

Case Report

Primary clear cell carcinoma of nasal cavity: a case report and review of literature

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Abstract: Primary Clear Cell Carcinoma (CCC) of nasal cavity is rare and is often misdiagnosed as a malignant or benign lesion frequently. We reported a case of primary clear cell carcinoma of nasal cavity, with the complaint of epiphora in right eye, nasal obstruction and bleeding. CCC often confused with the metastatic renal clear cell carcinoma (RCC) of the nasal cavity, pathology and immunohistochemistry are the gold standards of Clear Cell Carcinoma could help us to make a definite diagnosis. Surgery, radiotherapy and chemotherapy are the main treatment methods.

Keywords: Primary, CCC, immunohistochemistry, radiotherapy

Introduction

Primary clear cell carcinoma (CCC) of nasal cavity is a rare disease that often leads to head and face complications. This disease mainly originates from the salivary gland and clear cell squamous cell carcinomas [1]. However, Negahban et al reported that this cancer may emerge from the nasal mucosal surface covering the epithelium because tumor cells are observed in this area; moreover, the nasal ciliated cell surface border areas appear as transparent cytoplasm. Nasal malignant tumor accounts for 0.3% of all tumors and 3% of all head and neck cancer cases; nasal tumors are usually primary tumors and rarely metastatic lesions. Nevertheless, the CCC of the nasal cavity is usually transferred from the kidneys [2], and few primary clear cell carcinomas of nasal cavity were reported in recent years.

Case report

A 59-year-old male patient was admitted in April 2016 for epiphora of the right eye, nasal congestion, and nasal bleeding from the right nostril. Nasal endoscopy presented bilateral nasal mucosal chronic congestion with a yellowish-white scab shell and membrane on the right side of the middle turbinate. A severely

hyperemic polypoid mass in the right nasal cavity was noted, and both the middle turbinate and the hook were protuberant because of the mass. Nasal CT scans showed soft tissues in the right maxillary sinus, frontal sinus, ethmoid sinus, sphenoid sinus, and right nasal cavity. A cystic shadow was also observed on the right side of the ethmoid sinus, which obscured the surrounding bone, protruded towards the eye socket, and consequently impinged on the eye medial rectus muscle (**Figure 1**). The diagnosis results were as follows: (1) mass in the right nasal cavity and (2) sinusitis.

Surgical treatment was performed 4 days after admission. During surgery, the amount of hemorrhage was 600 mL, and pink neoplasms were observed in the ethmoid sinus and right middle nasal meatus. The middle nasal meatus was observed on the right maxillary sinus, along with the mucosal adhesion of the sphenoid sinus. Histopathological findings (**Figure 2**) revealed the large tumor cells. Abundant transparent cytoplasm, capillary, and blood sinus also appeared in the intercellular substance. Immunohistochemistry results were as follows: vimentin negative (**Figure 3A**), S-100 negative (**Figure 3B**), CD10 positive (**Figure 3C**), and CK7 negative (**Figure 3D**). The patient exhibited

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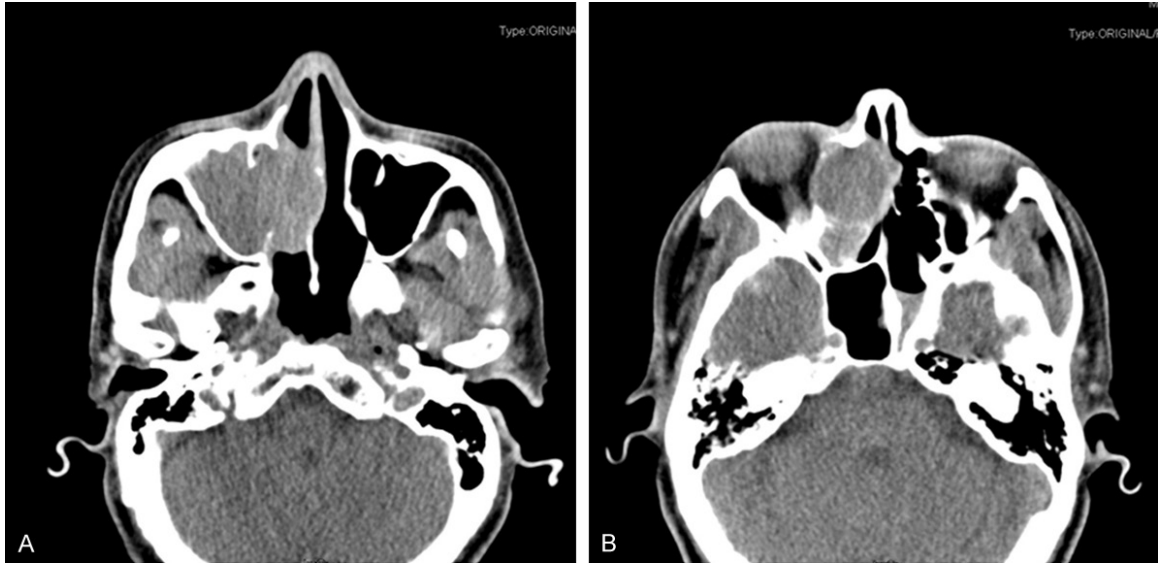


