Int J Clin Exp Pathol 2018;11(3):1581-1586
www.ijcep.com /ISSN:1936-2625/IJCEP0070777

Original Article

Sinonasalteratocarcinosarcoma: a report of two cases and clinicopathological analysis

Shaohua Chen*, Ting Zhou*, Ruxue Yang*, Nan Li, Zhaogen Cai, Gengsheng Su

*Department of Pathology, The First Affiliated Hospital of Bengbu Medical College, Bengbu Medical College, Bengbu, Anhui, P. R. China. *Equal contributors.*

Received December 11, 2017; Accepted January 7, 2018; Epub March 1, 2018; Published March 15, 2018

Abstract: Sinonasalteratocarcinosarcoma (SNTCS) is a highly malignant and aggressive neoplasm which can quickly damage the local soft tissue, bone tissue, and invade orbital and intracranial tissues. It also can result in local lymph node and distant organ metastasis. The data from 2 cases of SNTCS from the First Affiliated Hospital of Bengbu Medical College (China), treated with radiotherapy and chemotherapy followed by cranio-facial resection, were analyzed since 2016. The main symptoms of the two patients were of the nasal cavity with nasal congestion and runny nose. There was no recurrence after surgery. Microscopic examination showed that the composition of tumor tissue was very complex, as different degrees of differentiation of the origin of the organization could be seen in the tumor tissue. It was mixed with teratoma and cancer sarcoma components and undifferentiated/primitive tumor cells could also be seen in local tumor stroma. SNTCS is a very rare complex tissue composition of malignant tumors, because of its complex pathological morphology and high possibility of misdiagnosis. Pathological features and immunohistochemical markers can contribute to the diagnosis and differential diagnosis of the disease.

Keywords: Nasal cavity, sinonasalteratocarcinosarcoma, immunohistochemistry

Introduction

SNTCS is a highly malignant tumor combining the features of teratoma and carcinosarcoma, which is very rare in clinical practice. Most of the neoplasm occurs in the nasal cavity and paranasal sinuses. SNTCS is a serious disease due to its highly malignant potential, local invasion, and distant metastasis ability. It has been reported that the 3-year period survival rate is about 40% and the average survival period is less than 2 years [1]. The most common symptoms of the disease are nasal congestion and epistaxis. Most of the tumors can infiltrate into adjacent tissues and organs [2]. There are just a few cases that have been reported in the literature since WTO officially named "nasal teratocarcinoma sarcoma" in 2005.

Materials and methods

We collected 2 cases of sinonasalteratocarcinosarcoma in the First Affiliated Hospital of Bengbu Medical College from January 2009 to July 2016. The patients were one male and one female, aged 47 and 50 years. Both cases were sent to one of the authors for consultation. H&E-stained sections (4 um thickness) were reexamined to evaluate the tumor's histological features and immunohistochemistry was performed with the Elivision technique. Antibody details are given in **Table 1**. Clinical demographics and followup data were obtained from medical records and from referring physicians.This study was approved by the Ethics Committee of the First Affiliated Hospital of Bengbu Medical College and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

Results

Clinical features

Both patients initially presented with complaints of intermittent nasal obstruction and occasional epistaxis concomitant headaches for about two months and four months, particularly in occipitalis of the head. Both cases with nasal cavity showed the left nasal red and white

Table 1. Sources of the antibodies used in the immunohistochemistry analysis

Source	Antibody
Vimentin	Monoclonal, clone V9
EMA	Monoclonal, clone E29
CK	Monoclonal, clone AE1/AE3
NSE	Monoclonal, clone E27
Syn	Monoclonal, clone SP11
S-100	Monoclonal, clone4C4.9
Ki-67	Monoclonal, clone MIB-1
Desmin	Monoclonal, clone D33
CD99	Monoclonal, clone O13
CgA	Monoclonal, clone SP12

All antibodies were obtained from Maixin Biotech, Inc. (Fuzhou, China), and were ready to use.

new creatures. One case of the tumor was located in the left nasal cavity, the other in the left nasal cavity and paranasal sinuses.

Local computed tomography (CT) scan showed that an inflammatory nasal polyp on the left side of the maxillary sinus, ethmoid sinus, and valerian sinus and inferior turbinate hypertrophy of both sides with bending of the nasal septum. Further biopsy showed that the possibility of mucous epidermoid carcinoma could not be ruled out. Nasal CT showed (**Figure 1A**, **1B**): left nasal irregular soft tissue density filled, bilateral lower turbinate hypertrophy, left maxillary sinus, frontal sinus mucosa thickening, slightly increased sinus density, and skull base and sinus wall no obvious abnormality. Our hospital considered the diagnosis of sinonasalteratocarcinosarcoma by pathological biopsy. The neck ultrasound showed visible enlarged lymph nodes of which the boundary was clear. We resected the tumor via a lateral rhinotomy approach. After surgery, the patients were treated with radiotherapy and chemotherapy, radiotherapy program for docetaxel plus neda platinum. One patient was treated with ifosfamide + epirubicin + Changchun Dixin + prednisone for one cycle.

