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Case Report

Alveolar rhabdomyosarcoma of nasopharynx and paranasal sinuses with metastasis to breast in a middle-aged woman: a case report and literature review

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Abstract: Alveolar rhabdomyosarcoma (ARMS) is a common soft tissue tumor in children which can rarely metastasize to the breast in adults. Here we report the rare case of a 42-year-old Asian woman, who was diagnosed with ARMS of the nasopharynx and paranasal sinuses, and got a complete remission (CR) after surgery and chemoradiotherapy. Then the patient relapsed in the unilateral breast seventeen months later. Histology and immunohistochemistry of the primary sites and the breast lesions, combined with FISH, have been performed to confirm the diagnosis of metastatic alveolar rhabdomyosarcoma. With a rational therapeutic regimen of surgery, chemotherapy and radiotherapy, the patient has got a complete remission again.

Keywords: Breast metastasis, alveolar rhabdomyosarcoma, nasopharynx and paranasal sinuses

Introduction

Breast involvement from distant foci is seldom. The incidence of breast metastasis in malignancies has been reported accounting for only 0.5-2% [1, 2]. The most common metastatic diseases of the breast are malignant melanomas, lymphoma and leukemia [1]. Rhabdomyosarcoma (RMS) is a very common soft tissue sarcoma in the pediatric age group, which most often occurs in the head and neck areas, the extremities and the urogenital organs [3]. Here we report a case of breast metastasis of alveolar RMS in a 42-year-old woman. Breast examination, imaging study, histopathological features combined gene testing are used to identify the diagnosis. To the best of our knowledge, it is the first case described that alveolar rhabdomyosarcoma of the nasopharynx and paranasal sinuses metastasize to the breast in middle-aged woman.

Case report

A 42-year-old woman was admitted to our Ear Nose Throat (ENT) department for a year history of nasal obstruction and recurrent epistaxis. The nasal endoscopic examination revealed the presence of a 10×10 mm mass in the nasopharynx. And the head computed tomography (CT) scan found a destructive soft-tissue mass in the right ethmoid sinus and frontal sinus (**Figure 1**). There was also a palpable submandibular lymph node on the right side through neck examination.

Endoscopic complete excision of the mass in the nasopharynx and paranasal sinuses was done for surgical treatment, and the right submandibular lymphadenectomy was conducted at the same time. Histologic examination showed sheets of small round cells arranged in an alveolar pattern. Immunohistochemical examination of the mass and lymph node presented positive reaction for desmin, myogenin and CD-56 (**Figure 2**), but negative reaction for EBER-ISH, PCK, EMA, synaptophysin and CD-99. Fluorescence in situ hybridization (FISH) analysis revealed the FOXO1 (FKHR) mutation.

Investigations after the surgery included a full blood count, biochemical tests and PET-CT.

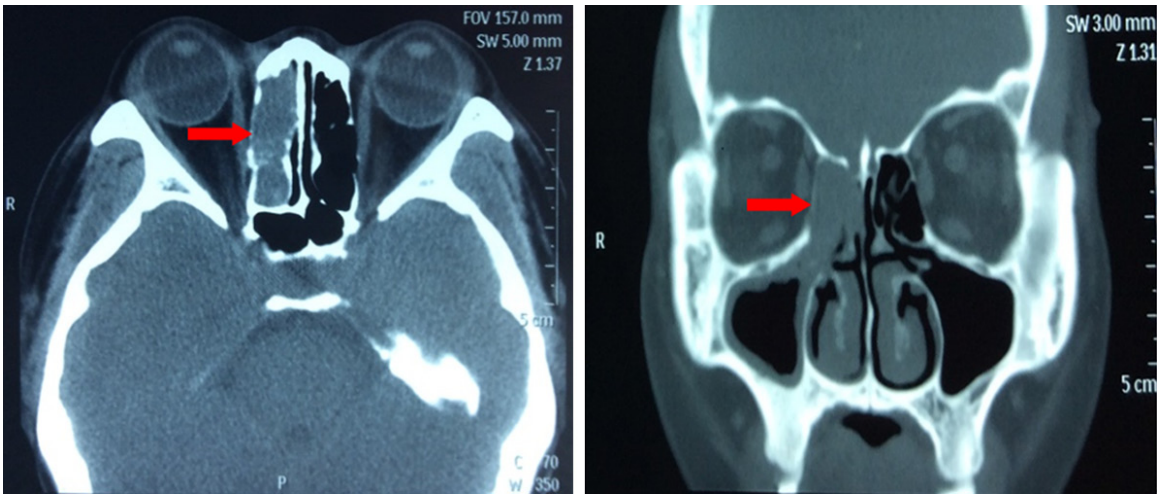

Figure 1. The head computed tomography (CT) scan showed a destructive soft-tissue mass (arrow) in the right ethmoid sinus and frontal sinus.

