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SMARCB1-Deficient Sinonasal Carcinoma: A Case Report and Review of the Literature

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1. Abstract

This article reports a case of SMARCB1 (INI-1)-Deficient Sinonasal Carcinoma. The patient went to the doctor with "blood streaks in the right nasal discharge and swelling and pain on the right cheek". Sinus imaging showed occupying the right maxillary sinus and surrounding bone destruction. The new biopsy of the right maxillary sinus orifice under nasal endoscopy considered cancerous lesions. After complete removal of the right maxillary sinus mass, immunohistochemistry and fluorescence in situ hybridization (FISH) were performed, and the final diagnosis of SMARCB1 (INI-1)-deficient sinonasal carcinoma was confirmed. Postoperative oncology department received radiotherapy and concurrent chemotherapy with etoposide and cisplatin. No recurrence of the right maxillary sinus mass was found during the follow-up treatment, and the patient's right facial pain disappeared. He was satisfied with the treatment effect. After 6 months of follow-up, there was no tumor recurrence or metastasis.

2. Case Report

A 62-year-old male presented with 1-month history of right blood-tinged rhinorrhea and swelling and pain in the right cheek, and right eye pain but no vision changes, no eye proptosis or diplopia. He had no personal history of head and neck cancer, radiation exposure, or workplace environmental exposures. He was a never-smoker. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) performed at an outside hospital revealed a sinonasal mass centered on the right maxillary sinus, with destruction of the inner wall of the maxillary sinus and the orbital floor. The nasal endoscopy at our hospital showed that the right maxillary sinus orifice was red and new organisms were prominent (Figure 1). A biopsy of the right maxillary sinus orifice mass was performed and the immunohistochemical examination results: INI-1 (lost), CK5/6 (focal, +), P40 (diffuse nuclear medium intensity +), P63 (focal, +), CgA (-), CD56 (-), AE1/AE3 (strong diffuse cytoplasm +), Syn (partially colored), P16 (partially colored), Fluorescence in situ hybridization: EBER (-). The tumor cells were negative (deficient) for SMARCB1 (INI-1). Hence, the diagnosis was amended to SMARCB1 (INI-1)-deficient sinonasal carcinoma (Figure 2A-C). There was no evidence of regional or distant metastasis. He underwent complete resection of the tumor and resection of the inner bony wall of the right maxillary sinus by nasal endoscopic pre-lacrimal crypt approach combined with middle nasal passage approach, and the margins of each wall of the maxillary sinus were frozen and no cancer was found. Postoperatively the second immunohistochemistry examination showed the tumor cells were negative (deficient) for SMARCB1 (INI-1), and genetic testing is recommended. It was sent to Guangzhou Jinyu Medical Testing

Center for fluorescence in situ hybridization (FISH) detection, and the result showed that the SAMRCB1 gene was missing, which further supports the diagnosis of SMARCB1-deficient sinonasal carcinoma (Figure 2D). Postoperatively, the patient was treated with radiation therapy (total radiation dose 66Gy, 2Gy/day, 5 days/week) with adjuvant cisplatin and etoposide chemotherapy. The patient has recovered well after treatment and was currently being followed up for 6 months. There is no recurrence or metastasis of the tumor. The patient is currently living in good condition and is continuing to follow up.

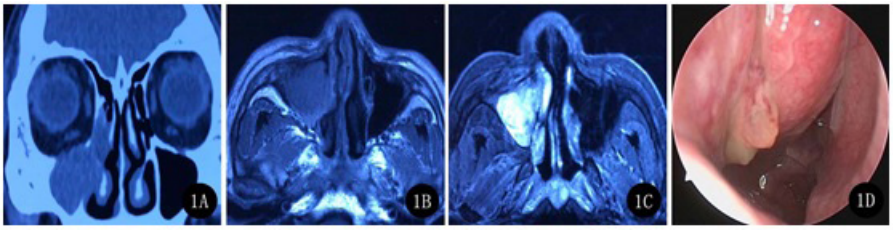

Figure 1: CT, MRI images and endoscopy of the patient's sinuses showed masses in the right maxillary sinus and surrounding bone destruction, Malignant tumors may be. **A**: Coronal CT; **B**: Horizontal MRI-T1 shows isosignal shadow; **C**: Horizontal MRI-T2 enhancement showed high-intensity shadow; **D**: endoscopic showed new creatures at the right maxillary sinus.