Gross and histological features

Generally, the tumor was a pile of gray-red polypoid tissue, part of which was slightly beige. The surface was relatively smooth, section was red, soft or medium quality, and the local area seemed to be jelly-like. Microscopic examination showed that the tumor had a variety of tissue components derived from two or three germ layers and showed a different maturity, in addition to being mixed with cancerous or sarcomatous components. The two cases contained microscopic epithelial components, spindle cell sarcoma, and undifferentiated/primitive tumor cell components. The surface of the tumor tissue was non-keratinized squamous epithelium (**Figure 2A**, **2B**) or pseudo-stratified ciliated columnar epithelium. The differentiation of the tumor had the characteristics of mufti-directional andnaïve. The squamous cell nest neuroepithelial cell-like cells were still obviously visible in some areas. Partial squamous cell nest differentiation was more mature, with visible keratosis, the mature epithelial components and irregular glandular structures could be seen in the local area. In some areas, there were also adenocarcinomas and the structure of a poorly differentiated adenocarcinoma with a cord-like and nest-like distribution (**Figure 2C**). The spindle-like cells can be seen around the squamous cells (**Figure 2D**). There were a lot of immature trabecular bone structures in some areas, among which focal and patchy distribution of juvenile small cells could be seen.

As mentioned above, the ectodermal component in the tumor is often keratinized and non-keratinized squamous epithelium. Typically the immature cytoplasmic transparent squamous cell nest has definite significance for the pathological diagnosis of the tumor. The inner endodermal composition of the tumor is often rich in mucus pseudostratified ciliated columnar epithelium and arranged in the adenoid-like structure of the digestive tract epithelium.

Adenocarcinoma, squamous cell carcinoma, sarcomatoid carcinogenic components, and carcinoidsyndrome could be seen in the tumor. The nerve tissue components in the tumor wereusually the olfactory neuroblastoma and the neurofibrillary component. A neural tube-like structure, authenticity, and pseudomonas also could be seen.

The mesodermal components in the tumor can be cartilage, smooth muscle, rhabdomyosarcoma, fibrosarcoma, the original interstitial tissue, and visible fibroma-like and myxoid tumor-like areas. The above mentioned various components of the tumor and other components such as adenocarcinoma, squamous cell carci-

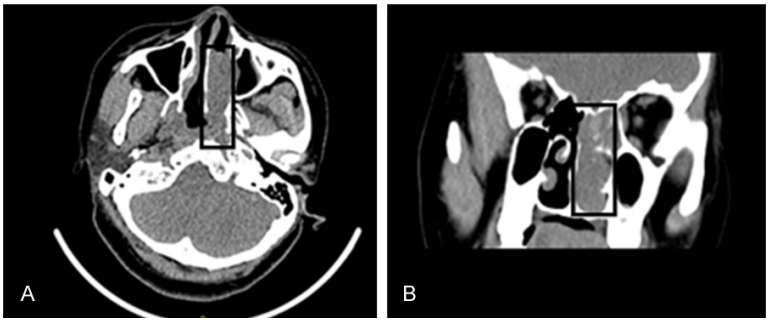

Figure 1. CT scan of the mass. A. CT scan showing a mass involving the left side of the nasal cavity. B. CT flat scan showing the left nasal irregular soft tissue density shadow filling.

