

Undifferentiated Subtype of Non-keratinizing Carcinoma of the Nasopharynx Metastasizing to the Breast: A Case Report and Literature Review

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ABSTRACT

Nasopharyngeal carcinomas (NPCs) have a particularly high risk for aggressive clinical behavior. Metastatic tumors or secondary malignant neoplasms to the breast are uncommon. Breast metastasis of NPCs is very rare. We report a case of NPC in a 17-year-old female patient presenting with a mass in her left breast. The tumor consisted of an inflammatory infiltrate rich in lymphoplasmacytic cells and composed of carcinoma cells having large, vesicular, round to oval nuclei with single, centrally located, eosinophilic nucleolus with eosinophilic cytoplasm. The epithelial tumor cells were strongly positive for pancytokeratin and CK19 and negative for CK7, CK20, progesterone, and estrogen receptors. NPCs are predominantly seen in adults with an average age of 50 years at diagnosis, and they are slightly more common in men than in women. The etiology of NPCs is generally multifactorial, such as genetic predisposition, Epstein-Barr virus infection, and environmental factors. A review of the literature on NPC yielded eight cases of metastasis to the breast. Excessive radical surgery is not suitable for metastatic tumors in the breasts of these patients, but isolated success has been obtained with a combination of local surgery and radiation therapy.

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Introduction

Metastatic tumors in the breast arise for the most part in malignant melanoma, lymphoma, lung cancer, and carcinoma of the ovary^[1]. Metastases from the head and neck region from malignant tumors are uncommon^[1]. For nasopharyngeal carcinomas (NPCs), the relationship between race, geographical areas, and multifactorial etiology should be noted. Worldwide, NPC constitutes approximately 65,000 new cases per year and accounts for 38,000 cancer cases death annually. The vast majority of neoplasms in this category are non-keratinizing carcinomas, which itself are the most common subtype of undifferentiated carcinomas^[2]. Occasionally, patients with NPCs have presented with lymphadenopathy, and the most frequent metastatic sites are retropharyngeal and level II lymph nodes^[3]. Distant metastases occur most often to bone, lung, liver, and retroperitoneal lymph nodes^[4]. To the best of our knowledge, only eight cases have been reported previously in the medical literature^[1, 5, 6, 7, 8] (Table 1). The clinicoradiological findings and pathological features of this unusual presentation are reported here.

Case report

A 17-year-old female arrived at the surgery department of a state hospital with non-specific, systemic symptoms, such as breast pain and palpable breast mass was detected. Breast ultrasonography and upper abdomen computed tomography (CT) imaging revealed the presence of a 7.8 cm × 4.8 cm solid mass in the left breast region, suspicious for a neoplasm and therefore was resected completely. We report a case; which was diagnosed in 2011 in a patient, he was diagnosed with stage I (T1N0M0) nasopharyngeal carcinoma (NPC) with tumor confined to nasopharynx. Magnetic resonance imaging was performed on the nasopharynx posterior wall and lateral walls, following an injection of intravenous contrast. T1a weighted signal due to post-contrast scans are performed; hypointense and T2a weighted signal due to hyperintense. The patient was diagnosed with NPC and developed a left breast mass (Fig. 1A, B, C, D). The tumor measured 4 cm × 1 cm × 1 cm

in diameter, and serial sections of the surgical specimen did not reveal tumor infiltration to the peripheral compartment. Its gross appearance was a soft, grayish-white tissue, which was a well-localized, well-demarcated, smooth mass. The cut surface of the tumor revealed ill-defined, solid areas that were focally prominent and gray with myxoid changes (Fig. 2). Microscopically, the tumor consisted of a prominent, chronic inflammatory infiltrate rich in denselymphoplasmacyticinfiltrate with less eosinophilic background and composed of carcinoma cells having large, vesicular, round-to-oval nuclei with single, centrally located eosinophilic nucleoli with eosinophilic cytoplasm. composed of sheets of cohesive epithelial cells with only small foci lacking cohesive tumor cells. Immunohistochemically, the epithelial tumor cells were diffusely and strongly positive for pancytokeratin and CK19. The cells were focally positive for CK5/6 but negative for CK7, CK20, progesterone receptors, and estrogen receptors (Fig. 3A, B, C, D,E). Absence of in situ breast (ductal or in situ lobular) carcinoma.

