Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 27 (2015) 216–220

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Case Report

A case of sinonasal undifferentiated carcinoma treated without radical resection

Takahisa Ohta[a,*], Masayuki Motohashi[a], Yasunori Muramatsu[a], Shinichiro Sumitomo[a], Jun-ichi Tanuma[b], Michio Shikimori[a]

[a] Department of Oral and Maxillofacial Surgery, Division of Oral Pathogenesis and Disease Control, Asahi University School of Dentistry, Japan
[b] Department of Oral Pathology, Division of Oral Pathogenesis and Disease Control, Asahi University School of Dentistry, Japan

ARTICLE INFO

Article history:
Received 13 December 2012
Received in revised form 21 August 2013
Accepted 7 October 2013
Available online 25 November 2013

Keywords:
Paranasal
Sinonasal undifferentiated carcinoma
Intra-arterial chemotherapy
Radiation therapy

ABSTRACT

Sinonasal undifferentiated carcinoma (SNUC) is a rare and highly aggressive neoplasm of the paranasal sinuses. SNUC is characterized by rapid expansion with high rates of recurrence and metastasis to cervical lymph nodes and distant sites. The patient was a 65-year-old woman who complained of persistant pain at the right maxilla. She had undergone endodontic therapy at the right first molar by her primary dentist. Imaging studies, including computed tomography (CT) and magnetic resonance imaging (MRI), showed a lesion occupying the right maxillary sinus and extending into the nasal cavity and ethmoid sinus. A malignant tumor of the maxillary sinus was suspected, and a biopsy was performed. The lesion was diagnosed as sinonasal undifferentiated carcinoma.

The patient was treated with chemoradiation therapy. After 4 cycles of chemoradiation therapy, CT and MRI showed shrinkage of the lesion and changes consistent with necrosis. Histological examination of a repeat biopsy specimen after the 4 cycles of chemoradiation did not contain tumor cells. 2 more cycles of chemoradiation therapy were added.

Six months after the initial diagnosis, CT finding suggested residual tumor in the ethmoid sinus. We performed another biopsy and the histopathological analysis was negative for tumor. The patient has been followed for 33 months since completing chemoradiation therapy, and there has not been any further evidence of disease.

1. Introduction

Sinonasal undifferentiated carcinoma (SNUC) is a rare malignant neoplasm of the paranasal sinuses. The age range is broad, and there is a male predominance (2–3:1) [1]. The most common symptoms of SNUC are facial pain, nasal obstruction, epistaxis and proptosis [2]. SNUC grows rapidly, frequently destroying sinus walls and penetrating into the cranial cavity or the oral cavity at an advanced stage. Patients with SNUC experience high rates of recurrence and metastasis to cervical lymph nodes and distant sites [1–4]. SNUC is a highly aggressive malignancy and it has a poor prognosis with a 5-year survival rate of less than 20%. Multimodality treatment, including surgical resection, has been recommended by most authors [1].

There are few prior reports regarding therapeutic strategies for SNUC. Here, we report a case of an SNUC of the maxillary sinus that was treated with chemotherapy by super-selective intra-arterial administration of cisplatin.

2. Case report

A 65-year-old woman was referred to the Department Of Oral Surgery, at our institution in February 2010 complaining of pain at her right maxilla. She had noticed a swelling for a month and had been going for endodontic therapy in the right first molar by her home dentist. She had also been under medical treatment for diabetes and hypertension.

Intraoral examination revealed marked tenderness with diffuse swelling of the gingiva in the right maxillary molar region from the ala of nose. Imaging studies including computed tomography (CT), contrast-enhanced CT, magnetic resonance imaging (MRI), and Gadolinium-enhanced MRI showed a lesion occupying the maxillary sinus and extending into the nasal cavity and ethmoid sinus (Fig. 1A–E). There were no abnormal findings in any other regions and there was no clinical evidence of cervical or distant metastasis. Laboratory data showed no abnormalities.

☆ AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

* Corresponding author at: 1851 Hozumi, Mizuho-City, Gifu 501-0296, Japan. Tel.: +81 58 329 1472; fax: +81 58 329 1472.
E-mail address: takaohta@dent.asahi-u.ac.jp (T. Ohta).

