Clinical Case Report

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Intracranial immature teratoma invading the nasal cavity mimicking olfactory neuroblastoma

A case report

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Abstract

Rationale: Primary intracranial immature teratoma accounts for majority of congenital central nervous system germ-cell tumors, but it is extremely rare in patients older than 15 years.

Patient concerns: A 27-year-old woman was referred to our hospital for headache, nasal congestion, and decreased olfactory sensation. Imaging showed a mass measuring approximately 5 cm × 4 cm in the right frontal lobe, which also filled the right nasal cavity. Histopathologically, the intracranial tumor tissues were composed of both mature tissues, including glands and squamous epithelial cells and immature neuroectodermal components. However, the tumor tissues in the nasal cavity were mainly immature neuroectodermal components that mimicked olfactory neuroblastoma. The cells stained positively for neuron-specific enolase, Alpha Thalassemia/Mental Retardation Syndrome X-Linked, and Oligodendrocyte transcription factor on immunostaining, proving a neuroectodermal differentiation.

Diagnoses: According to these findings, the tumor was diagnosed as a primary intracranial immature teratoma that also involved the nasal cavity after excluding the metastatic tumors.

Interventions: The patient underwent 2 surgeries. The first surgery was via the subfrontal approach, followed by a second endoscopic sinus surgery performed 22 days later.

Outcomes: The patient had no recurrence within a 6-month follow-up after the last surgery.

Lessons: When an intracranial immature teratoma involves the nasal cavity, the lesions in the nasal cavity may mimic other tumors including olfactory neuroblastoma. We suggest that thorough examination of tumor tissues and identification of variable components are critical for the appropriate diagnosis of intracranial immature teratoma, a rare tumor.

Abbreviations: CNS = central nervous system, CT = computed tomography.

Keywords: case report, immature teratoma, intracranial, nasal cavity, olfactory neuroblastoma

1. Introduction

Primary intracranial immature teratoma is a type of central nervous system (CNS) germ-cell tumor.[1] CNS germ-cell tumors are rare intracranial tumors that account for only 0.3% to 0.5% of primary intracranial tumors in the United States and 2% in Europe.[1] Immature teratoma is histologically characterized by an embryonic incompletely differentiated tissue, irrespective of the proportion of this component.[1] The immature tissues are mainly neuroectodermal components.[1] Most of the patients with CNS germ-cell tumors are under 20 years old, and patients older than 30 years only account for 2% of all the patients.[1] The peak ages of the patients are from 11 to 20 years.[1] However, most cases of immature teratoma are congenital, and patients older than 15 years are extremely rare.[2,3] CNS germ-cell tumors are mainly located in the central line similar to the tumors in other extragonadal sites.[1] However, primary intracranial immature teratomas in rare sites including the lateral ventricle and cerebral basal ganglia have been reported.[3,4] Congenital tumors usually involve a relatively wide area of the brain.[5,6] The prognoses of primary intracranial immature teratomas in the fetus and newborn are generally poor,[4,7–11] while prognostic data in adults are currently lacking. Herein, we report a rare case of primary intracranial immature teratoma in a 27-year-old woman. The case is unique in that the patient was older and that the tumors involved both the brain and the nasal cavity. The lesion in the nasal cavity was mainly composed of immature neuroectodermal components that mimicked olfactory neuroblastoma and could have led to a diagnostic pitfall.

2. Case report

The patient was a 27-year-old woman who developed right-sided headache, nasal congestion, and decreased olfactory sensation