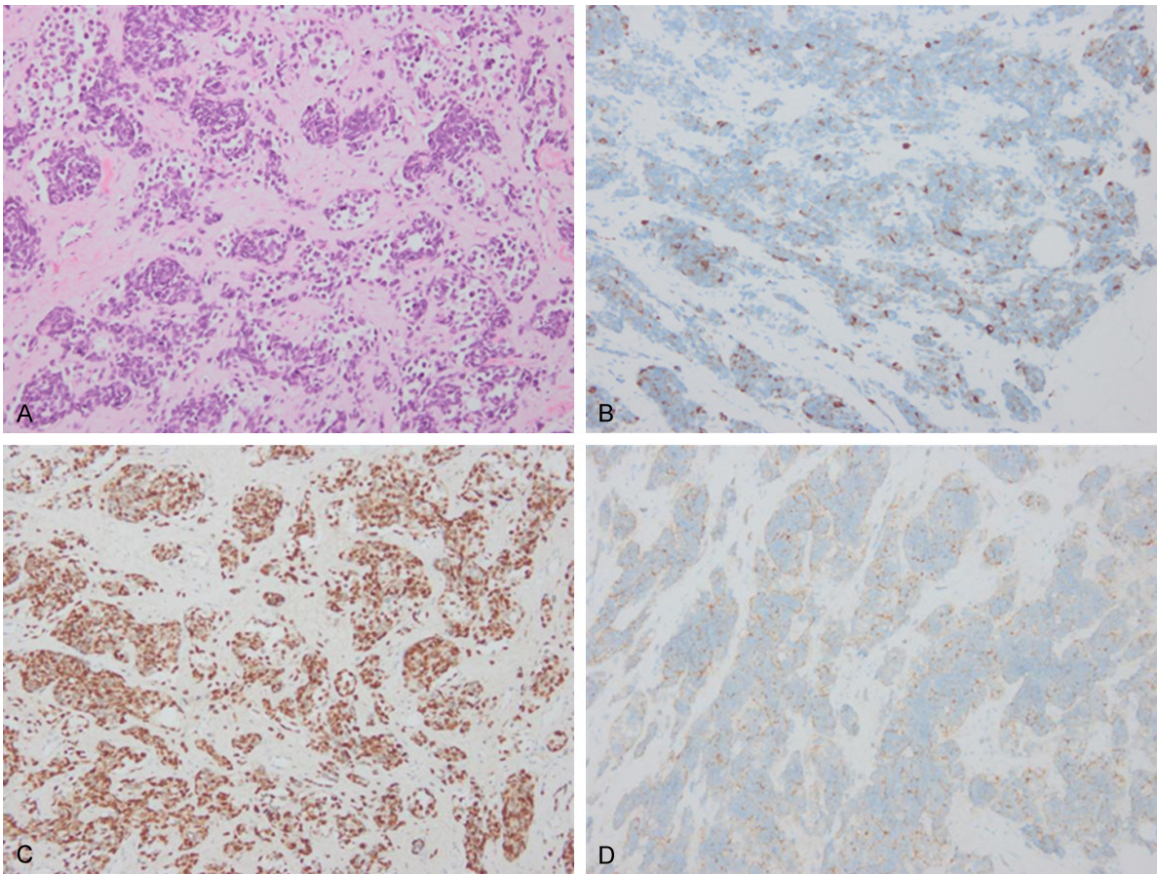

Figure 2. A. Histologic examination showed sheets of small round cells arranged in an alveolar pattern. (H&E, ×200). B. Immunostaining revealed positive result of desmin in the tumor cells. (×200) C. Immunostaining revealed positive result of myogenin in the tumor cells. (×200) D. Immunostaining revealed positive result of CD-56 in the tumor cells. (×200).