2212-5558/$ – see front matter
http://dx.doi.org/10.1016/j.ajoms.2013.10.001

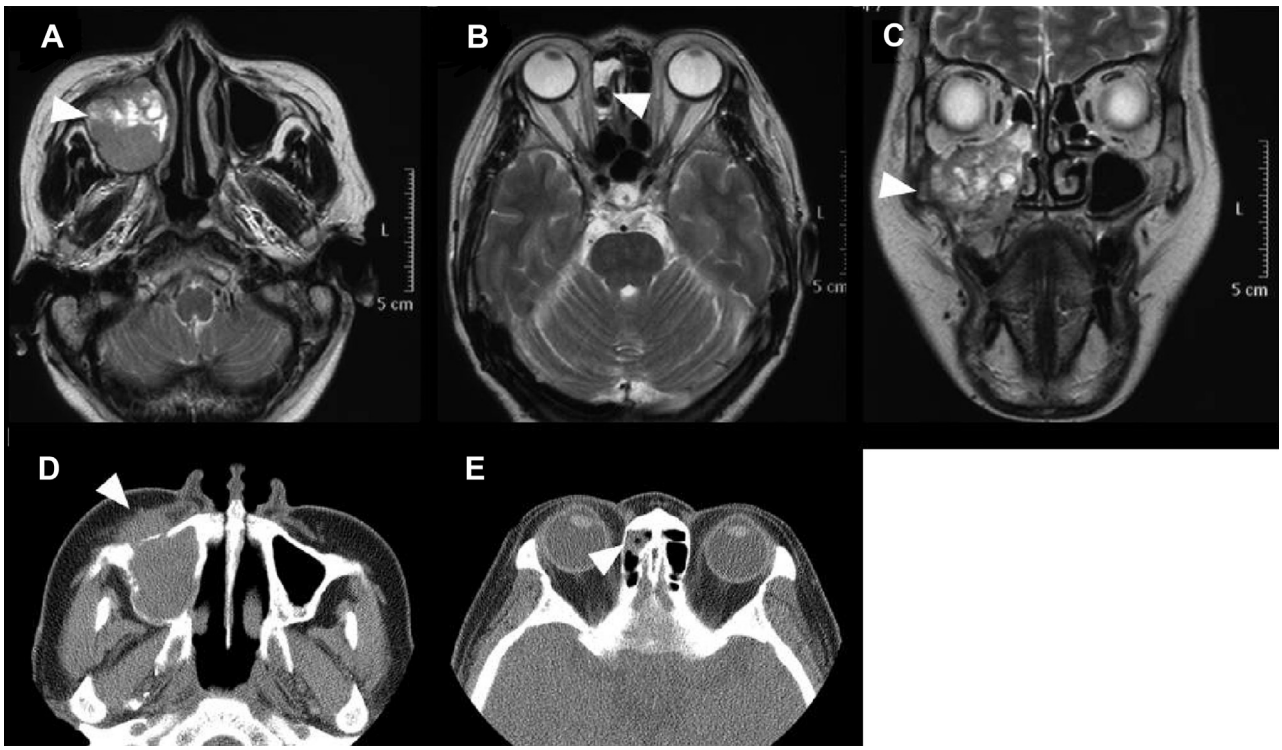

Fig. 1. Imaging studies of the patient before chemoradiation therapy. (A–C) MRI revealed the tumor showed isointensity and hyperintensity intermixed on T2-weighted images. (D and E) CT revealed the lesion filled in the right maxillary sinus with bony erosion and extended to ethmoid sinus and nasal cavity.

The patient underwent a biopsy of the maxillary sinus mass. The histopathological findings revealed invasive growth of alveolate tumor tissue. Neither squamous nor glandular differentiation was found in the nests and sheets of tumor cells. The tumor cells showed a high N/C ratio and nuclear pleomorphism with a marked increase in atypical mitotic figures. There was no evidence of permeation of the tumor into the blood or lymphatic vessels. The histological diagnosis of the biopsy specimen was sinonasal undifferentiated carcinoma classified as T3N0M0 (Fig. 2A and B).