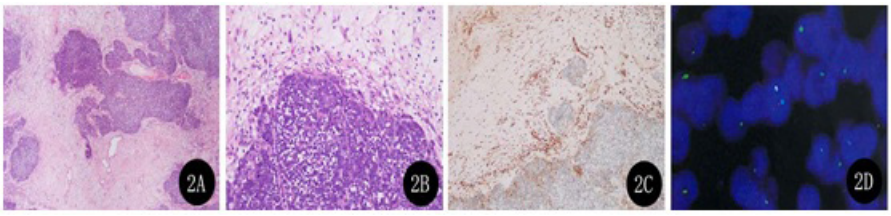

Figure 2: Immunohistochemical examination and fluorescence in situ hybridization (FISH) detection results **A (HE, 40X):** low magnification shows that tumor cells are arranged in irregular nests, surrounded by dense fibrous stroma, no obvious glands are seen tubular differentiation or squamous epithelial differentiation; **B (HE, 200X):** tumor cells are basal-like or clear cell-like at high magnification; **C (immunohistochemistry INI-1, 100X):** tumor cell INI-1 immune group at the bottom right of the picture negative analysis, suggesting that SMARCB1 (INI-1) is missing, and the non-tumor stromal cells on the upper left side are positive for INI-1; **D (FISH):** detects SMARCB1 gene deletion, green fluorescent marker EWSR1 (22q12) probe, red fluorescent mark the SMARCB1 (22q11) probe.

3. Discussion

SMARCB1 (INI1)-Deficient Sinonasal Carcinoma (SDSC) is a newly reported type of rare nasal cavity and paranasal sinus carcinoma characterized by the loss of nuclear INI1 expression. It was developed by Agaimy et al [1] and Bishop et al [2] First reported and named at the same time in 2014.At present, there are few case reports and related studies on SDSC. Nasal cavity and paranasal sinus cancer accounts for about 3%-5% of the entire head and neck tumors, and SDSC is even rarer. The latest literature reports about 82 cases of this disease in the world [3], The disease was reported for the first time in my country in 2018, and currently there are only 2 reports in Chinese search [4, 5]. In 2019, Goda et al [6] reported the disease for the first time in Japan. In the 2017 WHO classification of head and neck tumors, this tumor has not yet been independently classified as a new name. It is only regarded as a subclass of nasal cavity and sinus undifferentiated cancer.

The age of onset of SDSC is 19-89 years (median age is about 52 years), and the ratio of male to female is about 1.5:1. The most common site of tumor is the ethmoid sinus, which often invades the surrounding sinuses, orbits, anterior skull base, intracranial or far Metastasis with nasal congestion, nosebleeds, headache, diplopia and other corresponding clinical symptoms [7]. On imaging, SDSC often showed invasive growth. Half of the cases showed invasive bone destruction images on CT. MRI showed low to moderate signal on T2WI with obvious uneven enhancement [8].

In terms of tissue morphology, most SDSCs appear as basal-like cells and rhabdoid-like cells. According to the mixed composition of basal cell-like cells and rhabdoid cells, Agaimy et al [1] histologically divided them into basal cell-like type (accounting for about 60%), rhabdoid type (accounting for about 36%), and sarcoma type (accounting for about 4%).Basal cell-like tumor cells have less cytoplasm, high nuclear-to-cytoplasm ratio, scattered nuclear chromatin, and more obvious nucleoli. This case belongs to this subtype. The characteristic immunophenotypes of SDSC include diffuse expression of CKpan and complete loss of INI1 protein expression. The positive rate of CKpan is 97%-100%. Basal cell-like cells are often CK5/6 (+), P63 (+), P40 (+), Vimentin (-), and striated muscle-like cells are CK5/6 (-), P63 (-), P40 (-), Vimentin (+); CK7 positive rate is 48%, but it is usually focal positive; neuroendocrine markers Syn, CgA, CD56 are partially positive, and a small number of cases can express both neuroendocrine markers at the same time; the positive rate of P16 17%, but high-risk

HPV tests are all negative; EBER in situ hybridization tests are all negative[1,7].The immunohistochemical examination of this patient found that the lack of INI1 protein expression has tended to diagnose the disease, while CK5/6 (focal, +), P63 (focal, +), P40 (focal, +) support basal cell-like sub Type diagnosis.