These were all normal except for a suspicious right submandibular lymph node of 19 mm in diameter, with the MAX SUV 3.1 (**Figure 3**). It confirmed the diagnosis of a stage III ARMS

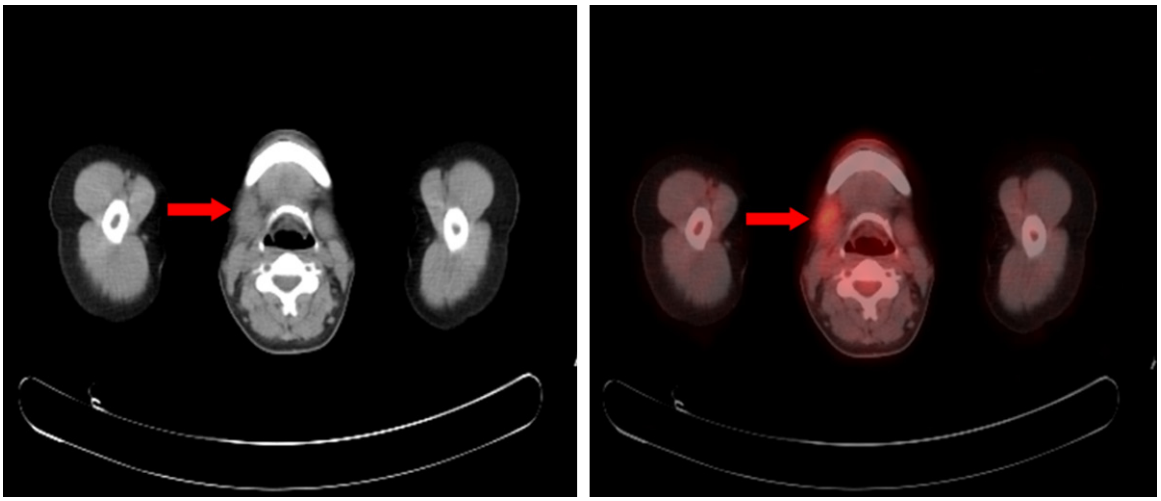

Figure 3. PET-CT showed a suspicious right submandibular lymph node (arrow) of 19 mm in diameter, with the MAX SUV 3.1.

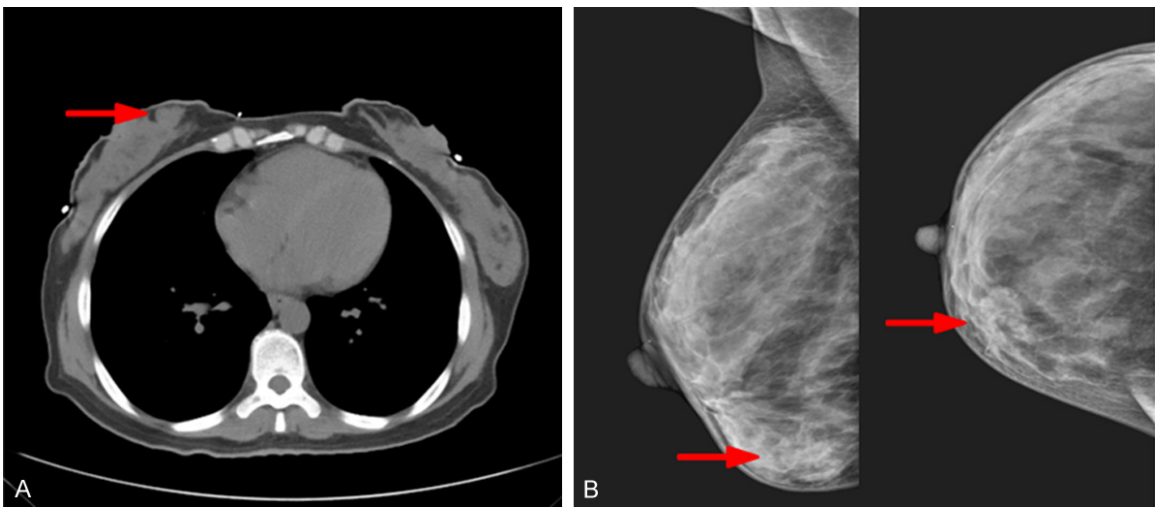

Figure 4. Chest CT scan (A) and breast mammography (B) showed masses (arrow) in the patient's lower inner quadrant of her right breast, and the size of the bigger one was 18×25 mm.

based on the Intergroup Rhabdomyosarcoma Study (IRS) TNM Pretreatment Staging System [4].

A multidisciplinary team meeting determined the patient's following treatment regimen, 2 cycles of consolidation chemotherapy including pirarubicin, ifosfamide and dacarbazine, followed by the irradiation of the nasal area and neck at a dose of 70 Gy in 33 fractions of 2.12 Gy over a period of 7 weeks. Chemoradiotherapy was well-tolerated by the patient and the subsequent restaging showed that she got complete remission (CR).

17 months later, the patient noted a lump in the lower inner quadrant of her right breast. Chest computed tomography (CT) scan, breast mammography and breast ultrasonography revealed two masses in the patient's right breast, and the size of the bigger one was 18×25 mm (**Figure 4**).