Immunohistochemically, the tumor cells were positive for AE1/AE3 (Fig. 2C), epithelial membrane antigen (EMA), cytokeratin (CK) 7 and vimentin. The Ki67 (Fig. 2D) labeling index was >90%. Leukocyte common antigen (LCA), CD56, chromogranin A, synaptophysin, carcinoembryonic antigen (CEA), human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), CK20, and Epstein-Barr virus (EBV) were negative (Table 1).

Table 1
Immunohistochemical staining result.

Antibodies	Results
AE1/AE3	Nearly 100% (+)
EMA	(+)
CK7	(+)
Vimentin	(+)
Ki67	(+)
LCA	(−)
Chromogranin A	(−)
Synaptophysin	(−)
CEA	(−)
HCG	(−)
CK20	(−)
AFP	(−)
EBV	(−)

The tumor cells showed positive for AE1/AE3, EMA, CK7 and vimentin. The Ki67 labeling index was >90%. LCA, CD56, chromogranin A, synaptophysin, CEA, HCG, CK20, AFP and EBV were negative in tumor cells.

In March 2010, the patient underwent catheter placement in the right maxillary artery. The catheterization was performed using a microcatherter (Prowler 14, Cordis Neurovascular Inc., USA), which was placed subcutaneously into the superficial temporal artery and advanced into the maxillary artery under fluoroscopic guidance. Catheter placement was confirmed by injection of contrast medium and indigo carmine (Fig. 3).

The patient then underwent super-selective intra-arterial infusion of cisplatin (5 mg/m^2, 7 mg/body/day, 5 days weekly) via the internal maxillary artery along with external beam radiation therapy (2 Gy/day, 5 days/weekly). The same regimen was repeated for four cycles on a weekly basis.

After this course of chemoradiation therapy, CT and MRI showed shrinkage of the lesion and changes consistent with necrosis (Fig. 4A–D). We performed maxillary antrotomy and resection for definitive diagnosis. Histologically, the biopsy specimen showed inflammatory fibrous connective tissue, without tumor. The patient had achieved a complete response to the chemoradiation therapy.

Two more cycles of chemoradiation therapy of the same regimen were added in lieu of radical resection (total CDDP 189 mg, RT 60 Gy). The patient tolerated the additional chemoradiation well and was discharged on post-chemoradiation therapy day 2.

A month after the treatment, follow-up CT was suggestive of residual tumor in the ethmoid sinus (Fig. 5A and B). We again performed biopsy, and the pathological analysis was negative for tumor. We continued to follow the patient carefully, and by 33 months after the initial chemoradiation therapy she remained well and without any local or regional evidence of tumor recurrence or metastasis (Fig. 5C and D).

3. Discussion

Malignant neoplasms of the paranasal sinuses and nasal cavity including metastatic disease are rare, comprising only 3% of all head and neck malignancies [5]. Among these, SNUC is a highly