SMARCB1 (also known as INI1 or BAF47) is a tumor suppressor gene located on chromosome 22q11.2[9]. Its gene expression product INI1 protein is widely expressed in the nucleus of normal cells and can be detected by routine immunohistochemistry. Fluorescence in situ hybridization (FISH) detection revealed the SMARCB1 gene Homozygosity or loss of heterozygosity is helpful for further accurate diagnosis of the disease[10].The LBP-SMARCB1 gene deletion probe used for detection is a counting probe, green fluorescently labeled EWSR1 (22q12) probe, red fluorescently labeled SMARCB1 (22q11) probe, the normal signal pattern is 2G2R, and the typical positive signal pattern is 2G1R or 2G(Note: G is green signal, R is red signal).First, the pathologist will evaluate the morphology of the tissue HE slides, select the tumor area, use the LBP-SMARCB1 gene deletion probe to perform fluorescence in situ hybridization, analyze the tumor area, and count 200 divisions in at least two fields of view Phase cells. The signal patterns of the 200 interphase cells analyzed in this patient are as follows: 1G0R 88.5%, 2G0R 10.0%, 2G2R 0.5%, and 1G1R 1.0%, which are consistent with SMARCB1 gene deletion changes.

Loss of INI1 protein expression caused by inactivation of INI1 gene is related to the occurrence of many malignant tumors (collectively referred to as INI1-deletion tumors), including atypical teratoid/rhabdoid tumor (AT/RT) of the central nervous system , kidney and soft tissue malignant rhabdoid tumors, renal medullary carcinoma, epithelioid sarcoma, epithelioid malignant peripheral nerve sheath tumors, myoepithelial carcinoma and extraosseous mucinous chondrosarcoma, et al. SDSC is a newly recognized malignant tumor of the nasal cavity and paranasal sinuses, and it is a new member of the INI1-deletion tumor family [11].Basal cell-like INI1-deficient sinonasal carcinoma needs to be differentiated from basal cell-like squamous cell carcinoma, lymphoepithelial carcinoma and NUT carcinoma; rhabdoid INI1-deficient sinonasal carcinoma needs to be differentiated from rhabdoid meningioma, rhabdomyosarcoma , AT/RT, extraosseous mucinoid chondrosarcoma, dedifferentiated chordoma; sarcoma-like type INI1-deficient sinonasal carcinoma needs to be differentiated from spindle cell squamous cell carcinoma, fibrosarcoma, leiomyosarcoma and spindle cell rhabdomyosarcoma. SDSC lacks the typical features of squamous differentiation and squamous epithelial dysplasia such as intercellular bridges and keratinized beads. Loss of INI1 nuclear expression, negative EBER, and comprehensive immunohistochemical examination. Tumor cells do not express S-100, SMA, Calponin, Desmin, MyoD1, Myogenin, CD34 and NUT can be distinguished from the above diseases; FISH detection technology has good sensitivity and specificity in terms of gene breakage and rearrangement, but it is impossible to determine whether the gene is broken or rearranged if the fluorescently labeled region is missing. Therefore, each detection method has certain limitations. It needs to be combined with the results of other detection methods to make an accurate diagnosis and differential diagnosis.

SDSC lacks an effective treatment plan. Surgery to completely remove the tumor, combined with postoperative radiotherapy and chemotherapy is the main treatment at present. Agaimy et al [7] reported 9 survivors of 39 SDSC patients during follow-up, and 7 of them received radical surgery plus radiotherapy. Wasserman et al [12] reported that 2 cases of SDSC patients received adjuvant radiotherapy and chemotherapy before surgery and the tumor volume was significantly reduced, which helped complete tumor resection and improved patient survival. Kakkar et al [13] reported 4 cases of SDSC patients with cisplatin-based adjuvant chemotherapy and achieved good short-term results.INI1 is related to a variety of key protein channels, and the research on these channel proteins provides application prospects for targeted drug therapy [14].