Discussion

The incidence of breast involvement by other non-mammary malignancies is very rare (approximately 0.4% to 1.3%). The most common sources of metastases to breast are primary neoplasms from adverse effects of breast lymphoma or leukemia and malignant melanoma^[9]. First described by Dawson (1936), metastases, the stomach signet ring cell carcinoma, is situated at the lymphatic channel in the breast. With these characteristics, the median interval to the development of a breast metastasis is approximately 2 years for cases with previously treated cancer. Metastatic disease, defined as a single lesion in the breast region, is seen in approximately 85% of cases^[10]. It is more common in Southern Chinese and African populations, in which the annual incidence rises to 30–50 per 100,000 persons^[11] and 23.3 and 8.9 cases per 100,000 persons per year for men and women, respectively^[4]. The age distribution is similar in men and women; however, it occurs predominantly in males^[2]. Although the etiology is multifactorial, including genetic predisposition and specific

Table 1: Data of the published cases of NPC metastasis to the breast.

References	Year	Age(years)	Gender
Sham [5,20]	1986	39	F
Sham[5,20]	1987	51	F
Driss [1]	1999	25	F
Que [19]	2003	41	F
Yeh [6]	2004	44	F
Vaishnav[7]	2012		F
Liang[8]	2013	49	M
Leach [5]	2013	49	F
This case	2013	17	F

Table 2: Chronological history (treatment and diagnosis) of the the case.

Treatment or diagnosis processes	Diagnosis and treatment	Date	Radiology	Stage
The initial presentation	NPC	11.10.2011	Magnetic resonance imaging (MRI)	Stage I (T1N0M0)
Treatment:conventional radiotherapy	Head and neck region: -Radiotherapy: 43 days, total dose 70 Gy. -Chemotherapy: Cisplatin 178 mg/first day (100mg/m2), 5 Fluorouracil 1780 mg/5 day (1000 mg/ m2) every 21 days.			
Breast metastasis	NPC	19.06.2013	Computed Tomography (CT)	
	Preoperative -Radiotherapy: 15 days, total dose 70 Gy			
Surgery:Pathologic diagnosis	Undifferentiated Subtype of Non-keratinizing Carcinoma of the Nasopharynx	14.08.2013		Stage IVC (T1N0M1)
After surgery	Local excision, Postop. -Chemotherapy: Docetaxel 100 mg/ one day (60mg/m2), 5 Fluorouracil 2500 mg/2 day (1000 mg/m2), Carboplatin (AUC 5), four cycles, every 21 days.			
At the end of the 21-month follow-up period	The patient was disease-free and continuing to come in for routine physical examinations.	14.05.2015	MRI, CT	

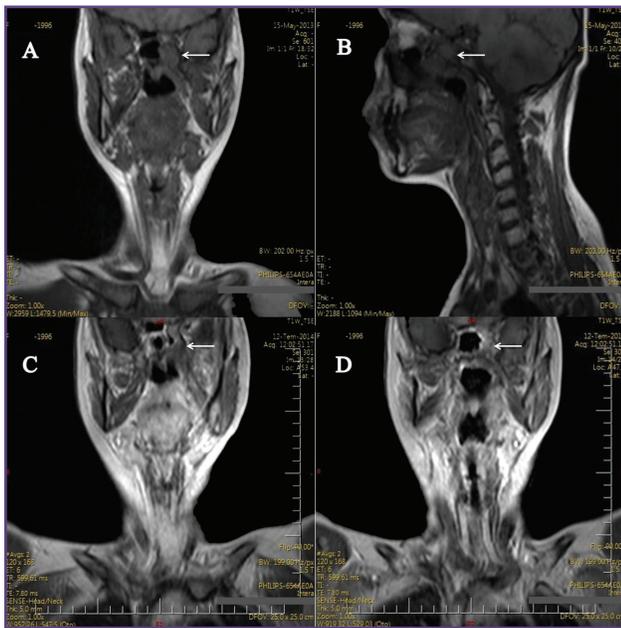


Fig. 1: Magnetic resonance imaging (MRI). (A, B) Preoperative MRI. (A) Axial post-contrast T1-weighted MRI showing a nasopharyngeal carcinoma (B) Sagittal T1 weighted MRI. C,D; postoperative MRI and postoperative local radiotherapy. (C, D) Axial post-contrast T1-weighted MRI.