Figure 1. Nasal CT scans. We can see the soft tissues in the right maxillary sinus, frontal sinus, ethmoid sinus, sphenoid sinus, and right nasal cavity. A cystic shadow was also observed on the right side of the ethmoid sinus.

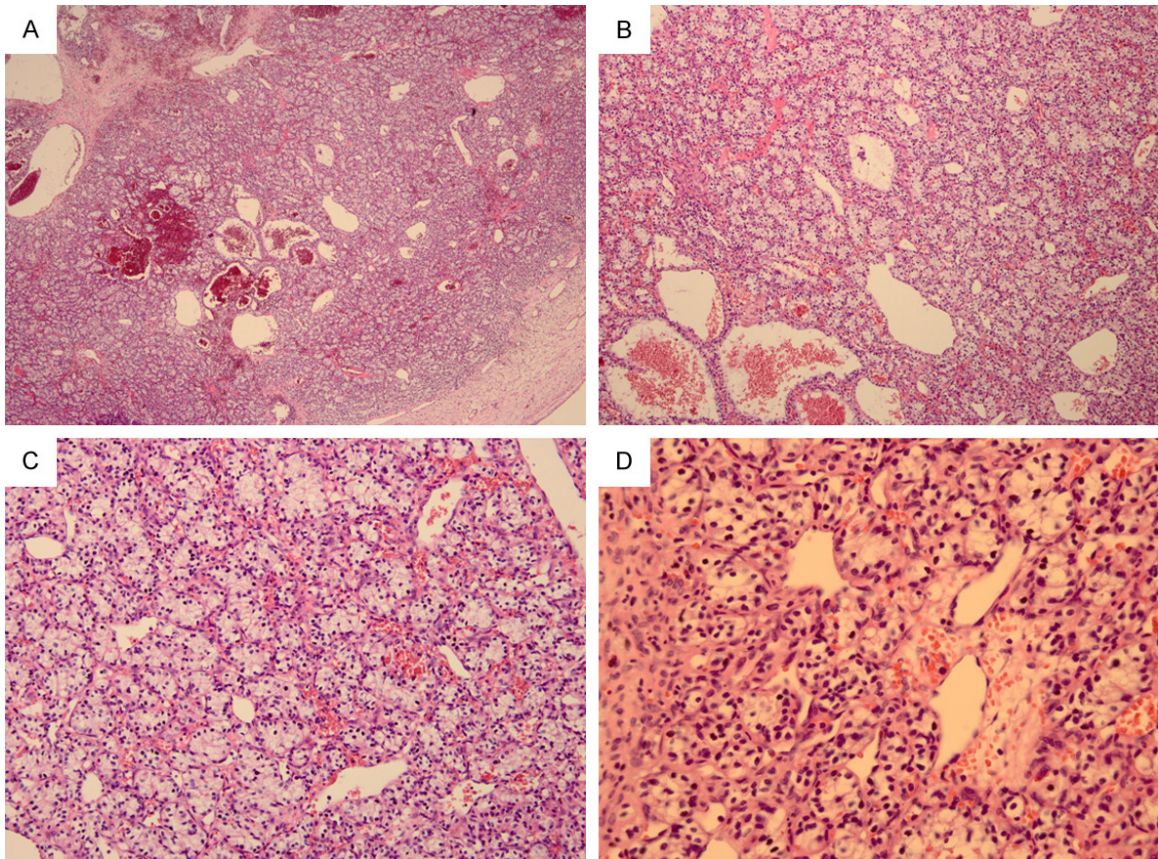


Figure 2. Histopathological. We can see the large tumor cells, transparent cytoplasm, capillary, and blood sinus appeared in the intercellular substance.