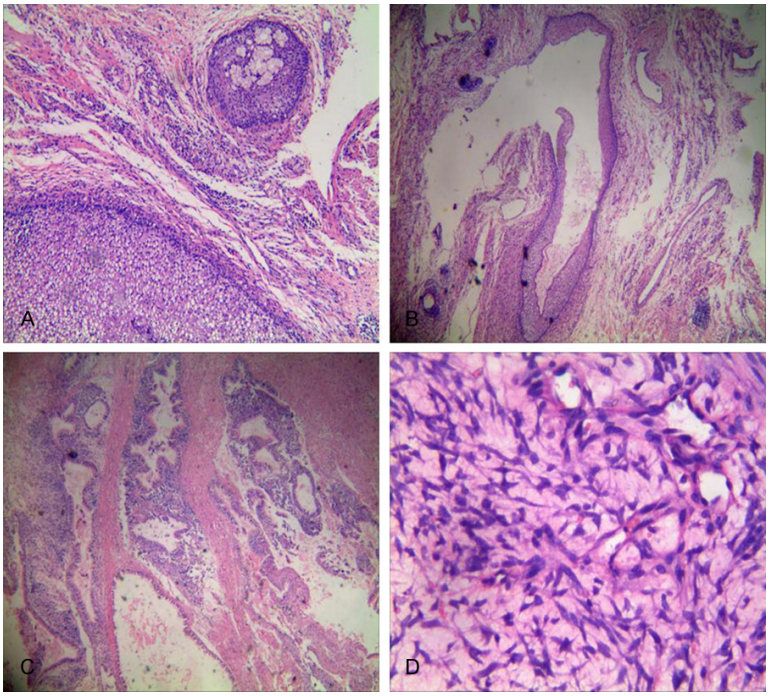

Figure 2. Histological features of the tumors. A. Immature squamous cell nests (magnification, ×100). B. Differentiated mature epithelium (magnification, ×100). C. Photomicrograph showing malignant epithelial cells arranged in glandular pattern (magnification, ×100). D. Photomicrograph showing spindle cell sarcoma. The tumor cells have nuclear atypia and mitosis (magnification, ×400).

noma and sarcomatoid carcinogenic components, and even nerve tissue were all mixed in different proportions. The tumor cells can differentiate well and the dysplasia was not obvious. The heterotypicity was more obvious and there were more mitotic figures, often hemorrhage and necrosis in the tumor.

Immunohistochemical features

The results of immunohistochemical markers derived from the different components of the germ layers are also different. Epithelial composition can generally express CK, EMA, and other positives (**Figure 3A**, **3B**). Nerve tissue components can express NSE, S-100, CD99, CgA, and other positives (**Figure 3C**). Undifferentiated/primitive tumor components can express CgA positive, CD99 negative, and-Syn weakly positive. Undifferentiated spindle cell sarcoma components can express Vimentin positive (**Figure 3D**), while the expression of Desmin and SMA were negative.

Diagnosis

Combined with the clinical manifestations of patients, pathological biopsy, and immunohistochemical results after the general discussion by ourdepartments, we made the diagnosis of sinonasalteratocarcinosarcoma.

Follow up

These patients are currently alive and well without evidence of recurrence and metastasis.

Discussion

SNTCS is an insidious, rare, and highly malignant neoplasm which has the characteristics of fast invasive growth, with diversified histological characteristics, and prone to distant metastases. Patients commonly have a poor prognosis. Brudrukkar and others reported that 11 of the 14 patients had local recurrence and the median recurrence time was 7 months [3].

Heffner and Hyams first proposed the tumor as teratogenic sarcoma in 1984 [4]. The tumor was officially named after “nasal sinuses terascarcinosarcoma” due to the complex histological model, in 2005. Histologically, SNTCS has one or more epithelial and mesenchymal components (benign and malignant). It is different

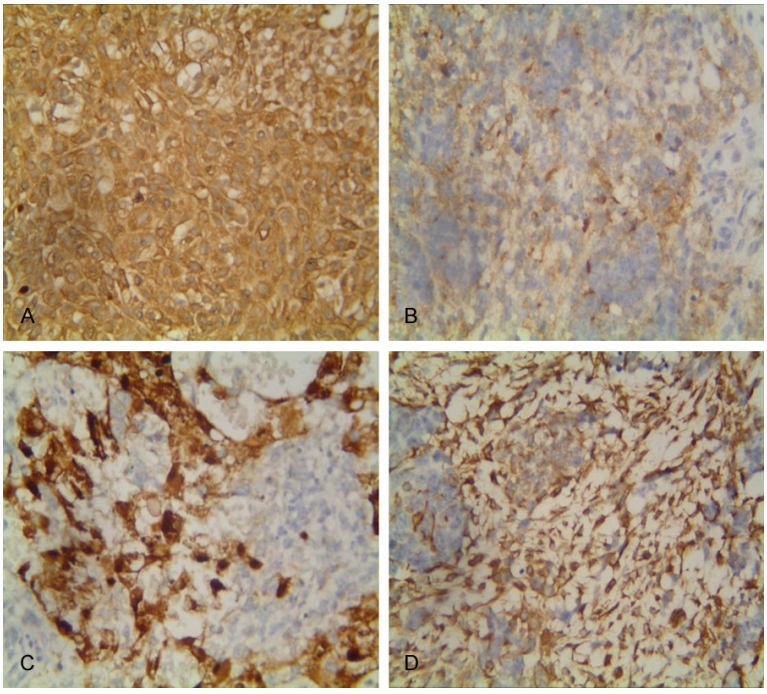

Figure 3. Immunohistochemical features of the tumors. A. Epithelial cells in tumor positive for CK18 (magnification, ×400). B. Epithelial cells in tumor positive for EMA (magnification, ×400). C. Neural cells in tumor positive for S-100 (magnification, ×400). D. Undifferentiated spindle cells positive for Vim (magnification, ×400).

from some single malignant epithelial tissue and the single real carcinosarcoma of malignant stromal elements.