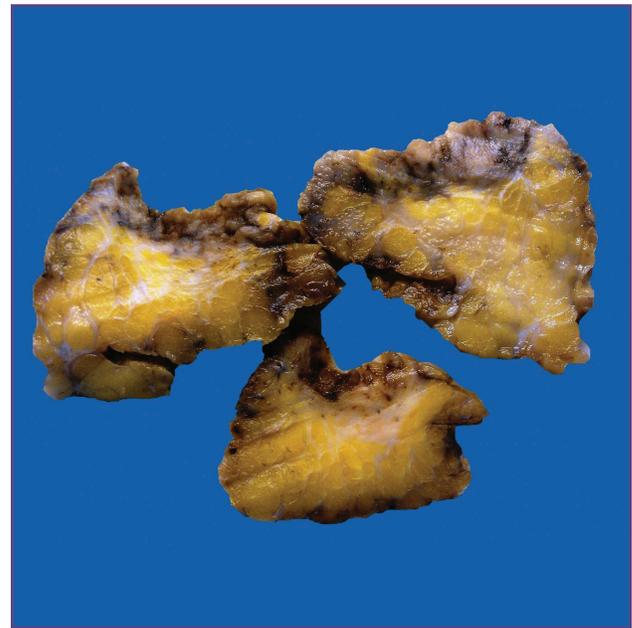


Fig. 2: Gross appearance of breast specimen.

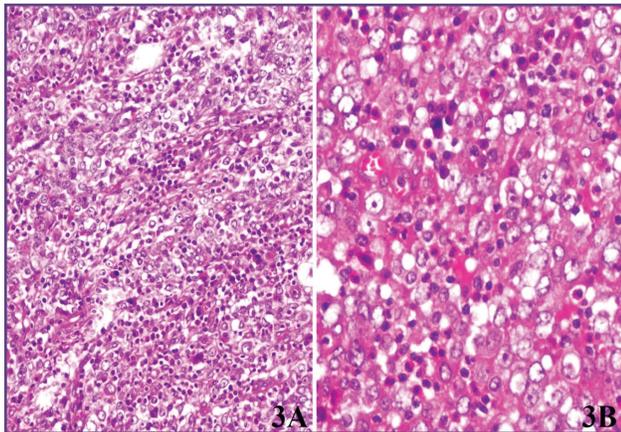


Fig. 3: (A) Undifferentiated nasopharyngeal carcinoma composed cells growth in a syncytial pattern and dense prominent lymphoplasmacytic infiltrate (H&E, 100×).

Fig. 3: (B) Undifferentiated nasopharyngeal carcinoma composed of tumor cells of oval to round large vesicular nuclei, with eosinophilic nucleolus (H&E, 200×).

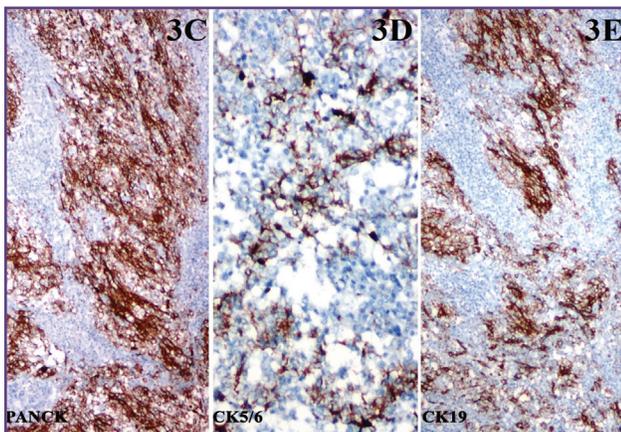


Fig. 3: (C,D,E) Immunohistochemically positive for pancytokeratin, CK5/6 and CK19 (100×).