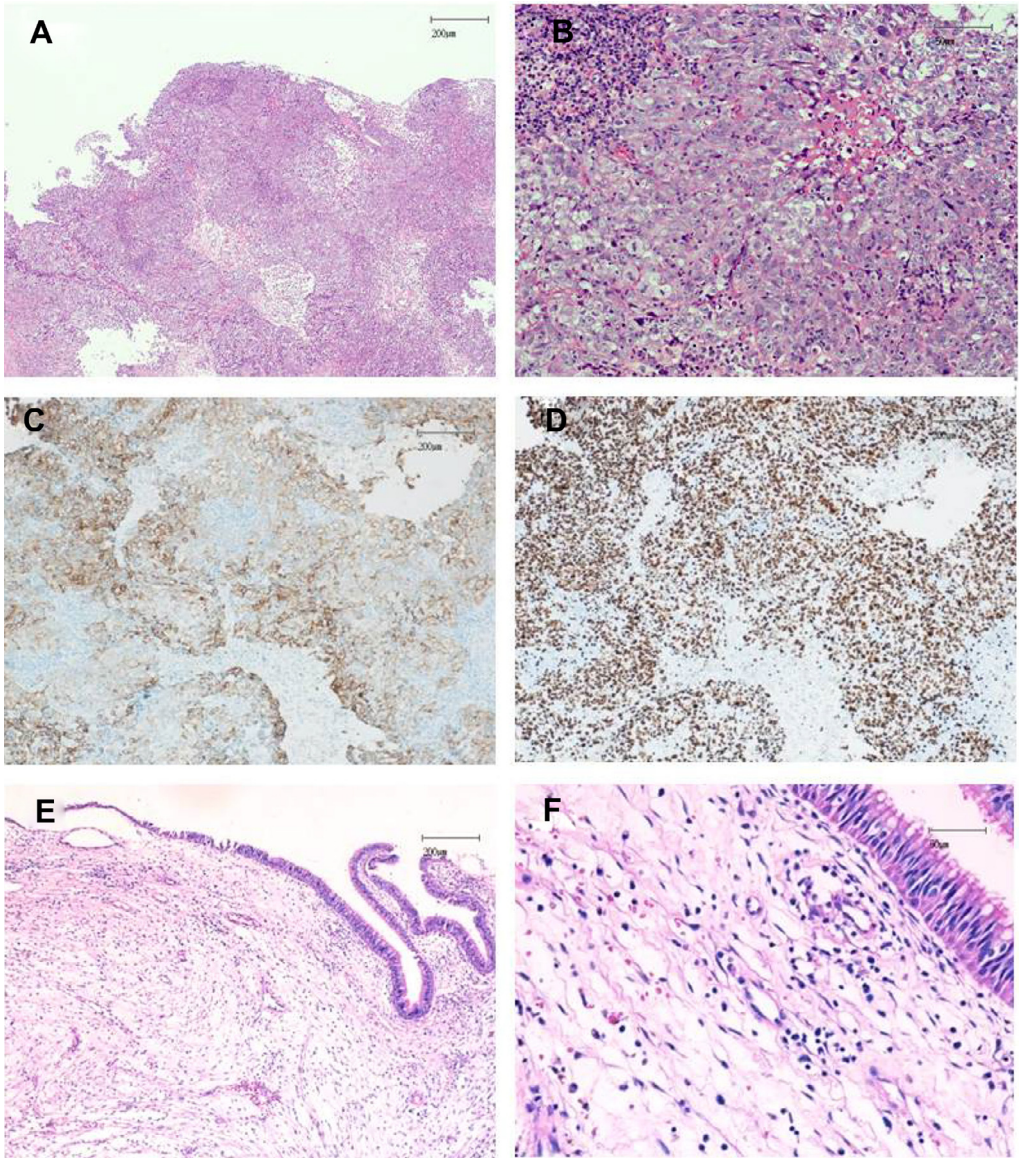

Fig. 2. (A and B) Before treatment, the tumor formed sheets with large size atypical cells. The cells were lacking of cornification, and revealed prominent atypism. The tumor revealed lymphocytic infiltration, prominent fission and apoptosis. (C) Immunohistochemical staining of AE1/AE3 showing positive reaction in the tumor. (D) The Ki-67 labeling index was >90% in tumor cells. (E and F) After 4 cycles chemoradiation therapy, the biopsy specimen showed inflammatory connective tissue, without tumor.

aggressive malignant neoplasm of the paranasal sinuses. Early symptoms of SNUC are similar to benign sinus disease. The lesion may remain undetected until patients present with nasal obstruction, epistaxis, or visual complications from orbital involvement. Dural and intraparenchymal brain involvement is often seen [6]. SNUC is believed to derive from the lining epithelium of the paranasal sinuses and nasal cavity. It was first classified as a separate entity in 1986 [7]. A recent study at the University of Michigan over 13 years reported an overall survival rate of 22% at 5 years, and estimated that 5 years distant metastasis free survival was 35% [1]. Other reports describe SNUC occurring with a 25–30% risk for distant metastasis [8]. Also 10–30% patients with SNUC have been shown to have clinically positive regional lymph nodes at the time of primary surgery or after treatment [3,9]. Lin et al. have suggested that the cervical lymph node basin must be addressed, even if neck disease is not clinically apparent [1].

Clinical, radiological, and immunohistochemical evidence can help in the differential diagnosis. Destruction of maxillary sinus walls can be identified radiographically in many cases of maxillary sinus malignant neoplasm, and SNUC is difficult to diagnose by panoramic radiography alone. Still, CT and MRI are beneficial aids to diagnosis of sinus lesions. CT shows an expansive lesion with bony erosion. MRI shows isointensity with gray matter on T1 weighted images, and slight hyperintensity on T2 weighted images [10].