A breast mass excision was performed. Histopathological examination combined with immunohistochemistry showed these small round tumor cells were immunoreactive for desmin (**Figure 5C**) and myogenin (**Figure 5D**), which confirmed the diagnosis of metastatic ARMS.

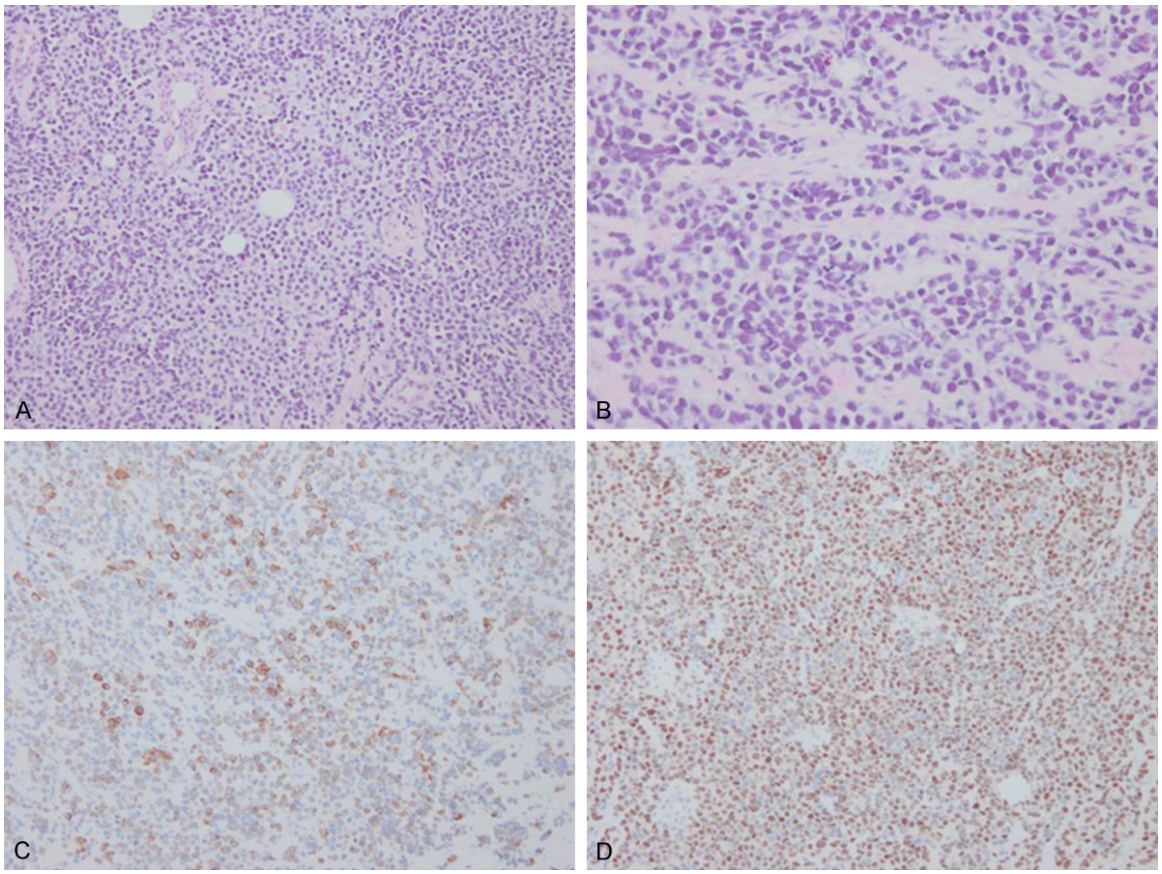

Figure 5. A. Histologic examination showed sheets of small round cells arranged in an alveolar pattern, a few residual breast ducts were presented on the up-left side. (H&E, ×200). B. Histologic examination showed nuclei with various morphological variations in these small round cells. (H&E, ×400). C. Immunostaining revealed positive result of desmin in the tumor cells. (×200). D. Immunostaining revealed positive result of myogenin in the tumor cells. (×200).

After the incomplete breast mass excision, she received 4 cycles of second-line chemotherapy, consisting of pirarubicin, cisplatin and dacarbazine. And the right breast beam concurrent radiotherapy was performed, at a dose of 60 Gy in 30 fractions of 2 Gy, using sIMRT. After 8 months, Chest computed tomography (CT) scan and the breast ultrasonography showed no mass in her breasts. At the time of this paper written, the patient is still doing well and gets CR again since she was diagnosed with breast metastasis.