abdominal CT scan 3 days after the surgery. Results showed no disease on abdominal

organs, and the patient presented no history of kidney disease. Combined results of immuno-

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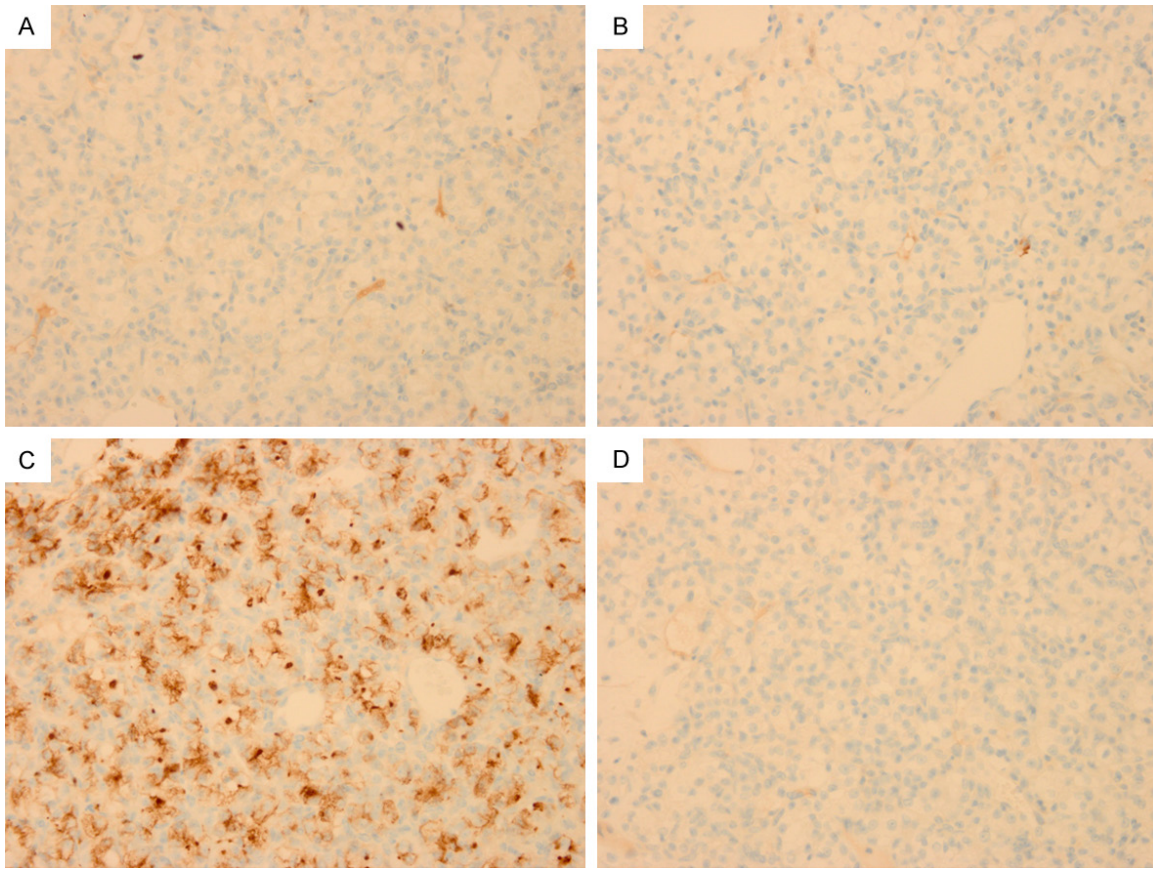


Figure 3. Immunohistochemistry. The picture indicates vimentin (A), S-100 (B) are negative, CD10 is positive (C), and CK7 is negative (D).

histochemistry and histopathology showed that the final diagnosis was primary CCC of maxillary sinus. A three-month follow-up of the patient was conducted to confirm the diagnosis. Additionally, results showed no discomfort of the kidney and whole body. And continuous radiation was performed (1.8-2.0 Gy every time, 5 times a week, total radiation amount is 66-76 Gy) after the operation. And there is no recurrence or metastasis was observed in the one year of follow-up period.

