: AE1/AE3 cytokeratin (dilution 1:200, Thermo Scientific), vimentin (dilution 1:400 Thermo Scientific), CD117 (dilution 1:150, Dako), CD34 (dilution 1:50, Dako), S-100 protein (1:6000, Dako), epithelial membrane antingen (EMA) (dilution1:150, Dako), chromogranin A (dilution 1:100, Thermo Scientific) and synaptophyisin (dilution 1:20, Dako).

Results

From histopathological point of view both tumors were interesting all layers of the intestinal wall, with mucosal ulceration and tumor invasion until the subserosa.

Microscopically, in HE staining, both tumors were consisting of two components, an epithelial and a mesenchymal one. Most part of the epithelial component was formed by a proliferation of tumor cells arranged in sheets or as isolated cells. Only in a small part of the epithelial component was observed a proliferation of atypical glands with a narrow lumen delineated by cuboidal-columnar tumor cells. Tumor cells of the epithelial component showed atypical cytological and nuclear features – large, vesicular nuclei with pronounced pleomorphism and an obvious nucleolus, with high mitotic activity (25/5 hight power field, HPF). From place to place some tumor cells appeared as giant multinucleated cells (osteoclast-like cells).

Among the elements of the epithelial component the mesenchymal component was also present, consisting of spindle shaped tumor cells arranged in bundles. Here and there cells were polygonal or oval in shape, showing a pronounced cytonuclear pleomorphism (Figure 1).

Using periodic acid-Schiff and alcian blue stain, in the cytoplasm of tumor cells a small amount of alcian positive mucin could be observed. The surrounding stroma was scant with scattered inflammatory cells. There was no evidence of vascular, lymphatic or perineural invasion, while the lymph

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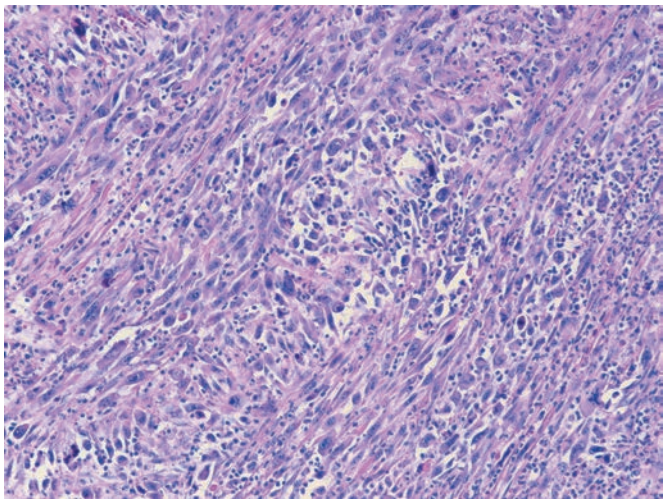

Fig. 1. Carcinosarcoma – tumor cells of the epithelial component and spindle shaped cells of the mesenchymal component. HE 10x.

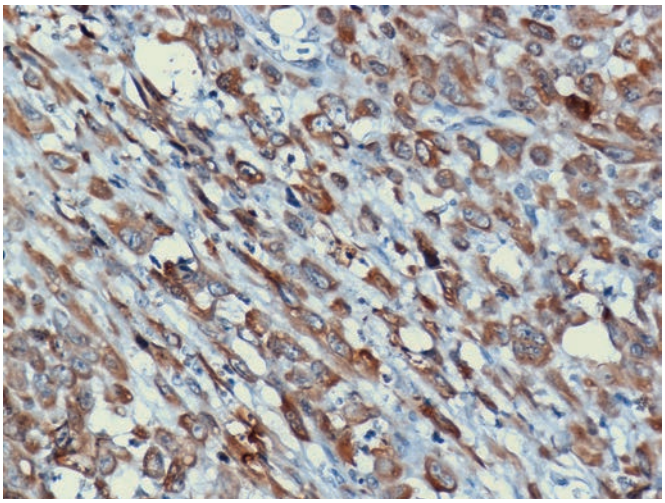

Fig. 2. Tumor cells of the epithelial component and spindle shaped tumor cells of the mesenchymal component immunopositive for AE1/AE3 cytokeratin, 20x.

