

# Perfect prognosis of a boy with alveolar rhabdomyosarcoma of the nasal wing treated with brachytherapy and chemotherapy

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*To the Editor:* Alveolar rhabdomyosarcoma (ARMS) of nasal wing with distant metastasis has a very poor prognosis. Because it is difficult to achieve complete surgical excision of the primary site of the nasal wing, distant metastasis is not easy to control. Here, we present an unusual case of a 29-month-old boy with ARMS in the left nasal wing accompanied by bone metastasis who was treated with systemic chemotherapy as well as <sup>125</sup>I interstitial brachytherapy, and this special multidisciplinary management resulted in a perfect prognosis and mild long-term side effects.

A 29-month-old boy with a 10-month history presented with a gradually increasing mass in the left nasal wing. No rhinorrhea and no nasal congestion or other symptoms were observed. The mass was located in the left nasal wing and alar root and was palpable on examination. It measured approximately 1 cm in diameter and felt hard in texture. The localized skin showed no signs of inflammation. The other systemic examinations were unremarkable.

Enhanced magnetic resonance imaging (MRI) examination of the paranasal sinuses showed a mass in the left nasal wing [Figure 1A], which showed a soft tissue density shadow from the subcutaneous left nasal root to the left nasal wing (12\*17 mm). The bone scan showed metastasis to the ninth lumbar vertebra [Figure 1C]. After biopsy of the left nasal alar tumor, the pathologic diagnosis was ARMS with positive immunohistochemical staining of desmin and myogenin [Figure 1F and 1G], and hematoxylin-eosin staining showed small round blue cells [Figure 1E]. Fluorescence *in situ* hybridization revealed a positive paired box 3-forkhead box protein O1 (*PAX-FOXO1*) fusion gene [Figure 1H]. No regional nodes were involved, and no other sites showed metastasis, including

the lung and bone marrow. Considering the primary site and bone metastasis, we proposed a treatment strategy for the patient with systemic chemotherapy and <sup>125</sup>I interstitial brachytherapy. After biopsy, one cycle of chemotherapy was given, followed by six seeds of <sup>125</sup>I implanted into the local mass. The particle dose was 12000.0 cGy, and the activity of each particle was 0.70 mCi. Radioactivity detection showed that the maximum dose of the six seeds was 62761.5 cGy. Seven days after <sup>125</sup>I implantation, five cycles of sequential chemotherapy were given. The chemotherapy regimens were as follows: “pirarubicin (25 mg/m<sup>2</sup>, d2, 9) + vincristine (1.5 mg/m<sup>2</sup>, d1, 8) + cyclophosphamide (300 mg/m<sup>2</sup>, d1–3) + cisplatin (90 mg/m<sup>2</sup>, d1),” and “ifosfamide (1.5 g/m<sup>2</sup>, d1–5) + actinomycin-D (300 μg/m<sup>2</sup>, d1–5) + etoposide (100 mg/m<sup>2</sup>, d1–3) + vincristine (1.5 mg/m<sup>2</sup>, d1).” The two schemes were alternated. No mass was found in the left nasal wing, and the metastasis to the ninth lumbar vertebra disappeared after the multidisciplinary treatment.

At the five-year follow-up, local control of the left nasal wing had improved, as shown by evidence provided by enhanced MRI of nasal sinus [Figure 1B]. A review of the whole-body bone scan showed that there was no sign of metastasis in the ninth lumbar vertebra [Figure 1D]. Visual acuity, cornea, lens, fundus, visual electrophysiology, and tear function tests were within normal limits. The nasal acoustic reflection and nasal resistance showed that the left nasal cavity resistance was higher than the right nasal cavity resistance. The face and nasolabial folds were symmetrical. As of September 2019, the boy had been in complete remission for 8 years and 9 months. The development of the teeth and alveolar bone was normal.

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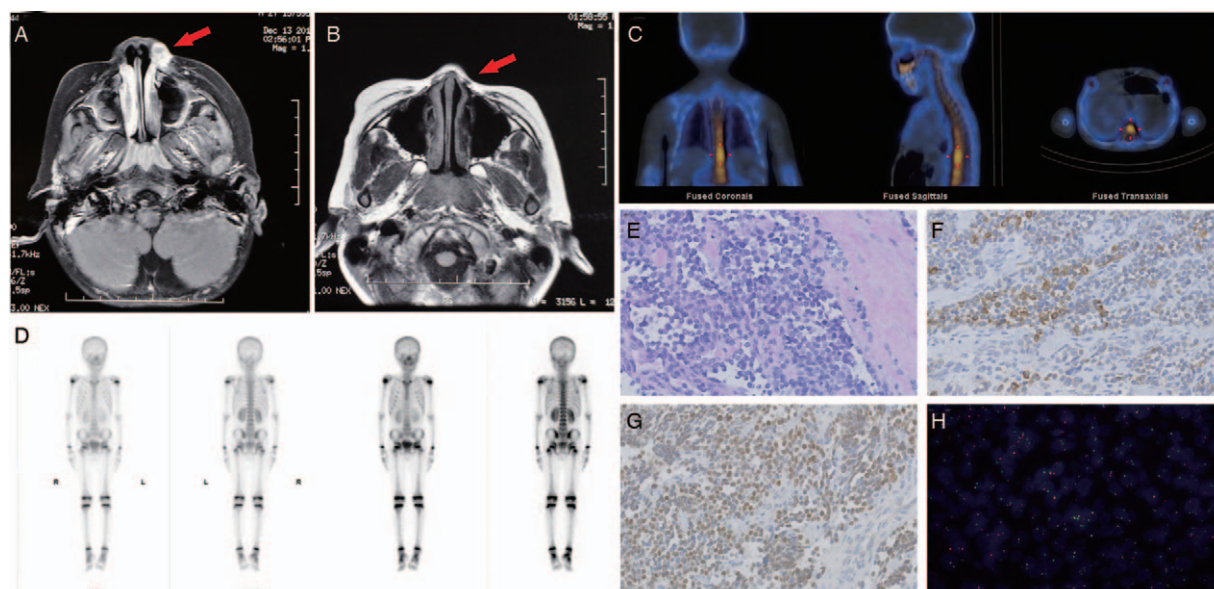
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**Figure 1:** Representative images of the patients. (A) Enhanced MRI of the sinuses before treatment: the soft tissue density shadow was in the left nasal wing, and the border was not clear. (B) Enhanced MRI of the sinuses after 5 years of treatment: no obvious tumor in the left nasal wing. (C) The HAWKEYE fusion image of the whole-body bone scan before treatment: the T9 radioactivity area was increased, and malignant lesions were involved. (D) The results of whole-body bone scans after 5 years of treatment were normal. (E) HE staining image showing small round blue cells (original magnification  $\times 400$ ). (F) Immunohistochemical staining for desmin (original magnification  $\times 400$ ). (G) Immunohistochemical staining for myogenin (original magnification  $\times 400$ ). (H) FISH test image of the *PAX-FOXO1* fusion gene. FISH: Fluorescence *in situ* hybridization; HE: Hematoxylin-eosin; MRI: Magnetic resonance imaging; *PAX-FOXO1*: Paired box 3-forkhead box protein O1.