Discussion

The primary CCC of nasal cavity is a malignant tumor that often starts with nasal bleeding and nasal congestion, which is accompanied with complications, such as bone destruction, sinusitis, and epiphora [3]. And the tumor cells may metastasize by blood and lymph. The deterioration of nasal bleeding is the most significant symptom of the tumor that is the main complain of the patients [4]. It can also cause facial

pain and deformity because of the invasion into ethmoid sinus and maxillary sinus. Furthermore, vision loss even blindness may occur after a few weeks to several months. The involvement of the sphenoid sinus may cause headaches and increased risk of optic nerve, and internal carotid artery damage [5].

CCC manifestations start with nasal symptoms that are nonspecific, and many of the indications begin with epistaxis and sinusitis [6]. CT scan shows no obvious characteristic features, such as soft tissues or bone destruction, during early stage. Thus, it is complex to distinguish secondary sinusitis from tumor tissue [7]. However, MRI can be a better option. The preoperative pathological biopsy under endoscope is recommended in the case of full hemostatic facilities.

Primary CCC has also been found in the larynx, minor salivary gland, nasopharynx, thyroid gland, ovary, uterus, cervix, and vagina. In

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Table 1. Immunohistochemistry for differential diagnosis of CCC

	Mucoepithelial carcinoma	Myoepithelial carcinoma	Acinic cell carcinoma	Renal cell carcinoma	Sinonasal renal cell-like adenocarcinoma	Clear cell carcinoma
CK	+	+	+	+	Variable	+
CK5/6	n/a	+	-	-	n/a	+
CK7	n/a	-	Variable	Variable	+	+
CK20	n/a	-	-	-	Variable	-
AE1/3	n/a	+	+	Variable	+	-
S-100	-	+	Variable	Variable	n/a	-
Calponin	+	+	n/a	n/a	n/a	-
Vimentin	n/a	+	n/a	+	-	-
GFAP	n/a	-	-	-	-	Variable
CD10	-	-	-	+	Variable	+
Ki-67	Variable	Variable	Variable	Variable	Variable	Variable
Mucin	+	-	-	-	n/a	n/a
EMA	+	Variable	+	+	n/a	+
p63	n/a	n/a	+	Variable	n/a	+
SMA	-	+	+	-	n/a	+
PAS	Variable	-	+	+	n/a	+
PAS-D	-	-	+	-	n/a	n/a

+: positive. -: negative. n/a: not applicable.

Table 2. Review of literatures describing CCC of nasal cavity and treatment

Literature	Cases	Age (yrs)/sex	Pathogenesis	Clinical manifestation	Treatment	Results
Zhao W. 2014 [1]	1	28/F	5 months	Congestion + bleeding	Surgery + radiotherapy	*Free for follow-up
Zhao W. 2014 [1]	2	60/M	1 year	Blood in nasal discharge + congestion	Surgery + radiotherapy	*Free for follow-up
Zhao W. 2014 [1]	3	33/M	2 months	Blood discharge	Surgery + radiotherapy + chemotherapy	*Free for follow-up
Zhao W. 2014 [1]	4	60/M	5 months	Blood in nasal discharge + congestion	Surgery + radiotherapy	*Free for follow-up
Zhao W. 2014 [1]	5	58/F	1 year	Blood in nasal discharge + congestion	Surgery + radiotherapy + chemotherapy	*Free for follow-up
Zhao W. 2014 [1]	6	49/F	6 months	Blood in nasal discharge + congestion	Surgery + radiotherapy	*Free for follow-up
Takayuki. 2016 [10]	7	80/M	4 months	Blood in nasal discharge + congestion	Surgery	Free for 1 year follow-up
Davina. 2015 [7]	8	60/F	6 months	Congestion + bleeding	Surgery	Free for 10 months follow-up
Hong J. 2013 [17]	9	34/F	1 year	Bleeding	Surgery + radiotherapy + chemotherapy	Free for 1 year follow-up
Hong J. 2013 [17]	10	57/F	6 months	Blood in nasal discharge + congestion	Surgery + radiotherapy + chemotherapy	Free for 6 months follow-up
Hong J. 2013 [17]	11	78/F	2 months	Congestion	Surgery + radiotherapy + chemotherapy	Died
Hong J. 2013 [17]	12	66/F	1 month	Congestion	Surgery + radiotherapy	Free for 2 years follow-up
Hong J. 2013 [17]	13	34/F	1 year	Congestion + headache	Surgery + radiotherapy	Free for 2 years follow-up
Huang XJ. 2011 [8]	14	54/M	3 months	Blood in nasal discharge	Surgery	Free for 1 year follow-up

*no full detailed time of follow-up, the follow-up time ranged from 4 to 22 years, with an average of 11 years.