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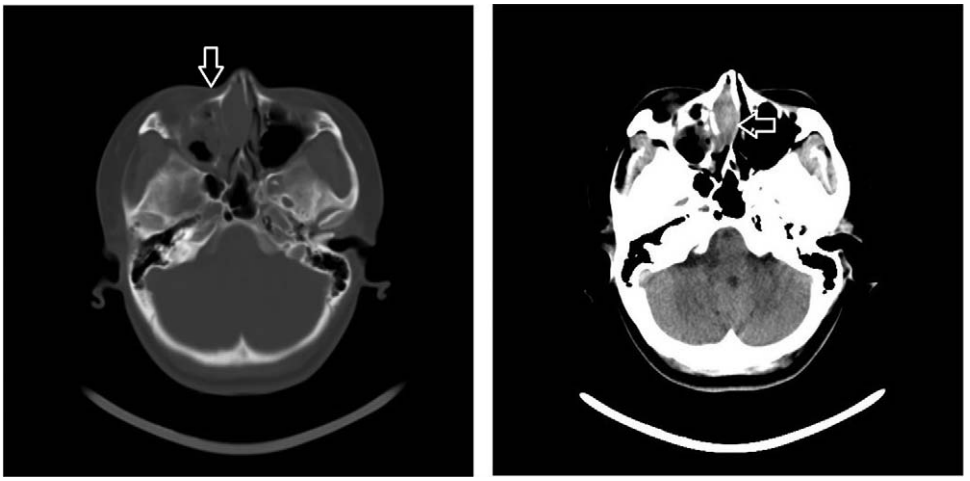

Figure 1. Computed tomography imaging of the tumor. A mass measuring approximately 5 cm × 4 cm was detected in the right frontal lobe and involved the genu of the corpus callosum (arrow). The mass also filled the right nasal cavity (arrow). The nasal septum and ethmoid bone were compressed and bent.

without obvious cause 20 days prior to consultation. The symptoms lasted for 1 day without relief. The headache was a severe persistent right-sided frontal pain that was not relieved by oral analgesics and was only mildly relieved by intravenous injection of mannitol. Computed tomography (CT) and magnetic resonance imaging examination in another hospital detected an intracranial mass. The patient then came to our hospital for further diagnosis and treatment. The patient had no fever and weight loss. Blood test showed a slightly low level of granulocyte count (6.62×10^9/L), lymphocyte ratio (17.5%), and granulocyte ratio (77.3%). The liver function test also showed a slightly low level of aspartate aminotransferase (12 U/L).

This study was prospectively performed and approved by the institutional Ethics Committees of China Medical University and was conducted in accordance with the ethical guidelines of the Declaration of Helsinki. The patient has provided informed consent for publication of the case.

The CT imaging showed a mass approximately 5 cm × 4 cm in the right frontal lobe that involved the genu of the corpus callosum. The right lateral ventricle was compressed by the tumor and narrowed. The structures of the central midline shifted left focally. No abnormalities were detected in the cerebellum and brainstem. The right nasal cavity was filled with mass, and the nasal septum and ethmoid bone were compressed and bent. The images of the tumor are shown in Figure 1. The patient underwent 2 surgeries. The first surgery was via the subfrontal approach. During the surgery, the mass was found to have attached to the brain closely; it grew along the sieve plate, and invaded the nasal cavity. Grossly, the tumor was approximately 6 cm × 5 cm without capsule. It was gray-red in color and had rich blood supply, with moderate hardness. The second surgery was an endoscopic sinus surgery performed 22 days later. The tumor was found to involve the top of the nasal cavity, turbinate mucosa, nasal septum mucosa, posterior wall of the frontal sinus, and anterior wall of the sphenoid sinus.

The tumor samples were examined via hematoxylin and eosin staining and immunohistochemistry as described previously.[12] The histopathologic features of the tumor are shown in Figure 2. The tumor contained differentiated mature glands (Fig. 2A) and squamous epithelial cells (Fig. 2B). The immature tissues were mainly composed of immature neuroectodermal components and surrounded by primitive mesenchymal tissues (Fig. 2C). The immature neuroectodermal cells were mainly arranged in nests and were very dense (Fig. 2D). The cells were relatively small and short shuttle like in shape. They were quite uniform in size and shape. The karyoplasmic ratio increased, and the nuclear staining was deep. Some neural tube-like structures were found in the tumor tissues (Fig. 2E). The tumor tissues in the nasal cavity were mainly composed of cell nests consisting of small round cells that mimicked olfactory neuroblastoma (Fig. 2F).

