A Case of Olfactory Neuroblastoma (Esthesioneuroblastoma) Presenting with Anemia Due to Nasal Bleeding

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A 69-year-old man was referred to our hospital because of occasional nosebleeds over a period of 6 months. Physical examinations were unremarkable except for anemia. Laboratory findings on admission indicated a hemoglobin level of 7.8 g/dL. Magnetic resonance imaging revealed a mass occupying the right nasal cavity and infiltrating the bones of the paranasal sinus. Histological findings revealed olfactory neuroblastoma (esthesioneuroblastoma) and the disease was diagnosed to be at a locally inoperable advanced stage. Concurrent chemoradiotherapy (cisplatin plus etoposide and 60 Gy in 30 fractions of 2.0 Gy) was performed. Chemoradiotherapy failed to show significant tumor size reduction, but the nosebleeds stopped. The patient remains disease-free over 3 years after treatment. Although olfactory neuroblastoma is an extremely rare nasal tumor, we should be aware of the disease as a potential cause of nasal bleeding and anemia. Shinshu Med J 64 : 247—252, 2016

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I Introduction

Olfactory neuroblastoma (ONB), or esthesioneuroblastoma, is a rare tumor originating from the olfactory neuroepithelium, which was first described by Berger et al. in 1924. ONB accounts for approximately 2%-3% of all sinonasal tumors with an incidence of approximately 0.4 cases per million. Clinically, ONB presents most commonly as a large, unilateral, polypoid, glistening, red-gray mass in the superior nasal cavity. Therefore, the primary clinical symptoms are unilateral nasal obstruction and epistaxis. We encountered a case of ONB with occasional epistaxis over a period of 6 months and subsequently presenting with persistent nasal bleeding after biopsy examination. The patient was treated with chemoradiotherapy and remains disease-free over 3 years after treatment. Here, we describe the clinical course and discuss the disease and therapy.

II Case Presentation

A 69-year-old man was referred to our hospital because of occasional nosebleeds over a period of 6 months. Physical examinations were unremarkable except for anemia and identification of a mass in the right nasal cavity. There was no superficial lymph node swelling. Laboratory findings indicated a hemoglobin level of 8.7 g/dL (MCV 83.0 fl, MCH 24.6 pg, MCHC 29.7%). Computed tomography (CT) and magnetic resonance imaging (MRI) showed a hypervascular mass occupying the right nasal cavity and infiltrating the bones of the paranasal sinus (Fig. 1, 2). After biopsy of the right nasal mass, the patient went home. Two days later, he had a persistent nosebleed and was taken by ambulance to our hospital where he was admitted. Gauze packing and intravenous hemostatic drugs
were applied. The bleeding showed marked reduction, but his anemia progressed and his hemoglobin level decreased to 7.8 g/dL. Histological findings showed groups of atypical small round cells with hyperchromatic nuclei under the epithelium (Fig. 3). The immunohistochemical findings revealed that the atypical cells were negative for cytokeratin (CK) AE1/AE3, S-100 protein, and melanoma-associated antigen (HMB) 45 (Fig. 4), and positive for chromogranin A and synaptophysin, neuron-specific enolase (NSE) (Fig. 5). These observations were consistent with the histological findings of ONB, although Flexner-Wintersteiner and/or Homer Wright rosettes were not observed. In addition, tumor cells were negative for CD 99 and bcl2 in immunohistochemical examination, distinguishing them from Ewing sarcoma and primitive neuroectodermal tumor. Ki-67 labeling index was 7 % in
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Fig. 3 Hematoxylin and eosin staining, low- (A) and high-power fields (B). Groups of atypical small round cells with hyperchromatic nuclei were observed under the epithelium. Flexner-Wintersteiner and/or Homer Wright rosettes were not observed in the present case.

Fig. 4 Immunohistochemical findings indicated that malignant cells were negative for cytokeratin (CK) AE1/AE3 (A) or S-100 protein in the low-power field (B). S-100 protein-positive cells were observed in the high-power field (C), but these cells seemed to be sustentacular cells.
Fig. 5 Immunohistochemical findings indicated that malignant cells were positive for chromogranin A (A) and synaptophysin (B).