nodes were free of metastatis. (TNM stage pT4N0, Mx). From immunohistochemical point of view, the tumor cells were strongly positive for cytokeratin AE1/AE3 as well as for vimentin (Figure 2, Figure 3). They were negative for epithelial membrane antigen (EMA), CD117, CD34, S100, chromogranin-A and synaptophisin (Figure 4).

Discussions

Small intestine carcinoma is a rare entity in current practice, as represented in general by adenocarcinoma and only exceptionally by the sarcomatoid carcinoma [3,10–12]. Only 23 cases of small intestine SC are described in the literature. The patients related general data showed that SC is more frequent in the male gender (M/F=2/1) while the average age of onset is 55 years. Regarding the localization it was more frequent described in the ileum and jejunum (12 and 11 cases respectively), and only one case was found in the duodenum. Macroscopically it appears as a single tumor mass, with size of about 8 cm. Most of these tumors recorded in the literature were polypoid, pedunculated, or exophytic, the infiltrative appearance being rarely described [3,10,13].

The multifocal nature [2] of the primary tumor was described only in two cases, a situation encountered also in our patient, the two tumor masses being located from each other at a distance of 30 mm. Even though both tumors were small, because of their endophytic nature they were protruding on the surface of the serosa.

Histogenesis of malignant tumors in literature represents an uncertain and very controversial topic. Some of the authors are of opinion that carcinomatous proliferation can also induce an excessive stromal proliferation – theory of stromal induction/metaplasia/fusion -, while other researchers support the theory that malignant epithelial and mesenchymal proliferation/ hyperplasia occurs simultaneously but separately – collision tumors theory – the two components originating from different stem cells [14,15]. The third group of researchers are sustaining the concept of the existence of a "totipotent stem cells", capable of epithelial and mesenchymal differentiation. These issues are also reflected

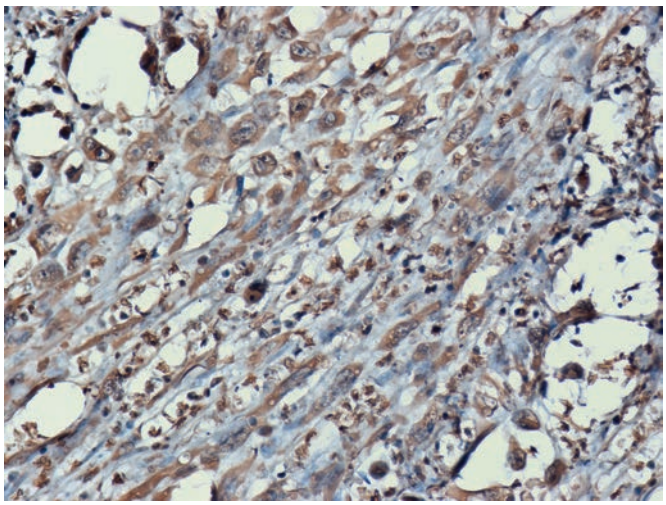

Fig. 3. Positive immunoexpression for vimentin of the tumor cells, 20x.