The immature tissues stained positively for alpha fetoprotein (AFP) and Alpha Thalassemia/Mental Retardation Syndrome X-Linked. Meanwhile, the mature glands and squamous epithelial cells stained positive for cytokeratin (CK). Glial fibrillary acidic protein and human chorionic gonadotropin (HCG) staining yielded negative results. The Ki-67 index in the immature neuroectodermal components was extremely high at >90%. The immature neuroectodermal tissues showed diffuse positive staining of neuron-specific enolase; NeuN staining yielded negative results. The mature squamous epithelial cells showed positive staining only for P63. Placental alkaline phosphatase (PLAP) staining was negative or only very weak. Focally positive S-100 staining was observed only around the immature neuroectodermal cell nests. Both the mature and immature tissues showed positive SALL4 staining. Immature neuroectodermal cell nests showed focally and weakly positive synaptophysin staining, and diffuse and strongly positive vimentin staining. The immunostaining pattern of the intracranial part of the tumor is shown in Figure 3.

The CD56 staining was only focally positive around the cell nests. CD99 staining was very weak. Chromogranin A and CK staining yielded negative results. The Ki-67 index was higher than 90%. S-100 staining yielded positive results in the cells around the tumor cell nests. Synaptophysin and TT-1 staining yielded negative results, while vimentin staining was focally positive. Figure 4 shows the immunostaining pattern of the tumor tissues in the nasal cavity. The patient had no recurrence during a 6-month follow-up after the last surgery.

3. Discussion

Intracranial immature teratoma is a type of CNS germ-cell tumors. The pathogenesis of these tumors remains unclear to date. Increased levels of gonadotropin in blood circulation may

