

# Application of Chemotherapy in Patients with Advanced Olfactory Neuroblastoma with Multiple Metastases: A Case Report and Review of Literatures

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Esthesioneuroblastoma; Multiple metastasis; Chemotherapy

## 1. Abstract

**1.1. Background:** Olfactory neuroblastoma or esthesioneuroblastoma (ENB) is a rare malignant tumor arising from the olfactory epithelium, which is commonly treated by surgery and radiotherapy (RT). However, the benefit of chemotherapy has not been clearly addressed. Therefore, this case report focused on the potential role of chemotherapy in late-stage ENB patients with multiple and recurrent metastasis.

**1.2. Case Report:** A 46-year-old male was diagnosed with olfactory neuroblastoma by biopsy 2 years ago with suspected cervical lymph node and lung metastasis by ultrasound and thoracic enhanced CT. Considering lesions in multiple sites, we decided to perform endoscopic nasal lumpectomy to remove tumor, followed by systemic chemotherapy and thirty times of standard RT on both the cervical lymph nodes and the pulmonary metastatic nodules. The aforementioned treatment provided preferable outcome, both metastasis in the neck and lung were eliminated and the patient was discharged. However, 1 year after discharge, pulmonary nodules were found again in the right upper lobe and both lower lobes with lymph nodes enlargement in the right hilar. Therefore, a second time of chemotherapy was provided to get rid of the re-appearing lesions. Fortunately, the pulmonary nodules were quite sensitive to chemotherapy and they were successfully resected by thoracoscopy following chemotherapy. According to a long-term follow-up, the patient hasn't manifested any related clinical symptoms since the second discharge.

**1.3. Conclusion:** Through our experiences, we learned that patients with olfactory neuroblastoma could benefit from regular

chemotherapy, especially those with multiple organs metastasis or in advanced stage.

## 2. Introduction

Olfactory neuroblastoma or esthesioneuroblastoma (ENB) is a rare malignant tumor arising from the olfactory epithelium, which is commonly treated by surgery and radiotherapy (RT) [1-3]. Although some previous studies confirmed the positive efficacy of chemotherapy in patients with ENB, limited restriction on tumor growth and frequent occurrence of adverse effect has prevented more well-rounded application of chemotherapy. In recently years, with the ever widely accepted concept of precise medication, adverse effects of chemotherapy in ENB patients have caught the attention of clinicians worldwide, which inevitably restricted the use of chemotherapy. However, as far as we are concerned, chemotherapy is of paramount importance in down-regulating tumor stage so as to provide opportunities for surgeries in patients with late-stage or advanced tumor where surgeries are not primarily considered [4-5]. Therefore, to more detailedly understand the positive functions of chemotherapy in patients with ENB, we reported a case with ENB receiving two rounds of chemotherapy combined with two radical surgeries who seemed to have received preferable benefits of chemotherapy [6-7].

## 3. Case Presentation

A 46-year-old male suffering from olfactory neuroblastoma was admitted to the Department of Otolaryngology and Head-Neck Surgery of West China Hospital, Sichuan University. His history indicated that he developed left nasal discharge stained with blood 2 years ago, concomitant with left nasal congestion without dizzi-

ness, tinnitus, cough, or dyspnea. In our hospital, enhanced MRI of the brain was provided which indicated a lump in left ethmoid sinus and nasal cavity, highly foreboding malignant tumor. In the meantime, nasal endoscopy found a neoplasm in the left nasal cavity located at the nasal septum part of olfactory cleft region which was likely to be malignant. Therefore, the patient received endoscopic nasal lumpectomy and external transfer of inferior turbinate fracture and subsequent pathological and immunohistochemistry tests indicated the existence of neuroblastoma. However, neck and thoracic enhanced CT as well cervical ultrasound indicated suspicious metastasis of cervical lymph nodes and pulmonary nodules. Thus, subsequent PET-CT was arranged which indicated high glucose metabolism of the abovementioned lesions. To confirm this, we performed puncture of cervical lymph nodes and thoracentesis, which generated positive results indicating metastasis. Since metastasis was confirmed, even if surgery had been done, we believed accessory therapies should be added in order to prevent further metastasis and relapse. Therefore, 10 times of radiotherapy (RT) was applied to the pulmonary nodules and 8 times of RT was applied to cervical lymph nodes to get rid of metastatic lesions. Considering the complexity of the patient, phase I-II trials of EP chemotherapy regimens (etoposide 100mg D1-5, cisplatin 50mg, 50mg, 40mg), phase I-II trials of AI chemotherapy regimens (Pirarubicin hydrochloride 60mg D1 IVGTT, cyclophosphamide 1500mg D1-4 IVGTT, q3w), phase III-IV trials of EP chemotherapy regimens (etoposide 100mg D1-5, cisplatin 50mg, 50mg, 40mg) and phase III-IV trials of AI chemotherapy regimens (Pirarubicin hydrochloride 60mg D1 IVGTT, cyclophosphamide 1500mg D1-4 IVGTT, q3w) were applied subsequently. The patient recovered well after chemotherapy and was discharged under satisfactory body condition.