The disease occurs mostly within the nasal cavity and paranasal sinuses, the minority areas located in ethmoid sinus, sphenoid sinus, etc. Most of the patients are adult and the age ranges from 18 to 79, with the average age at about sixty [5, 6]. The cardinal symptoms of SNTCS include runny nose, nasal congestion, and intermittent nasal bleeding. When the tumor invades adjacent tissue there may be corresponding clinical symptoms such as facial swelling, lacrimation, exophthalmos, vision loss, headache, decreased sense of smell and consciousness, personality behavior changes, and so forth [7, 8]. Imaging manifestations of nasal and paranasal sinuses are in irregular places, the density is different, the signal strength is low or moderate intensity, with or without calcification, and a small number of rapid progresses can be seen at the skull base, cavernous sinus and other parts of the destruction of bone. The vast majority of patients do not have specific indicators in laboratory tests, therefore the diagnosis of the disease generally depends on pathological biopsy, immunohistochemistry, and other pathological examination.

The tumor was nodular or polypoid, the surface was dark red or gray-red, and soft or qualitative. It may become tough when invading into bone tissue or associated with calcification, with visible bleeding and necrosis on the section, and a few have been associated with ulcers [9, 10].

Microscopic examination has shown that the composition of the tumor was very complex, showing differentiation from the three germ layers of different organizations. The tumor in histology not only includedteratoid components such as glands, squamous epithelium, cartilage tissue, glial, etc. but also cancerous sarcomatoid components. Tumor tissue can be interspersed with nestle-like gland cancer and spindle cell sarcoma area. In addition, some patients may also have different degrees of differentiation of neuroepithelial cells and differentiation of naive small cells and the formation of similar olfactory neuroblastoma-like areas.

Typical tumors of SNTCS have benign and malignant epithelial, mesenchymal, and neural components. Epithelium is usually composed of keratotic or non-keratinized squamous epithelium, pseudo-stratified ciliated columnar epithelium; a glandular structure for the cubic or columnar cells may have mucus secretion. They commonly contain immature cells (embryonic cell-like) and immature squamous cell nests which are important diagnostic clues. It could be a lesion caused by primitive embryonic tissue or multicellular stem cells blurred in the upper respiratory tract during development, often mixed with cancerous and sarcomatous components [11].

Immunohistochemical studies have been done on SNTCS in our study which demonstrate that variable expression of neural (S-100 protein, neuron specific enolase, CgA, CD99), epithelial

(CK, EMA), and undifferentiated/primitive tumor components can express CgA positive, CD99 negative, and Syn weakly positive. The regular strong expression of vimentin has led to favoring an undifferentiated spindle cell sarcoma component while the expression of Desmin and SMA were negative.

Pathological examination and immunohistochemistry can contribute to diagnosis and differential diagnosis, however, there are similarities between the pathogenesis and pathological changes of the olfactory neuroblastoma. Diagnosis of SNTCS could be very difficult due to its heterogeneous composition [12], especially when sampling was not enough.

SNTCS is a rare and rapidly invading high-malignancy in clinical practice. It is less susceptible to distant metastasis and poor prognosis. It is a disease with a male preponderance. The ratio of male to female prevalence is 7:1 or 8:1. The age of onset is between 18 and 79 years old and the median age is 55 years old [13]. The disease has a poor prognosis. Patients have an average survival period of less than 2 years and recurrence usually within 3 years. Once diagnosed, patients need to be actively dealt with effective treatment. It has been reported in the literature that the most effective treatment is to regulate surgical resection combined with postoperative external exposure. The studies of Smith and others showed that 5 patients were treated with radical surgery plus postoperative radiotherapy. After having been followed up for 72-372 months, the patient was stable with no recurrence or metastasis [7]. However, if recurrence or metastasis exists, it is supplemented by chemotherapy. Adjuvant chemotherapy can improve survival because metastatic tissue usually contains sarcoma components [14].