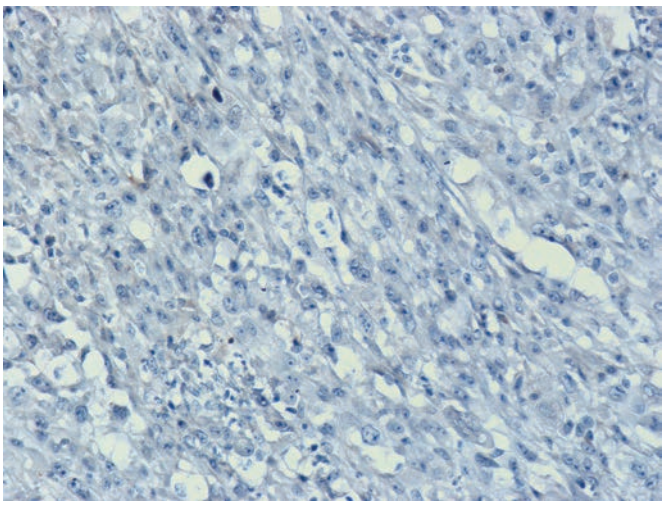

Fig. 4. Tumor cells were negative for CD117, 20x.

by the current histopathologic examination which describes SC of monophasic or biphasic nature [1]. Microscopically the typical biphasic SC includes the presence of the epithelial and mesenchymal components, cells of both components expressing epithelial markers such as cytokeratin and also markers of mesenchymal differentiation such as vimentin, from immunohistochemical point of view [8,13].

In terms of nomenclature this is also very diverse, due to the opinion of different researcher groups. Some authors in describing the SC considered the architecture, organization and the laying out of the two tumor components. In this respect the two components were arranged in distinct areas inside the same tumor, these being also called „true carcinosarcomas", while in other cases the two components were overlapping thus being described as "so-called carcinosarcomas" [13,14].

There is a certain classification of these tumors in three categories. In type 1 of the „collision tumors", there is a distinct boundary between the two tumor components. In type 2 or „combined tumors" the two components are coexisting, being confluent and present in all areas of the tumor, while the mesenchymal component shows no distinctive features. And in type 3 or "composite tumors" the two components of the tumor are present, the stromal component showing a different feature [3,8,15] .

Other researchers in the nomenclature of these tumors gave importance to the immunohistochemical profile. If the epithelial and stromal cells express the epithelial marker cytokeratin, the tumor is termed „sarcomatoid carcinoma", but if stromal cells do not express epithelial markers, the term „carcinosarcoma" is preferred [1,3,8,12,15]. In these cases it is important to asses some staining technical problems that may lead to misdiagnosis, respectively to carry out immunohistochemical reactions on several sections from different areas of the tumor.

The epithelial component is usually present in the form of glandular structures or organized in nests or cords, and rarely as isolated tumor cells. Cells of the epithelial component are large, polygonal cells with abundant, eosinophilic cytoplasm, and rounded or oval, vesicular nuclei, with an obvious nucleolus. Arrangement of epithelial tumor cells in the form of trabeculae may raise problems of differential diagnosis with neuroendocrine tumors. But the epithelial tumor cells do not express neuroendocrine markers, while in case of immunopositivity this is observed focally and isolated in some cells [12].

The mesenchymal component is composed of spindle cells arranged in bundles more or less organized, with a small amount of eosinophilic cytoplasm, and elongated, oval, vesicular nuclei, with obvious nucleoli, showing a marked mitotic activity. SC in that the mesenchymal component predominates can raise problems of differential diagnosis with gastrointestinal stromal tumors (GISTs), leyomyomas, leyomyosarcomas.

The immunohistochemical profile is important, SC being CD 117 and CD 34 negative tumors, what differentiates them from GISTs and do not express myoid differentiation markers, such as desmin or smooth muscle actin, markers that are positive in all benign and malignant tumors of muscular origin. This component may contain occasionally anaplastic cells of multinucleated gigantic cell type, and also various tissue components of differentiated mesenchymal origin such as the osteoid, chondroid, neural, adipose or rhabdoid type [7,10,15,16].

Regarding the management of these tumors, it is described that the only effective therapy method proved to be surgical resection due to early local recurrence and development of hepatic and lymphonodular metastasis, patients presenting an ineffective response to chemo- and radiotherapy [3,6,7,17].

Usually all small intestine carcinomas have very bad prognosis. Thus prognosis of SC is also poor, most of the cases described in the literature being large tumors, with local and distant metastasis, death in patients occurring within a range of 2–39 months after diagnosis.