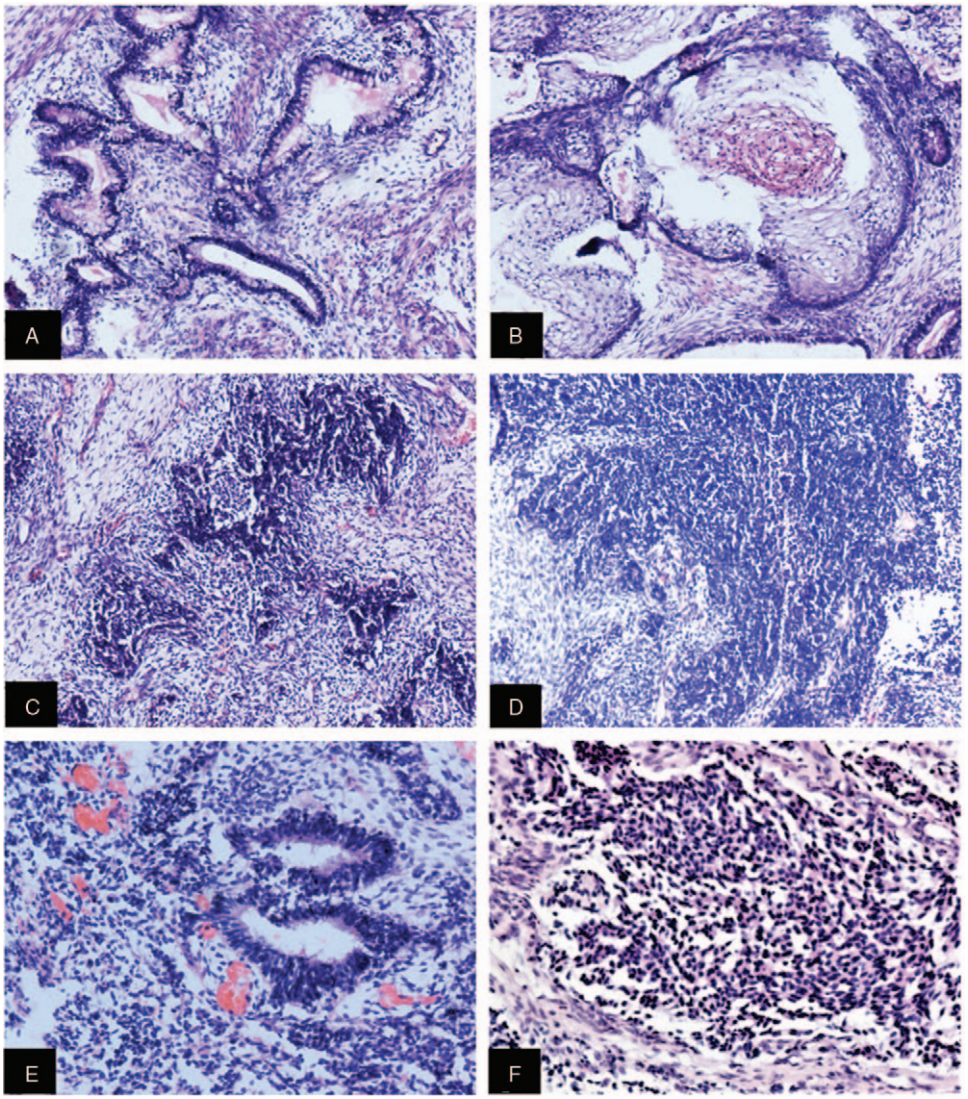

Figure 2. Histopathologic features of the tumor. The tumor contains both mature (A, B) and immature tissues (C–F). The mature tissues included glands (A) and squamous epithelial cells (B). Meanwhile, immature tissues comprised of immature neuroectodermal components including dense cell nests (C, D), neural tube-like structures (E), and primitive mesenchymal tissues (C). The tumor cells in the nasal cavity were round small cells that formed cell nests, which mimicked olfactory neuroblastoma (F). Scale bar: A, B, E, F: 10 μm; C, D: 40 μm.

be an important factor in the tumorigenesis.[1] Another possible factor is the increase in X chromosome, which is a characteristic of the genetic abnormalities in these tumors.[1]

Most patients with CNS germ-cell tumors are in their 20s.[1] However, intracranial immature teratomas usually occur in the fetus and frequently cause miscarriage.[13,14] Only a few cases of patients older than 15 years have been reported.[2,3] Here, we present a case of primary intracranial immature teratoma in a 27-year-old woman. The tumor in this patient was mainly located in the frontal lobe of the brain and also involved the nasal cavity. The clinical symptoms of intracranial immature teratoma vary according to its specific location in the brain,[1] but commonly include symptoms of brain tissue oppression.[1] In addition, some tumors can secrete hormones and lead to corresponding symptoms.[1] Most tumors lack specific imaging findings, and the diagnoses mainly depend on histologic examination.[1] An increase of some substances including AFP, β-HCG, and PLAP in serum and cerebrospinal fluid is crucial in the diagnosis of CNS germ-cell tumors including immature teratoma.[1]

Intracranial teratomas can be solitary or co-occur with other germ-cell tumors such as choriocarcinoma.[1,15] The histologic features of intracranial immature teratoma are consistent with tumors originating in the gonads and other extragonadal sites.[1] Therefore, it is necessary to exclude metastatic tumors. In the current case, the patient had no other symptoms except the intracranial and nasal cavity symptoms. No other tumors were detected except that in the frontal lobe of the brain and the nasal cavity. Thus, it was considered as a primary intracranial immature teratoma that involved the nasal cavity rather than a metastatic tumor. Moreover, the histologic and immunostaining features of the lesions in the nasal cavity were similar with those of olfactory neuroblastoma.