4. Summary

SDSC is an aggressive tumor. The effect of surgical treatment, radiotherapy and chemotherapy is not good, and the prognosis is poor. Most of them are locally advanced infiltrating and destructive growth. Local recurrence and distant metastasis often occur after treatment [15]. Agaimy et al [7] conducted a retrospective analysis of 39 SDSC patients and found that 56% of the patients died of the tumor within a few days to 102 months after diagnosis, with a median survival time of only 15 months; in 30 surviving cases during the 115-month follow-up (median 17 months), 33% of patients had local recurrence, and 37% (11 cases) had distant metastases, including lungs, pericardium, pleura, bone, and soft tissues of the thighs. SDSC is clinically rare. In patients who are characterized by the lack of INI1 protein cell expression in the clinic, the possibility of the disease should be considered. Therefore, strengthening the understanding of the disease will help early clinical diagnosis and active treatment, and improve the effective treatment rate of patients.

References

1. Agaimy A, Koch M, Lell M, et al. SMARCB1(INI1)-deficient sinonasal basaloid carcinoma: a novel member of the expanding family of SMARCB1-deficient neoplasms. Am J Surg Pathol. 2014; 38(9): 1274-81.
2. Bishop JA, Antonescu CR, Westra WH. SMARCB1 (INI-1)-deficient carcinomas of the sinonasal tract. Am J Surg Pathol. 2014; 38(9): 1282-9.
3. Parsel SM, Jawad BA, McCoul ED. SMARCB1-deficient sinonasal carcinoma: systematic review and case report. World Neurosurg. 2020; 136: 305-10.

4. Minghui Zhang, Yanhui Liu. A case of INI1-deficient sinonasal carcinoma and literature review. J Clin Exp Pathol. 2018; 34(12): 1386-8.
5. Shenjun Tang, Changwen Zhai, Cuncun Yuan, et al. SMARCB1 (INI1)-deficient sinonasal carcinoma: a clinicopathological analysis of six cases. Chin J Pathol. 2020; 49(1): 47-51.
6. Goda N, Haga H, Sumiyoshi S, et al. A case of SMARCB 1 (INI l)-deficient sinonasal carcinoma presenting as an ethmoid mass. Diagnostic pathology. 2019; 36(2): 125-9.
7. Agaimy A, Hartmann A, Antonescu CR, et al. SMARCB1(INI-1)-defificient sinonasal carcinoma: a series of 39 cases expanding the morphological and clinicopathological spectrum of a recently described entity. Am J Surg Pathol. 2017; 41(4): 458-71.
8. Shatzkes DR, Ginsberg LE, Wong M, et al. Imaging appearance of SMARCB1 (INI1)-deficient sinonasal carcinoma: a newly described sinonasal malignancy. AJNR Am J Neuroradiol. 2016; 37(10): 1925-9.
9. Hollmann TJ, Hornick JL. INI1-deficient tumors: diagnostic features and molecular genetics. Am J Surg Pathol. 2011; 35: e47–e63.
10. Owosho AA, Zhang L, Rosenblum MK, et al. High sensitivity of FISH analysis in detecting homozygous SMARCB1 deletions in poorly differentiated chordoma: a clinicopathologic and molecular study of nine cases. Genes Chromosomes Cancer. 2018; 57(2): 89-95.
11. Agaimy A. The expanding family of SMARCB1(INI1)-deficient neoplasia: implications of phenotypic, biological, and molecular heterogeneity. Adv Anat Pathol. 2014; 21(6): 394-410.
12. Wasserman JK-Dickson BC-Perez-Ordonez B-et al. INI1(SMARCB1)-deficient sinonasal carcinoma: a clinicopathologic report of 2 cases. Head Neck Pathol. 2017; 11(2): 256-61.
13. Kakkar A-Antony VM-Pramanik R, et al. SMARCB1(INI1)-deficient sinonasal carcinoma: a series of 13 cases with assessment of histologic patterns. Hum Pathol. 2019; 83: 59-67.
14. Carugo A, Minelli R, Sapio L, et al. p53 is a master regulator of proteostasis in SMARCB1-deficient malignant rhabdoid tumors. Cancer Cell. 2019; 35(2): 204-20.
15. McHugh KE, Policarpio-Nicolas MLC. Metastatic SMARCB1 (INI-1)-deficient sinonasal carcinoma diagnosed by endobronchial ultrasound-guided fine-needle aspiration(EBUS-FNA): a potential diagnostic pitfall and review of the literature. Acta Cytol. 2019; 63(5): 431-7.