Conclusions

The sarcomatoid carcinoma is a rare tumor, with a mixed, epithelial and mesenchymal, malignant component, whose microscopic appearance represents a real challenge for pathologists. Immunohistochemistry is a modern and very useful tool for positive and differential diagnosis, with a major importance in the subsequent management of patients.

The histopathological feature, tumor stage and the evolution indicates the fact that usually they are very aggressive tumors, with bad evolution characterized by rapid growth, local invasion, and early metastasis inducing death in patients shortly after diagnosis.

References

1. Randjelovic T, Filipovic B, Babic D, et al. Carcinosarcoma of the stomach: a case report and review of the literature. Word J Gastroenetrol. 2007;13(41):5533-5536.
2. Bak M, Teglbjaerg PS. Pleomorphic (ginat cell) carcinoma of the intestine: an immunohistochemical and electron microscopic study. Cancer. 1989;65:2557-2564.
3. Reid-Nicholson M, Muhammed I, Perino G, et al. Sarcomatoid carcinoma of the small intestine, a case report and review of the literature. Arch Pathol Lab Med. 2004;128:918-921.
4. Rascarachi G, Honrado E, Quiroga Prado L. Carcinoma sarcomatoide en paciente diagnosticado de síndrome de Sjögren. Gastroenterol Hepatol. 2009;32(3):150-154.
5. McCluggage WG. Uterine carcinosarcomas (malignant mixed Mullerian tumors) are metaplastic carcinomas. Int J Gynecol Cancer. 2002;12:687-690.
6. Sasaki K, Natsugoe S, Higashi M, et al. Esophageal carcinosarcoma with granulocyte colony-stimulating factor: a case report. Esophagus 2007;4:129-134.
7. Öztürk E, Yilmazlar T, Zerci Ö. A rare tumor located in the anorectal junction: Sarcomatoid carcinoma. Turk J Gastroenterol. 2006;17(3):236-239.
8. Kim JH, Moon WS, Kang MJ, et al. Sarcomatoid carcinoma of the colon: A case report. J Korean Med Sci. 2001;16:657-660.
9. Dikman SH, Toke C. Enetroblastoma complicating regional enteritis. Gastroenterology 1973;65:562-566.
10. Robey-Cafferty SS, Silva EG, Cleary KR. Anaplastic and sarcomatoid carcinoma of the small intestine. Hum Pathol. 1989;20:858-863.
11. Tsukadaria A, Koizumi T, Okubo Y, et al. Small-intestinal sarcomatoid

carcinoma with superior vena cava syndrome. J Gastroenterol. 2002;37:471-475.

12. Fukuda T, Kamishima T, Ohnishi Y, et al. Sarcomatoid carcinoma of the small intestine: histologic, immunohistochemical and ultrastructural features of three cases and its differential dignosis. Pathol Int. 1996;56:682-688.
13. Ikeda Y, Kosugi SI, Nishikura K, et al. Gastric carcinosarcoma presenting as a huge epigastric mass. Gastric Cancer. 2007;10:63-68.
14. Kayaselcuk F, Tuncer I, Toyganozu Y et al. Carcinosarcoma of the stomach. Pathol Oncol Res. 2002;8(4):275-277.
15. Regragui A, Lakhdar H, Belabbas M, et al. Carcinome sarcomatoide de l´oesophage: à propos d´un cas avec étude immunohistochimique et moléculaire. Gastroenetrol Clin Biol. 2004;28:487-489.
16. Rosati G, Ugolini G, Senatore G, et al. Sarcomatoid anaplastic carcinoma of the small bowel in cardiac transplant bearer. Minerva Chir. 2008;63(4):301-306.
17. Moriwaki Y, Sugiyama M. Severe anemia inducing preshock caused by sarcomatoid carcinoma of the small intestine. Int Surg. 2009;94(2):164-70.