2002, Zur KB et al, reported this disease as renal cell-like carcinoma of the nasal cavity for the first time [3]. However, only 12 cases have been reported in the last 30 years. The carci-

noma is often confused with other nasal neoplasms, such as clear cell metastasis of thyroid cancer, malignant melanoma, epithelial myoepithelial carcinoma, and malignant myoepithe-

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lioma [8], especially the metastatic renal clear cell carcinoma (RCC) of the nasal cavity. Abdominal and nasal CTs combined with pathological diagnosis can estimate the origin of the cancer [1]. In general, in the absence of kidney disease and with minimal enhancement, MRI generally indicates the primary CCC imaging characteristics. The majority of histopathological findings are usually characterized as the following: transparent cells arranged in nests, capillary-rich fibrous tissue space, small nucleus, less mitosis and vacuoles and fully connected cell body [9]. And we summarized the immunohistochemical staining of several kinds of tumors reported in literatures [1, 7, 10-14] (**Table 1**). These indicators can help us with diagnosis and differential diagnosis of the primary CCC of nasal cavity. The immunohistochemistry findings of the patients in our case are not typical. The abdominal CT and post-operation follow-up help us confirm the diagnosis.

According to reports in the previous literatures, surgery, radiotherapy and chemotherapy are still the main treatment methods (**Table 2**). There are no unified standards for the treatment of CCC at present. Nevertheless, surgery is the first recommended treatment in some cases. The tumor is rich in capillaries and blood sinus, and the intraoperative bleeding easily occurs. Moreover, interventional embolization and intraoperative controlled hypotension or general anesthesia can reduce bleeding. For some patients with early lesions and poorly differentiated malignant tumor, the survival rate of using endoscopic resection is similar to that with surgery combined with radiotherapy. The prognosis of nasal septum tumors is better than those of other parts. Early implementation of effective treatment exhibits a cure rate of more than 70%. The tumor with clear boundary is located in the nasal septum or lateral nasal wall boundaries can be completely resected. Nasal endoscopy combined with nasal lateral incision is a good option when the eyes or other parts of the body are invaded [15].

The scope of radiotherapy is determined by the security boundary, size and location of the tumour. In phases I and II, surgery or radiotherapy should be performed [8]. Primary focal region and neck lymph node of the same side should be included, preventive irradiation of bilateral lymph nodes when security boundary

is not enough after the operation. In phases III and IV, radiotherapy and chemotherapy are recommended. Radiotherapy of I-V lymph nodes in bilateral neck should be conducted when the tumor has metastasized to the neck or pharynx. In lymph node metastasis, cervical lymph node dissection of bilateral neck, therapeutic irradiation of focal lymph node and prophylactic irradiation of lymph node drainage area should be conducted. If the tumour invades the nasopharynx and parapharyngeal space, radiotherapy should include the anterior areas of bilateral areas. In the large tumor, surgery may be considered when the tumor has shrunk after radiotherapy. The radiation dose for the primary foci and invaded lymph node region is 60-76 Gy, and 45-55 Gy for preventive irradiation in surrounding intact lymph nodes. Chemotherapy is usually used in conditions as follows: (1) advanced stage or multiple metastases; (2) possible of lymph node metastasis; (3) adjuvant chemotherapy before surgery [16]; (4) to increase the sensitivity of radiotherapy.

The poor prognostic indicators include low performance status, thrombocytosis, neutrophilia, serum LDH levels higher than normal and low hemoglobin. Besides, the size, stage and metastasis of the tumor are related to the survival rate. And the prognosis of the patients with multiple metastases is poor, with a 5-year survival rate of 0% to 7%. For the early stage patients [6], radiation and chemotherapy combined with expanded resection can greatly improve its survival rate.

Disclosure of conflict of interest

None.

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