carcinogens, by far the most important known predisposing factor is infection with the Epstein-Barr virus (EBV) [11,12]. In this section, we present a simplified version, taking into account the etiopathogenetic correlation of precursor EBV and the undifferentiated form of NPC (WHO type III) [13]. NPCs are most common in the region of the lateral wall of the nasopharynx with particular frequency in the fossa of Rosenmüller. Grossly, most lesions present as exophytic, but it is rarely ulcerated. Patients may be asymptomatic or may present with a mass in the posterior cervical triangle or superior jugular chain of nodes and sometimes present in the otitis media, epistaxis, and nasal obstruction [14]. NPCs are generally characterized by more aggressive clinical behavior; most present with a metastasis with extensive locoregional involvement and hematogenous or

lymphatic spread [2]. Bones constitute the most common metastatic site (75%), followed by lung (46%), liver (38%), and retroperitoneal lymph nodes (10%) [4]. Previous studies demonstrate the mean age of breast metastases from undifferentiated NPCs is 42 years (25 to 51 years) (see Table 1). In the present case, we present the first 17-year-old case of breast metastases from NPC to expand the medical database; there are no previously described reports of this in the literature. NPCs can be subdivided into three distinct groups: non-keratinizing carcinoma (the most common form), undifferentiated subtype (WHO III), and the condition called lymphoepitheliomas [15]. Histologically, the undifferentiated subtype is characterized by solid sheets and nests of the epithelial cells with cytoplasmic eosinophilia and round or oval vesicular nuclei and large, central, and prominent nucleoli with a dense, prominent lymphoplasmacytic infiltrate [16].

There are patterns of growth of NPC: Schmincke type is characterized by small clusters or aggregates and Regaud type also occurs in the large syncytial cells [17]. The immunophenotype of NPC has the following characteristics: positive for EBER, pancytokeratin, CK5/6, 34βE12, CK8, CD56, CK13, CK19, p63, and p53, but usually negative for CK4, CK7, CK10, CK14, CK20, p16, and HPV [14]. The most specific markers of breast carcinoma are gross cystic disease fluid protein 15 (GCDFP-15). There is apparently a diagnostically useful difference in the immunoprofile of breast carcinoma in the sense that the former is usually positive for CK7, GATA3, ER, and GCDFP-15 and negative for CK20 [18]. In most instances, the differential diagnosis of the undifferentiated subtype of non-keratinizing carcinoma resembles a number of other small round cell neoplasms of the sinonasal tract, including neuroblastoma, lymphoma, rhabdomyosarcoma, melanoma, plasmacytoma, and other [15] poorly differentiated carcinoma in primary breast cancer [10]. Radiotherapy for NPC, therefore, is the gold standard for treatment, and the 5-year survival rate in this series was 70% [11]. In contrast, the median survival for patients with metastatic tumors in the breast was approximately 10 months after the diagnosis of the metastases, and the patients ranged in survival from 0.4 to 192.7 months [10]. The prognosis of these metastatic tumors in the breast is substantially worse [7]. Primary treatment of metastatic tumors in the breast is radiation therapy and wide excision supplemented, if necessary, with therapy and/or combined axillary dissection. Mastectomy is not recommended as the therapy of choice [10]. The patient was treated with conventional radiotherapy and received radiotherapy to the

head and neck region and during a follow-up appointment 20 months after the diagnosis of breast metastasis (Table 2). At the end of the 21-month follow-up period, the patient was disease-free and continuing to come in for routine physical examinations.

Conclusion

In conclusion, breast metastases are most frequently confused with benign lesions and primary breast cancer. Obviously, metastasis to the breast requires a multidisciplinary approach with close cooperation and dialogue among the clinician, oncologist, radiologist, and pathologist. There should be careful comparison of suspicious foci with the cytologic or radiologic pattern in the initial diagnostic core needle biopsy. Therefore, patients with metastatic breast lesions may have been treated by unnecessary excessive radical surgery.

Conflict of interest

No financial competing interests

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None

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