Discussion

RMS is the most common soft tissue sarcoma in childhood and adolescence, comprising 10-12% of all malignant solid tumors in children [5]. There are two major histological subtypes of RMS: alveolar rhabdomyosarcoma (ARMS) and embryonal rhabdomyosarcoma (ERMS) [6]. Alveolar rhabdomyosarcoma (ARMS) is an aggressive myogenic childhood cancer, of which prognosis is poor [7]. For ARMS in adults, the survival probability is even worse, not to mention those with breast metastasis [8]. Because most patients with breast metastasis often have already got widely disseminated diseases, who relapsed only in the unilateral breast as our patient are extremely rare.

Lung is the most common metastatic site of RMS, and then followed by bone, bone marrow and liver [9]. Breast involvement from distant foci is seldom. The incidence of breast metastasis in malignancies has been reported accounting for only 0.5-2% [1, 2]. Of the 1,399 female RMS patients, according to Intergroup Rhabdomyosarcoma Study (IRS), there were 19 breast metastatic individuals except for 7 primary breast RMS, comprising 1.4%. And the

most common primary RMS metastatic to breast is from extremities, followed by nasopharynx & paranasal sinuses and trunk [10].

ARMS with metastasis to breast often occurred in the pubertal girls. Daniel M et al reported all of the 26 IRS cases were female with ages ranging from 11.5 to 20.2 years, and 24 patients of them were ARMS [10]. W. H. Kwan et al also said that female with an alveolar subtype of RMS in the pubertal period may place a patient at higher risk of developing breast metastasis [11]. It is plausible that the increasing vascularity and rapidly growing mammary tissue during the pubertal development phase may be related with the preferential metastasis to breast, as most of these patients were younger women [12]. Yaren A. et al reported that a pregnant woman got metastatic rhabdomyosarcoma to the breast, which further supported that vascularity may be associated with the metastasis priority selection [13]. But the hypothesis above cannot be enough to explain why breast metastasis of ARMS happened in a 42-year-old woman in our case.

Histopathology manifested that the tumor cells were small and round cells which arranged in an alveolar pattern (**Figures 2A** and **5A**). Its probable misdiagnosed as other malignancies, such as malignant lymphoma, leukemia, and small cell carcinoma, for the lack of specific characteristics [9, 13, 14]. In our case, the non-Hodgkin lymphoma was once considered when the naive lymphocyte was found at beginning. Fortunately, with the use of immunohistochemistry (IHC) and FISH, final diagnosis of ARMS was made. RMS should be considered for this kind of histopathological manifestation, especially in the children and teen.

The accurate diagnose is the fundament of subsequent treatments. As classification based on histopathology does not always allow accurate diagnoses for an unambiguous subclassification, we combined IHC and FISH to distinguish ARMS from other soft tissue tumors and make a definite diagnosis. As it's not easy to make an accurate diagnosis for breast metastasis, we distinguish it from other tumors clinically and histologically.

Desmin and myogenin are particularly useful in identifying tumors with myogenic differentiation [6]. Dias P. et al reported ARMS expressed at least three folds more myogenin than ERMS averagely, which can be used for distinguishing between alveolar and embryonal RMS [15]. About 80% of ARMS are identified with chromosomal translocations (t(1;13) (p36;q14) or (t(2;13) (q35;q14)), which generates PAX7-FOXO1 or PAX3-FOXO1 fusion genes [16-18]. The FOXO1 gene is also called FKHR previously. Our patient in the case found the FOXO1 (FKHR) mutation, which provided a strong and precise evidence to guarantee the accurate diagnosis of ARMS from ERMS and other tumors. The genetic testing may play a much more important role in the future and guide the clinical application of prospective targeted therapy.

ARMS with breast metastasis case is very uncommon, but we should also pay attention to the breast lumps with a previous history of malignant tumor. The routine breast examinations, including breast ultrasonography, Chest CT scan, mammography or MRI, should be suggested in the follow-up assessment. Perlet et al reported that contrast-enhanced MRI can be successful in the detection of malignant hypervascular tumors, with sensitivity up to 95% [19]. Gene detection in conjunction with histopathology and IHC can be successful to ascertain the diagnosis and assess the prognosis. With these methods above, an appropriate, rational and effective therapeutic schedule would be provided without delay.

Conclusion

Here we report the case of 42-year-old woman presenting with metastatic ARMS of nasopharynx and paranasal sinuses in breast, which is extremely rare in adults. Histology, IHC and FISH have been used to confirm the diagnosis. A comprehensive therapy of surgery, chemotherapy and radiotherapy are performed to the patient. Although metastatic ARMS to the breast often presents a dismal prognosis, which has been described in most reports, the patient in our case has achieved complete remission (CR) and obtained a satisfactory outcome.

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Disclosure of conflict of interest

None.

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