Given the lack of other teratoma components, it may be mistaken as olfactory neuroblastoma. The peak incidence of olfactory neuroblastoma is from age 20 to 30 years,[16] which is also a pitfall for the current case. Without a complete pathologic examination of the intracranial lesions to determine the variable components of the tumor tissues, this tumor may also be

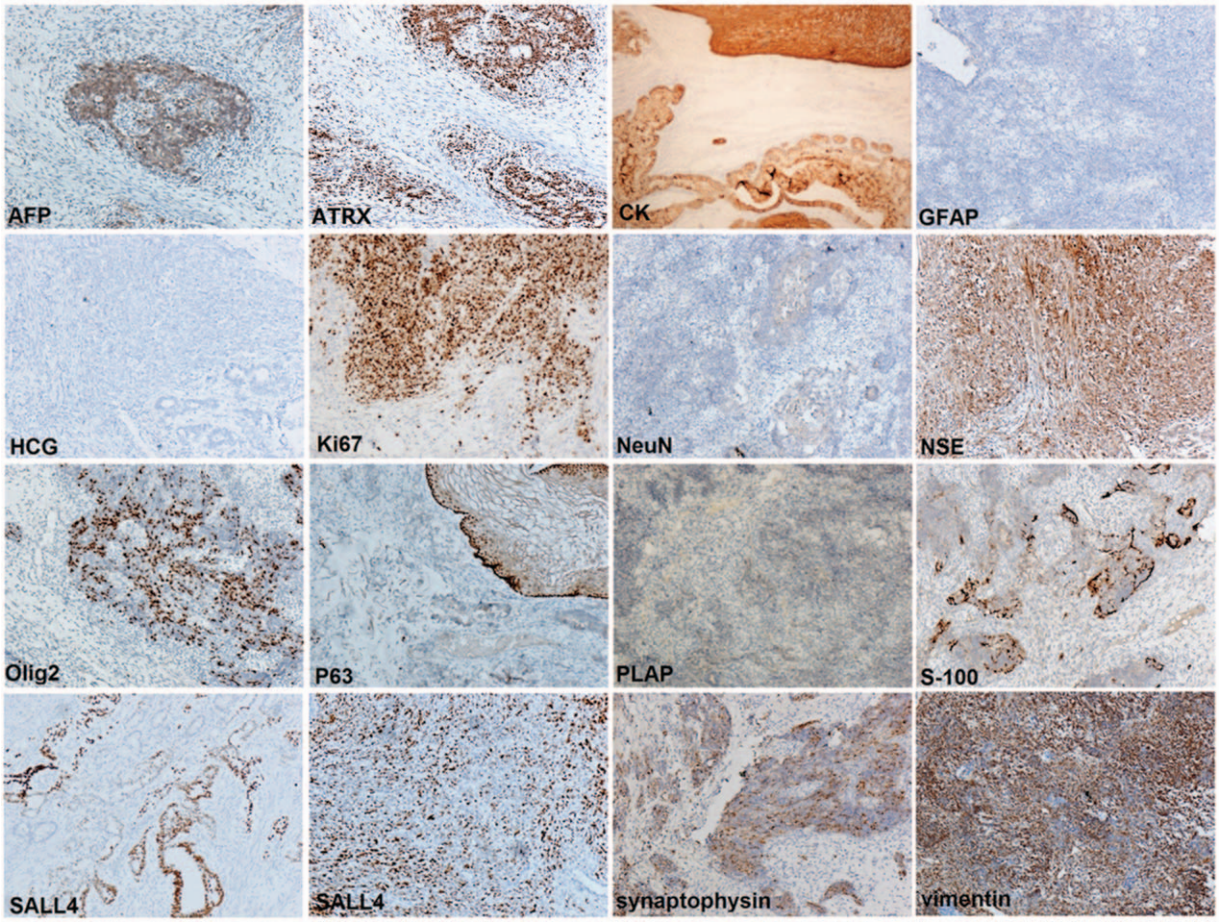

Figure 3. Immunostaining patterns of the intracranial parts of the tumor. AFP and ATRX staining yielded positive results in the immature components. CK staining yielded positive results in the mature glands and squamous epithelial cells. GFAP and HCG staining yielded negative results. The Ki-67 index in the immature neuroectodermal components was nearly 100%. NeuN staining yielded negative results. NSE staining was diffusely positive in the immature neuroectodermal tissues. P63 staining yielded positive results in the mature squamous epithelial cells. PLAP staining was negative or very weak. S-100 staining was focally positive around the neuroectodermal cell nests. SALL4 staining yielded positive results in both the mature and immature tissues. Synaptophysin staining was focal and weak in the immature neuroectodermal cell nests. Vimentin staining was diffusely and strongly positive in the immature neuroectodermal cell nests. Scale bar: 20 μm. AFP = alpha fetoprotein, ATRX = alpha thalassemia/mental retardation syndrome X-linked, CK = cytokeratin, GFAP = glial fibrillary acidic protein, HCG = human chorionic gonadotropin, NSE = neuron-specific enolase, PLAP = placental alkaline phosphatase.