Lymphoma, malignant melanoma, rhabdomyosarcoma, lymphoepithelial carcinoma, and olfactory neuroblastoma infrequently occur in the paranasal area. SNUC should be differentiated from these entities [11]. The definitive diagnosis is made by histological and immunohistochemical findings [6].

Histologically, SNUC forms nests, lobules, trabeculae and sheets in the absence of squamous or glandular differentiation. The nuclei are medium to large sized, surrounded by small amounts of eosinophilic cytoplasm. The diagnosis can be difficult based on light microscopy alone, and immunohistochemical characterization is necessary for definitive diagnosis [2]. The use of markers including keratin, vimentin, LCA, and S-100 has been beneficial.

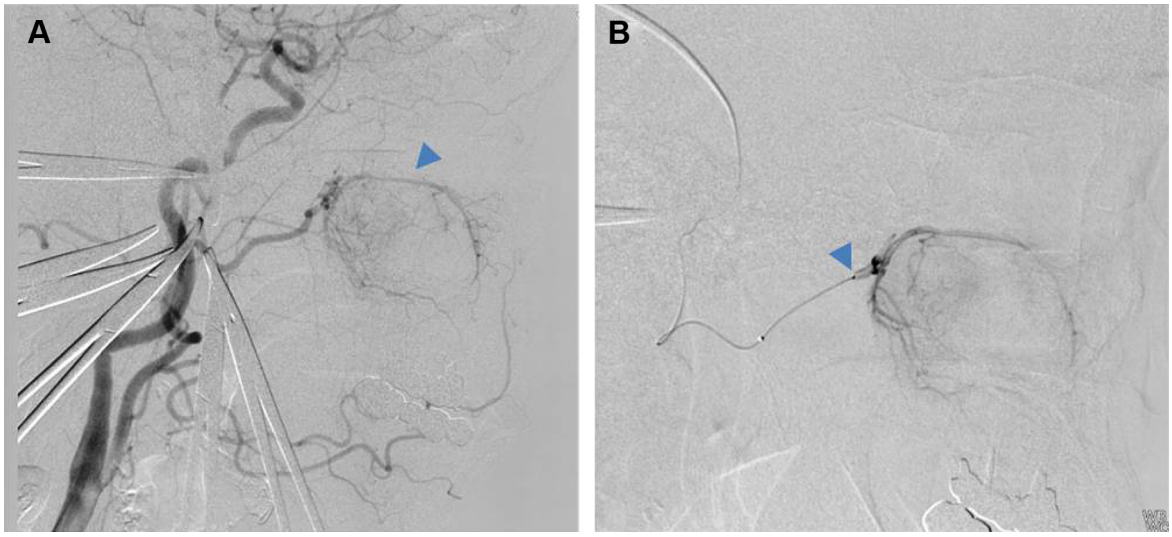

Fig. 3. (A) Transradial carotid angiogram was performed to define the feeding vessels (arrow head). (B) Catherization was performed through subcutaneously into STA, and advanced to maxillary artery. Arrow head indicates the tip of microcatherter.

In this case, we decided to delay surgical resection of the lesion at the time of the initial diagnosis. The patient was treated with super-selective intra-arterial chemotherapy and concurrent radiation therapy preoperatively. After chemoradiation therapy, CT and MRI revealed the lesion had changed in intensity and decreased in size. After treatment, there was no evidence of tumor cells in the repeat biopsy specimen.

We collected and compared recent case series that treated by surgery followed by postoperative chemoradiation therapy, chemoradiation therapy prior to surgery, or chemoradiation therapy without surgery, and we focused on the 5-year survival rates in those reports [1,12–15]. In these reports, patients treated with chemoradiation therapy without surgery had the best results, though this finding was not statistically significant. Our findings were similar to the studies of Lin et al. and Riscin et al. They suggested that patients with SNUC who underwent surgical resection prior to chemoradiation had a poorer prognosis and that perhaps surgical treatment delays the truly critical treatment for SNUC. Induction chemotherapy, such as administration of a platinum-based regimen concurrent with radiation therapy has been found to improve both locoregional control of the disease and to decrease distant metastasis [1,15].