However, 1 year after discharge, during follow-up in the outpatient department, the patient's thoracic enhanced CT indicated reappearing calcified nodules in the upper lobe of right lung and granuloma in the right lower lobe with scattered inflammation in both lobes without signs of lymph node enlargement of neck. Therefore, another round of chemotherapy was arranged in order to decrease the size of the nodules. After the nodules' sizes were reduced within resection capacity, we performed wedge resection of the upper and lower lobes of the lung and mediastinal lymphadenectomy. During the surgery, we found the nodules in right upper and lower lobes were 1.8 cm and 0.7 cm respectively, which were more than 2 cm distance to eminence. Biopsies of multiple lymph nodes and resected nodules indicated tumor metastasis and extensive fibrosis with neuroblastoma and chondrocyte or osteocyte hamartomas in the resected lung tissue. After surgery, the patient felt good, except for scattered inflammation in the lung manifested by enhanced CT.

#### 4. Discussion

According to guidelines, effective treatments recommended main-

ly include surgery and RT, among which chemotherapy is not adequately mentioned [8]. Although several studies reported the attempts to treat patients with olfactory neuroblastoma by chemotherapy, the actual effect remains unclear. In this patient, we chose chemotherapy to improve long-term survival after baseline treatment of surgery and RT [9]. Accordingly, the patient did get a 1-year disease free survival postoperatively. However, we did find disease recurrence in the lungs determined by pathological biopsy 1 year after discharge, thus we added another AI chemotherapy regimen to prevent a worse prognosis. After all chemotherapy regimens, long-term follow-up was conducted to make sure there would no longer be significant progression of tumor [10-11].

As we know, olfactory neuroblastoma was an uncommon nasal malignant tumor arising from neuro-epithelium, in which primary surgery followed by radiotherapy was the standard treatment, especially for higher grade lesion [12]. On account of the particularity of this patient, we added two chemotherapy regimens after the standard treatment even though the outcome of the chemotherapy regimen was not defined. We could not deny the effect of chemotherapy, because the patients didn't develop further metastasis after receiving two rounds of chemotherapy [13]. On the contrary, according to our recordings, chemotherapy actually restricted the development of pulmonary metastases and prompted the subsequent resection of nodules. Therefore, a combination of nasal surgical resection, definitive RT and adjuvant chemotherapy should be considered reliable [14]. However, during literature review, several studies showed that adjuvant chemotherapy following primary surgery and RT in neuroblastoma did not exhibit improved outcomes compared to primary surgery and RT alone. According to their studies, platinum-based adjuvant chemotherapy failed to provide more preferable outcomes regardless of Kadish stage from B, C to D, on condition that the tumor was not detected at an early stage [15]. However, other studies revealed that olfactory neuroblastoma was sensitive to chemotherapy and chemotherapy was especially useful for advanced, recurrent or metastatic tumor [16]. As a result, the exact role of chemotherapy in the treatment of neuroblastoma as the timing of such therapy was still unclear. However, in terms of treating outcome, this patient was in good condition after chemotherapy and resection of pulmonary metastases without further tumor development during AI and EP chemotherapy.

According to previous reports, cervical metastasis was often observed in advanced neuroblastoma patients [17]. What was special of the patient we described was that he had metastases in both the cervical and pulmonary regions. Literatures including guidelines only concluded that chemotherapy was not recommended in patients without advanced development. Thus, we suspected that chemotherapy might be an efficient pathway to treatment patients with more easily metastatic neuroblastoma or patients in more advanced conditions.

## 5. Conclusion

Through our experiences, we learned that patients with olfactory neuroblastoma could benefit from regular chemotherapy, especially those with multiple organs metastasis or in advanced stage.

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