mistaken as olfactory neuroblastoma with an intracranial invasion. One of the differential features is a concurrence of 2 tumors in the cranial and nasal cavities. However, surgical record of the first operation showed that the mass was mainly located in the frontal lobe and grew along the sieve plate and invaded the nasal cavity, which indicates that the mass in the cranial cavity and nasal cavity was connected and there was actually only 1 tumor.

Extracranial head and neck immature teratomas are often the manifestations of extended primary intracranial tumors.[17] Karaca et al reported a case of intracranial immature teratoma with craniofacial extension.[17] Large tumors, which are more common in congenital cases, can even extend into the oral cavity.[4,9,10,13,14] Another diagnostic problem for the current case was determining which mass was the primary tumor and which was the invading part for immature teratoma as both could originate in the nasal cavity.[16] The tumor tissues of immature teratomas in the invaded sites are usually mainly composed of immature components.[2]

In the current case, the tumor tissues in the nasal cavity were strongly similar and mainly composed of immature neuroectodermal components, supporting that this tumor was more likely an invading part of the intracranial tumor. Another reason that the intracranial tumor may be the primary one is that it comprised majority of the tumor. The intracranial mass was closely located to the central line, which is also consistent with a primary CNS germ-cell tumor. According to these findings, we first considered this tumor to be an intracranial immature teratoma, although the possibility of a tumor in the nasal cavity that invaded the cranial cavity cannot be fully ruled out. Excluding a metastasized immature teratoma is particularly important. The patient did not have symptoms in other sites including the abdomen and chest cavity, and no other mass was detected on physical examinations, findings that support a primary intracranial tumor.

At present, surgical resection is the most important treatment for intracranial immature teratoma.[3] The significance of postoperative chemoradiotherapy in improving patient survival remains controversial. In Garrè report, chemotherapy achieved good results in a patient with recurrent tumor.[18] Some studies also indicated that chemotherapy was useful in shrinking tumors to facilitate resection.[19,20] Meanwhile, Huang study showed