Treatment of SNUC continues to present a challenge that requires a multidisciplinary approach, including otolaryngology head and neck surgery, neurosurgery, ophthalmology, radiation oncology, and medical oncology [13]. Further studies are necessary to elucidate the optimal treatment of SNUC.

Here we have reported a case in which a patient with SNUC was treated with chemoradiation therapy and achieved a complete response.

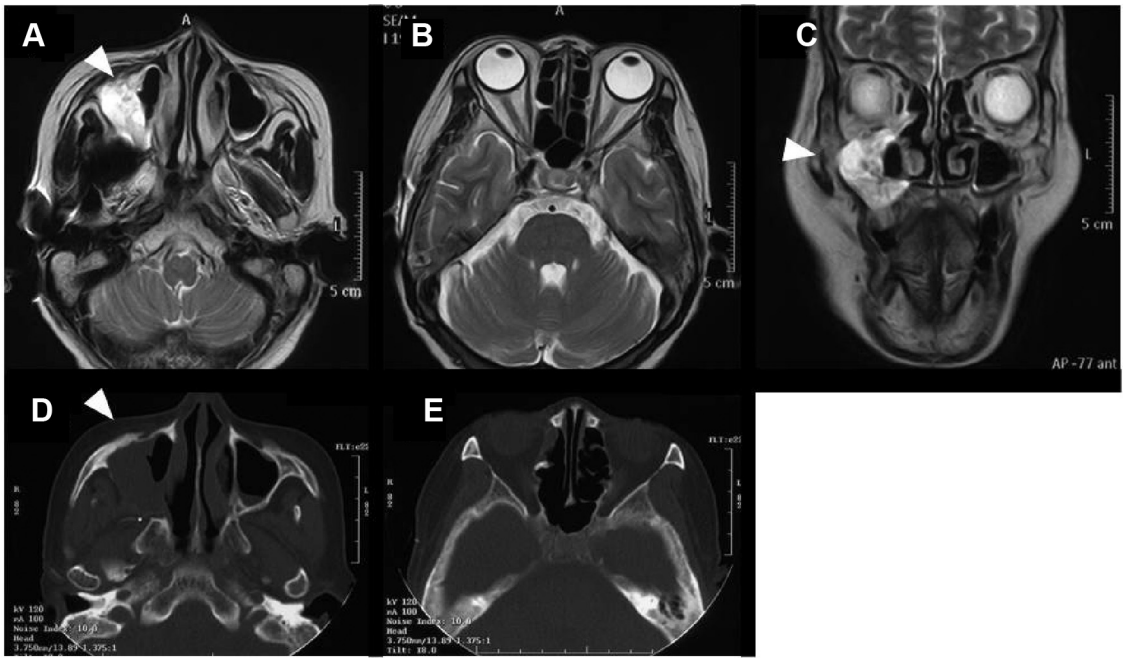

Fig. 4. (A–E) T2-weighted MRI and CT images of the patient after 4 cycles chemoradiation therapy, the lesion showed decreased volume and changed intensity on these images.