Only the left nasal wing was slightly smaller than the right, although there was no scar formation or pigmentation. The prognosis of the boy is perfect, and he is a student in primary school.

The incidence of rhabdomyosarcoma is approximately six cases per 1,000,000 population per year.<sup>[1]</sup> Rhabdomyosarcoma is the most common form of soft tissue sarcoma and is the third most common extracranial solid tumor in childhood.<sup>[2]</sup> On the basis of histology, two main rhabdomyosarcoma subgroups can be distinguished: ARMS and embryonal rhabdomyosarcoma (ERMS). Immunohistochemistry shows extensive myogenin-positive cases of ARMS and a few focal myogenin-positive cases of ERMS.<sup>[3,4]</sup> However, the fusion genes of *FOXO1* gene translocation with *PAX3* or *PAX7* are detected in 75% of ARMS cases. *PAX-FOXO1* fusion gene detection has specificity and sensitivity for the diagnosis of ARMS.<sup>[4,5]</sup> ARMS presents in approximately 25% of rhabdomyosarcoma patients, and a substantial fraction of patients with ARMS have metastasis at the time of diagnosis. ARMS commonly spreads to the lung, bone, bone marrow, and distal lymph nodes.<sup>[2]</sup> The *PAX-FOXO1* fusion gene and distant metastatic disease, which are present at onset, are risk factors that influence the prognosis of the disease.<sup>[2]</sup>

Currently, the treatment of rhabdomyosarcoma worldwide includes surgery, radiotherapy, and chemotherapy. Most patients with head and neck rhabdomyosarcoma (HNRMS) have unresectable tumors due to functional and/or cosmetic constraints, which also cause a very high risk of local relapse and influence the prognosis. For HNRMS, radiotherapy, and chemotherapy are the main treatment options to improve the prognosis, but the choice of timing and mode of radiotherapy can reduce local

recurrence. Radiotherapy includes external beam radiotherapy and brachytherapy. External radiotherapy can damage the surrounding normal tissues, and long-term toxic side effects, such as nasal external radiotherapy, can lead to facial development damages, visual impairments, and alveolar bone development abnormalities.<sup>[6]</sup> A literature report showed that brachytherapy used in head and neck tumors could improve prognosis and quality of life with few side effects.<sup>[7]</sup> However, brachytherapy plays an important role in select patients. Therefore, HNRMS requires a multimodal approach emphasizing the preservation of form and function and the decrease in long-term morbidity.<sup>[8]</sup> Rhabdomyosarcoma is sensitive to chemotherapy. Therefore, chemotherapy is one of the main treatments for rhabdomyosarcoma. Worldwide, vincristine, actinomycin D, and alkylating agents (cyclophosphamide or ifosfamide) are commonly used in rhabdomyosarcoma chemotherapy. The latest chemotherapeutic drugs are etoposide, carboplatin, and epirubicin.<sup>[9]</sup> In the treatment of distant metastasis cases, patients should be given intensive multidrug therapy.

The nasal wing is a rare primary site of HNRMS, so it is very difficult to achieve complete remission with the treatment for ARMS of nasal wing with distant metastasis. However, the boy was administered <sup>125</sup>I interstitial brachytherapy with concurrent chemotherapy. He has been in complete remission for more than eight years, and the face and nasolabial folds are symmetrical.

<sup>125</sup>I interstitial brachytherapy with concurrent chemotherapy was effective for a child with nasal rhabdomyosarcoma, and the long-term side effects were mild. We hope that there will be more pediatric cases such as this in order to provide multidisciplinary treatment in the coming years.

### Declaration of patient consent

The authors certify that they have obtained the patient's guardians consent form. In the form, the patient's guardians provided their consent for the images and other clinical information to be reported in the journal. The patient's guardians understand that patient's name and initials will not be published and efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

### Conflicts of interest

None.

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