Case Report

A 48-Year-Old Male with Cutaneous Metastases of NUT Midline Carcinoma Misdiagnosed as Herpes Zoster

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Keywords

NUT carcinoma · Skin · Cutaneous metastases

Abstract

NUT (nuclear protein of the testis) midline carcinoma (NMC) is a rare, poorly differentiated neoplasm with dismal prognosis. Though NMC are often metastatic by the time of presentation, cutaneous metastases have not been well described in the literature. We report a case of NMC in a patient who presented with grouped well-demarcated tender non-ulcerated erythematous nodules on the right mid-back. The lesions were initially diagnosed and treated as herpes zoster. Following failure to improve with antiviral therapy, imaging and skin biopsy revealed that the lesions were in fact cutaneous NUT carcinoma. Although NMC is an uncommon diagnosis, clinicians should be aware that affected patients can develop skin involvement to avoid unnecessary and harmful treatments.

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Introduction

NUT midline carcinoma (NMC), first described in 1991, is a rare, poorly differentiated neoplasm that portends a grim prognosis [1–3]. NUT carcinoma most often affects the midline upper aerodigestive tract structures, but can also affect the thymus, thorax, lungs, and mediastinum. NMC are uniquely defined by their genetics, rather than the tissue or site of origin. In almost all cases of NMC, NUT of chromosome 15 is abnormally fused to another gene, most commonly BRD4 of chromosome 19 (t15:19).

Here, we report a patient with known NUT carcinoma who had cutaneous metastases that were originally misdiagnosed and treated as shingles. Though disseminated disease with cutaneous involvement has been reported, characterization of these findings and corresponding histology is limited [4, 5].

Case Presentation

A 48-year-old male with known metastatic NUT carcinoma of the lung treated with cisplatin, etoposide, and radiation therapy presented to the hospital with 5 weeks of persistently painful and progressive nodules on his right flank. This rash had previously been diagnosed as shingles for which he was treated with 1 week of acyclovir and subsequently 1 week of valacyclovir without any improvement. Notable past medical history included gastroesophageal reflux disease and attention deficit disorder, for which he took omeprazole 20 mg and amphetamine-dextroamphetamine 20 mg daily. His family history was notable for lupus in his sister and arthritis in his mother. He was a current smoker with 30-pack-year tobacco history, occasional drinker, and occasional marijuana user.

On physical exam, there was a large firm, flesh-colored to erythematous dermal plaque with interspersed, grouped, well-demarcated, tender, non-ulcerated erythematous nodules on the right mid-back. No vesicles were present (Fig. 1).

Diagnosis and Follow-Up

Computed tomography of the chest revealed multiple soft tissue nodules and subcutaneous nodules, and edema along the right lateral abdominal wall with extension to a new fluid collection along the right lateral chest wall most concerning for metastasis. Punch biopsy of a nodule on the right mid-back confirmed the diagnosis of cutaneous NUT carcinoma, revealing a tumor composed of undifferentiated epithelioid cells with a very high nucleus-to-cytoplasmic ratio, hyperchromatic chromatin, and prominent nucleoli (Fig. 2).

Subsequent FISH evaluation demonstrated NUT rearrangement in 35 out of 50 nuclei, and immunohistochemical stain for NUT protein showed diffuse nuclear reactivity (Fig. 3). The sample stained positive for Pan-K, and negative for TTF-1 and napsin-A.

Following the diagnosis of cutaneous metastases, the patient's antiviral medication was stopped, and palliative care was consulted for management of his persistent pain.

Discussion

We report a case of NMC in a patient who presented with cutaneous metastases that were originally misdiagnosed as herpes zoster. The initial presentation of this painful rash in a pseudo-dermatomal fashion on the thorax in an immunocompromised patient led to an

incorrect diagnosis. Although secondary characteristics of zoster were present (pain, distribution), the primary lesions were not characteristic – firm, tender nodules instead of inflammatory papules with superimposed vesicles. Diagnoses of zoster that are made on secondary characteristics should be quickly revisited, especially if the patient does not improve with antiviral therapy.

NMC is a rare and aggressive subtype of squamous cell carcinoma [6]. Due to its nonspecific initial clinical presentation, diagnosis is often delayed, and as such NMC is often widely metastatic by the time of presentation. Currently, most patients receive combination chemotherapy and radiation; however, NMC is often refractory to conventional therapies, with a median survival time of approximately 9 months [7].

The rate of NMC with cutaneous involvement is unclear [4, 8]. Young et al. [5] described a case of cutaneous NMC metastases in an 11-year-old female who presented with pink-red dermal papules and plaques on the neck similar in nature to the findings of our patient.

Though it is a rare clinical presentation, clinicians should be aware that patients with NMC can develop cutaneous metastases to avoid unnecessary treatments and optimize pain control.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

References

- 1 Harms A, Herpel E, Pfarr N, et al: NUT carcinoma of the thorax: case report and review of the literature. *Lung Cancer* 2015;90:484–491.
- 2 Kubonishi I, Takehara N, Iwata J, et al: Novel t(15;19)(q15;p13) chromosome abnormality in a thymic carcinoma. *Cancer Res* 1991;51:3327–3328.
- 3 Kees UR, Mulcahy MT, Willoughby ML: Intrathoracic carcinoma in an 11-year-old girl showing a translocation t(15;19). *Am J Pediatr Hematol Oncol* 1991;13:459–464.
- 4 French CA, Kutok JL, Faquin WC, et al: Midline carcinoma of children and young adults with NUT rearrangement. *J Clin Oncol* 2004;22:4135–4139.
- 5 Young MR, Millington K, Clarke LE, Helm K: NUT midline carcinoma with cutaneous metastases. *J Am Acad Dermatol* 2012;67:323–324.
- 6 Chau NG, Hurwitz S, Mitchell CM, et al: Intensive treatment and survival outcomes in NUT midline carcinoma of the head and neck. *Cancer* 2016;122:3632–3640.
- 7 Al Diffalha S, Al Aukla N, Hasan S, Dickinson S, Khalil F: NUT midline carcinoma: a rare malignancy. *Cancer Control* 2017;24:202–206.
- 8 Stelow EB, French CA: Carcinomas of the upper aerodigestive tract with rearrangement of the nuclear protein of the testis (NUT) gene (NUT midline carcinomas). *Adv Anat Pathol* 2009;16:92–96.

Fig. 1. Right mid-back of patient. Multiple skin-colored and erythematous nodules overlying a skin-colored, firm plaque.

Fig. 2. Punch biopsy of the right mid-back. HE. $\times 600$. Undifferentiated epithelioid cells showing a very high nucleus-to-cytoplasmic ratio, hyperchromatic chromatin, and prominent nucleoli.

Fig. 3. Punch biopsy of the right mid-back. Immunohistochemical stain ($\times 600$) for NUT protein showed diffuse nuclear reactivity.