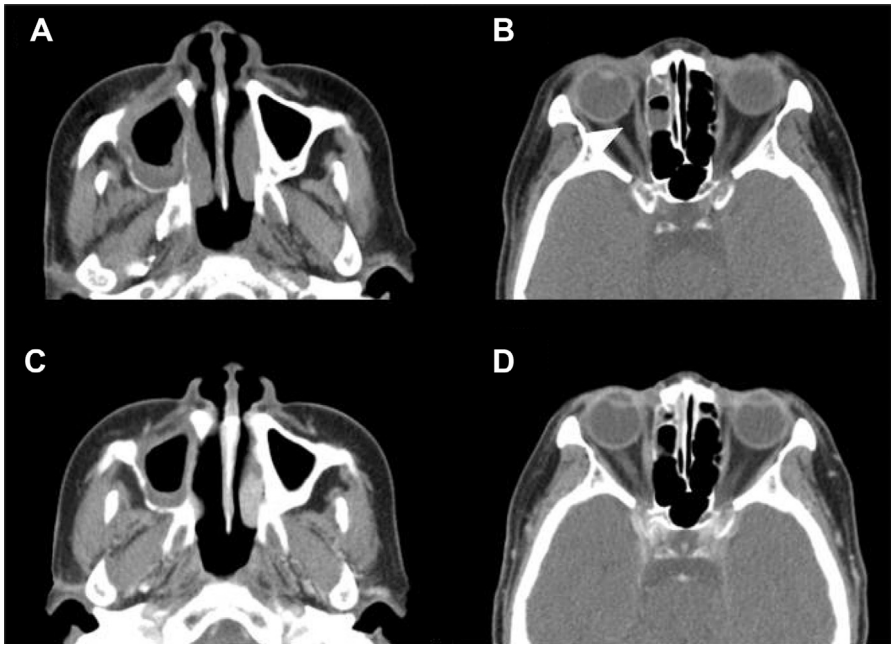

Fig. 5. (A and B) A month after additional chemoradiation therapy ended, follow-up CT was suggestive of residual tumor in the ethmoid sinus. But the pathological analysis was negative for tumor. (C and D) Recent CT images of the patient, there were no evidence of tumor recurrence or metastasis in the local or regional areas.

References

[1] Lin EM, Sparano A, Spalding A, Eisbruch A, Worden FP, Heth J, et al. Sinonasal undifferentiated carcinoma: a 13-year experience at a single institution. Skull Base 2010;20:61–7.
[2] Pitman KT, Costantino PD, Lassen LF. Sinonasal undifferentiated carcinoma: current trends in treatment. Skull Base Surg 1995;5:269–72.
[3] De Simone P, Coletti L, Campani D, Falcone A, Filipponi F. Liver transplantation for metastatic sinonasal undifferentiated carcinoma: a case report. Transplant Proc 2008;40:3821–2.
[4] Edwards PC, Hess SJ, Saini T. Sinonasal undifferentiated carcinoma of the maxillary sinus. J Can Dent Assoc 2006;72:163–7.
[5] Franchi A, Moroni M, Massi D, Paglierani M, Santucci M. Sinonasal undifferentiated carcinoma, nasopharyngeal-type undifferentiated carcinoma, and keratinizing and nonkeratinizing squamous cell carcinoma express different cytokeratin patterns. Am J Surg Pathol 2002;26:1597–604.
[6] Sohsman M, Yang HM, Cassarino DS. Sinonasal undifferentiated carcinoma metastatic to the skin. J Cutan Pathol 2010;37:1241–4.
[7] Frierson Jr HF, Mills SE, Fechner RE, Taxy JB, Levine PA. Sinonasal undifferentiated carcinoma. An aggressive neoplasm derived from Schneiderian epithelium and distinct from olfactory neuroblastoma. Am J Surg Pathol 1986;10:771–9.
[8] Gorelick J, Ross D, Marentette L, Blaivas M. Sinonasal undifferentiated carcinoma: case series and review of the literature. Neurosurgery 2000;47:750–4 [discussion 754–5].
[9] Tranzler Ed Morris CG, Orlando CA, Werning JW, Mendenhall WM. Management of sinonasal undifferentiated carcinoma. Head Neck 2008;30:595–9.
[10] Sharara N, Muller S, Olson J, Grist WJ, Grossniklaus HE. Sinonasal undifferentiated carcinoma with orbital invasion: report of three cases. Ophthal Plast Reconstr Surg 2001;17:288–92.
[11] Menon S, Pai P, Sengar M, Aggarwal JP, Kane SV. Sinonasal malignancies with neuroendocrine differentiation: case series and review of literature. Indian J Pathol Microbiol 2010;53:28–34.
[12] Revenaugh PC, Seth R, Pavlovich JB, Knott PD, Batra PS. Minimally invasive endoscopic resection of sinonasal undifferentiated carcinoma. Am J Otolaryngol 2011;32:464–9.
[13] Musy PY, Reibel JF, Levine PA. Sinonasal undifferentiated carcinoma: the search for a better outcome. Laryngoscope 2002;112:1450–5.
[14] Parbhu KC, Galler KE, Murphy BA, Pitchford CW, Mawn LA. Primary ocular presentation of sinonasal undifferentiated carcinoma. Ophthal Plast Reconstr Surg 2010;26:61–3.
[15] Riscin D, Porceddu S, Peters L, Corry J, Weih L. Promising results in chemoradiation with sinonasal undifferentiated carcinoma. Head Neck 2004;26:435–41.