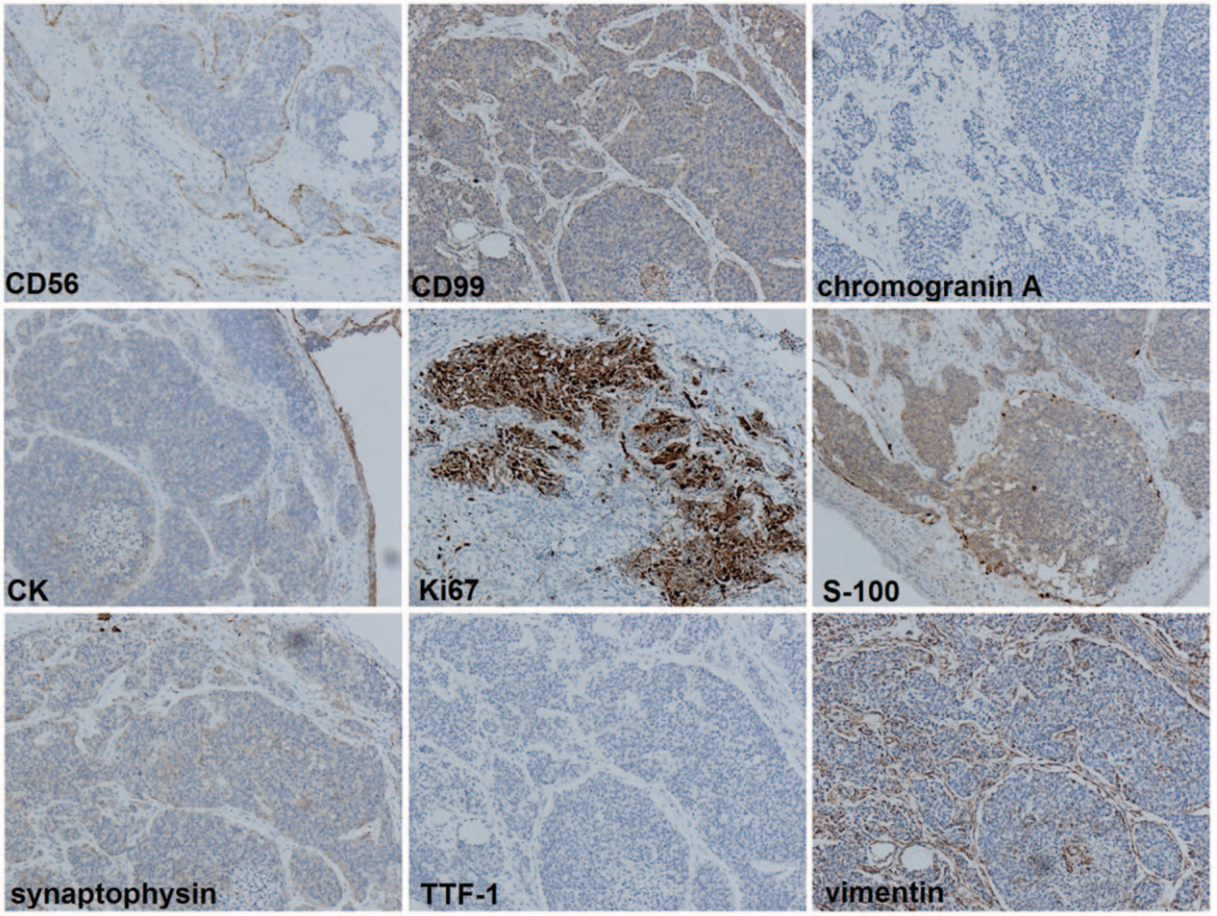

Figure 4. Immunostaining patterns of the tumor tissues in the nasal cavity. CD56 staining yielded positive results around the tumor cell nests. CD99 staining was very weak, and chromogranin A and CK staining yielded negative results. The Ki-67 index was nearly 100%. S-100 staining was focally positive around the tumor cell nests. Synaptophysin and TT-1 staining yielded negative results, and vimentin staining was focally positive. Scale bar: 20 μm. CK = cytokeratin.

that postoperative gamma knife surgery and not postoperative chemoradiotherapy significantly improved the patient's 5-year survival rate.[21] The prognosis of congenital intracranial immature teratoma is usually poor because the tumor is usually large and is accompanied by extensive invasion.[7–10,14] Late recurrence is uncommon in these patients,[22] but Mano et al reported a case of intracranial immature teratoma that recurred 21 years after the surgery of the primary tumor.[22] There are few reports of tumors in adults, and the prognosis in these cases remains to be studied.

4. Conclusion

Primary intracranial immature teratoma is a rare malignant CNS tumor particularly in patients older than 15 years. When it involves the nasal cavity, it may mimic neuroectodermal tumors including olfactory neuroblastoma and may lead to a diagnostic pitfall. As tumors in the nasal cavity and the brain are often closely related, complete imaging and pathologic examinations are crucial for appropriate diagnosis.

Author contributions

Conceptualization: Yuefeng Jiang, Xiaoyun Mao, Yang Zhao, Chuifeng Fan.
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Investigation: Yuefeng Jiang, Xiaoyun Mao.
Supervision: Chuifeng Fan.
Writing – original draft: Yuefeng Jiang, Xiaoyun Mao, Yang Zhao.
Writing – review & editing: Chuifeng Fan.

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