However, histological diagnosis is essential for ONB because of the broad and complex histological findings in tumors arising from the sinonasal tract, including squamous cell carcinoma, sinonasal undifferentiated carcinoma, small cell neuroendocrine carcinoma, rhabdomyosarcoma, Ewing sarcoma, lymphoma, malignant melanoma, etc. In addition, there are no specific clinical and radiographic findings in patients with ONB that could be useful for differential diagnosis from these nasal tumors. Histologically, primitive-appearing "small round blue cells" with finely granular chromatin, distinctive lobular and often coalescing architectural growth pattern are remarkable findings in ONB. Furthermore, immunohistochemical staining, including neuroendocrine immunophenotype without significant cytokeratin expression and positivity for S-100, confirm the diagnosis. These findings were consistent with those in the present case.

In general, ONB is a slow-growing tumor with long-standing symptomatology. The clinical symptoms are unilateral nasal obstruction and epistaxis, including pain, excessive lacrimation, rhinorrhea, visual disturbances, and anosmia. In our case, recurrent epistaxis was observed 6 months before admission. However, the patient presented with persistent nasal bleeding after biopsy and developed further anemia, which was a noteworthy clinical manifestation in the present case. Thus, extreme caution should be taken in the approach to the biopsy, due to the potential risk of significant bleeding.
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widely utilized and correlates well with prognosis. A study of 311 patients based on the Surveillance, Epidemiology, and End Results database showed that disease-specific survival at 10 years was correlated with “modified” Kadish staging (83%, 49%, 39%, and 13% for stages A, B, C, and D, respectively). In this analysis, original Kadish C was divided into stage C (beyond the sinuses, including the orbit or intracranial extension) and D (distant metastasis) in the “modified” Kadish staging.

Surgery followed by radiotherapy is generally accepted as the gold standard treatment in ONB regardless of Kadish stage, with the possible exception of disease metastasis. Several case series studies demonstrated the longest survival times in patients receiving the modalities, compared with either surgery or radiation alone. However, non-surgically treated or inoperable subjects were included among ONB patients with Kadish C, as in the present case. Takenaka et al. summarized 104 Japanese patients with ONB reported from 1990 to 2013 and found that approximately half of the patients were stage Kadish C. They reported that 40% were non-surgically treated patients and that survival was significantly poorer compared with surgically treated patients.

Combined modality treatment with chemoradiation has been increasingly adopted for these inoperable patients over the last two decades. The efficacy of chemotherapy using CDDP, cyclophosphamide, vincristine, doxorubicin, or VP-16, etc., with and without radiotherapy was reported, although there have been no broad reports of useful chemotherapy regimens in patients with advanced metastatic ONB to date. Fitzek et al. examined the usefulness of neoadjuvant CDDP + VP-16 chemotherapy in 19 cases of neuroendocrine tumors in the sinonasal tract, including nine cases of ONB. They found that 13 patients showed a significant response to two cycles of CDDP + VP-16 with a response rate of 68.4%. In addition, Gupta et al. reported a case of ONB with extensive involvement of the nasal cavities, nasopharynx, paranasal sinuses, and orbit that showed a complete response to concurrent chemoradiation with CDDP + VP-16 chemotherapy. The chemotherapy regimen with concurrent radiotherapy has been widely accepted in limited stage cases of small cell lung cancer, in which the tumor cells were of neuroendocrine origin as well as ONB. Therefore, we selected CDDP + VP-16 combined concurrent radiotherapy in the present case. Unfortunately, the combined chemoradiotherapy failed to reduce the tumor size and the residual mass was still inoperable. However, the patient has remained free of symptoms, including epistaxis, for over 3 years. Combined chemoradiation might be efficacious for local control of this disease.

In summary, we described a case of olfactory neuroblastoma that showed occasional epistaxis over a period of 6 months, and subsequently developed persistent nose bleeds after obtaining a biopsy specimen of the primary tumor. We should be aware of the disease as a cause of nasal bleeding, and further studies regarding therapeutic strategies for inoperable olfactory neuroblastoma are warranted.

References


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