In conclusion, as clinical symptoms of SNTCS and imaging manifestation are usually lacking in specificity, it is easy to make a misdiagnosis and to miss a treatment opportunity. The disease is extremely rare and has a high degree of malignancy and poor prognosis. Therefore, we should strengthen the understanding of the disease, taking into account the various aspects of the patient information to make the correct diagnosis andadminister timely and effective treatment. The immunohistochemical profile can aid in diagnosis. CK, EMA, S-100, and Vim appear to be the most sensitive markers and are expressed in most cases. However, currently the precise lineage of these distinctive neoplasms remains poorly understood.

Acknowledgements

We would like to thank Editage for English language editing. Thanks to Di-chen Li and Qun Xie (Department of Pathology, The Frist Affiliated Hospital of Bengbu Medical College) for their assistance with histopathological and immunohistochemical stain evaluations. This study was supported by the Natural Science Foundation of Anhui Province (No. 1608085QH207), Key Foundation of Excellent Young Talents in Colleges and Universities in Anhui province (gxyqZD2016161), and the Nature Science Key Program of College and University of Anhui Province (No. KJ2017A236).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Nan Li, Department of Pathology, The First Affiliated Hospital of Bengbu Medical College, 287 Changhuai Road, Bengbu 233000, Anhui, P. R. China. Tel: +86-552-3070209; E-mail: linanangel100@sina.com

References

[1] Sharma HS, Abdullah JM, Othman NH, Muhamad M. Pathology in focus: teratocarcinosarcoma of the nasal cavity and ethmoid. J LaryngolOtol 1998; 112: 682-6.

[2] Misra P, Husain Q, Svider PF, Sanghvi S, Liu JK, Eloy JA. Management of sinonasalteratocarcinosarcoma: a systematic review. Am J Otolaryngol 2014; 35: 5-11.

[3] Budrukkar A, Agarwal JP, Kane S, Siddha M, Laskar SG, Pai P, Murthy V, Sengar M, D'Cruz A. Management and clinicaloutcome of sinonasalteratocarcinosarcoma: single institution experience. J LaryngolOtol 2010; 124: 739-743.

[4] Heffner DK, Hyams VJ. Teratocarcinosarcoma (malignant teratoma?) of the nasal cavity and paranasal sinuses. A clinicipathological study of 20 cases. Cancer 1984; 53: 2140-2154.

[5] Yang S, Sun R, Liang J. Sinonasalteratocarcinosarcoma: a clinical and pathological analysis. Int J SurgPathol 2013; 21: 37-43.

[6] Salem F, Rosenblum MK, Jhanwar SC, Kancherla P, Ghossein RA, Carlson DL. Teratocarcinosarcoma of the nasal cavity and paranasal sinuses: report of 3 cases with assessment for

chromosome 12p status. Hum Pathol 2008; 39: 605-609.
[7] Smith SL, Hessel AC, Luna MA, Malpica A, Rosenthal DI, El-Naggar AK.Sinonasalteratocarcinosarcoma of the head and neck: a report of 10 patients treated at a single institution and comparison with reported series. Arch Otolaryngol Head Neck Surg 2008; 134: 592-5.
[8] Kim JH, Maeng YH, Lee JS, Jung S, Lim SC, Lee MC. Sinonasalteratocarcinosarcoma with rhabdoid features. PatholInt 2011; 61:762-767.
[9] Shorter C, Nourbakhsh A, Dean M, Thomas-Ogunniyi J, Lian TS, Guthikonda B. Intracerebral metastasis of a sinonasalteratocarcinosarcoma: a case report. Skull Base 2010; 20: 393-396.
[10] Misra P, Husain Q, Svider PF, Sanghvi S, Liu JK, Eloy JA. Management of sinonasalteratocarcinosarcoma: a systematic review. Am J Otolaryngol 2014; 35: 5-11.
[11] Thomas J, Adegboyega P, Iloabachie K, Mooring JW, Lian T. Sinonasalteratocarcinosarcoma with yolk sac elements: a neoplasm of somatic or germ cell origin? Ann Diagn Pathol 2011; 15: 135-139.
[12] Szudek J, Bullock M, Taylor SM. Sinonasalteratocarcinosarcoma involving the cavernous sinus. J Otolaryngol 2005; 34: 286-8.
[13] Wei S, Carroll W, Lazenby A, Bell W, Lopez R, Said-Al-Naief N. Sinonasalteratocarcinosarcoma:report of a case with review of literature and treatment outcome. Ann DiagnPathol 2008; 12: 415-425.
[14] Misra P, Husain Q, Svider PF, Sanghvi S, Liu JK, Eloy JA. Management of sinonasalteratocarcinosarcoma: a systematic review. Am J Otolaryngol 2014; 35: 5-11.