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Case report-Olgu sunumu
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Tdt positive small round cell tumor: Is this always lymphoblastic leukemia/lymphoma?

Tdt pozitif küçük yuvarlak hücreli tümör: Her zaman lenfoblastik lösemi/lenfoma mıdır?

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Abstract

Merkel cell carcinoma is a high-grade neuroendocrine carcinoma of the skin characterized by cells with a "blastic" appearance, scanty cytoplasm, evenly distributed chromatin. Terminal deoxy-nucleotidyl transferase is a DNA polymerase expressed by thymic T cells lymphoblastic lymphoma/leukemia and some cases of acute myeloid leukemia. Herein, we report a case of Terminal deoxy-nucleotidyl transferase positive small round cell tumor in consistent with Merkel cell carcinoma.

Keywords: Merkel cell carcinoma, terminal deoxy-nucleotidyl transferase, leukemia, lymphoma

Özet

Merkel hücreli karsinom dağılmış kromatine sahip, dar sitoplazmalı, blastic görünümde morfolojiye sahip derinin yüksek gradeli nöroendokrin tümörüdür. Terminal deoksinükleotidil transferaz lenfoblastik lösemi lenfoma ve bazı akut myeloid lösemilerde timik T hücrelerinden eksprese olan bir DNA polimerazdır. Burada terminal deoksinükleotidil transferaz pozitif merkel hücreli karsinom olgusu sunulmaktadır.

Anahtar sözcükler: Merkel hücreli karsinom, terminal deoksinükleotidil transferaz, lösemi, lenfoma

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Introduction

Merkel cell carcinoma (MCC) is an uncommon neuroendocrine cutaneous tumor which is highly aggressive [1]. It is most commonly seen in men in their 70s and on sun-exposed skin. Moreover, when it is found in immunosuppressed patients, the clinical course can be more fulminant [2]. The cell of origin remains elusive and the non- descript nature of the histology has led to various descriptions of the tumor, which include small cell cancer of the skin, trabecular cutaneous tumor, or anaplastic skin cancer [3]. The tumor is most often located in the head and neck region (50.8%) or the extremities (33.7%). The average size is 29 mm at presentation [4]. Terminal deoxy-nucleotidyl transferase (TdT) is an intranuclear enzyme, a template independent DNA polymerase, expressed in approximately 90% of acute lymphoblastic lymphoma, in a small subsed of acute myeloid leukemia and hematodermic CD56+/ CD4+ neoplasm and a significant number of pediatric small round cell tumors [5]. Herein, we report our experience with a case of a 69 year-old woman with MCC of arm with TdT positivity.

Case report

Clinicopathological features

A 69- year-old woman presented with a mass lesion in her left arm which was excised by a local surgeon. The received pathology specimen was examined and was found to particularly encapsulated irregular, tan-white colored lesion measuring 23x12x6 mm in diameter. Microscopically, the tumor exhibited a lobular growth patern (Figure 1a). A dermal based lesion composed of strands and nests of relatively uniform small round cells with scanty cytoplasm, round to oval nuclei, and powdery dispersed chromatin, as well as inconspicuous nucleoli (Figure 1b-d). There were numerous mitotic figures in the sections examined.

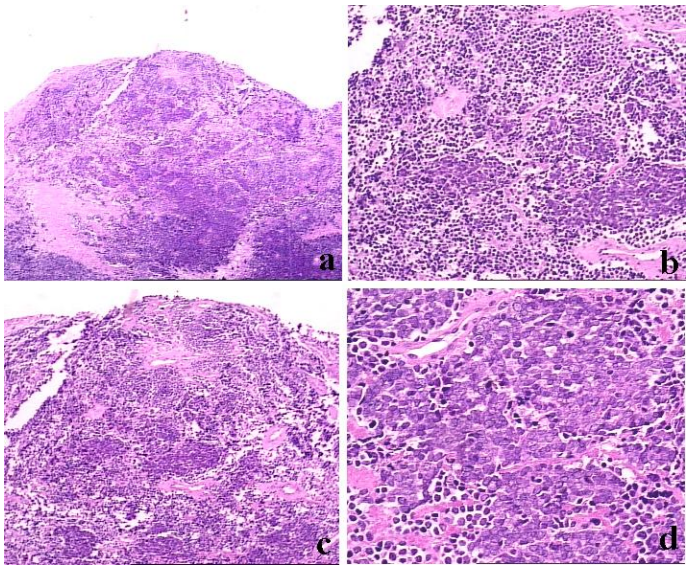

Figure 1a. The tumor exhibited a lobular growth patern. b-d. Dermal based lesion composed of strands and nests of relatively uniform, small and round cells with scant cytoplasm, round to oval nuclei, and powdery dispersed chromatin as well as inconspicuous nucleoli (H&E;X200).

Immunohistochemical analysis

Immunohistochemistry was performed on tissue sections by using Ventana Automated Immunostainer. The antibodies used included: EMA (GP1.4, NeoMarkers, 1/1000), CK 20 (Ks20.8, NeoMarkers, 1/150), Synaptophysin (27G12, NeoMarkers, 1/10), Chromogranin A (polyclonal, NeoMarkers, 1/1000), CD99 (HO36-1.1, NeoMarkers, 1/30), CD45 (C-Pan-LCA, NeoMarkers, 1/500), TTF-1 (8G7G3/1, Cell Marque, 1/250), Ki-67 (SP6, NeoMarkers, 1/200), and TdT (SEN 28, NeoMarkers, 1/30). Immunohistochemically, the neoplastic cells were positive for EMA, CK20 (dot like pattern), Synaptophysin, Chromogranin A, CD99, and also TdT (Figure 2). Ki-67 was positive in %100 of the tumor cells. The diagnosis of MCC was made.

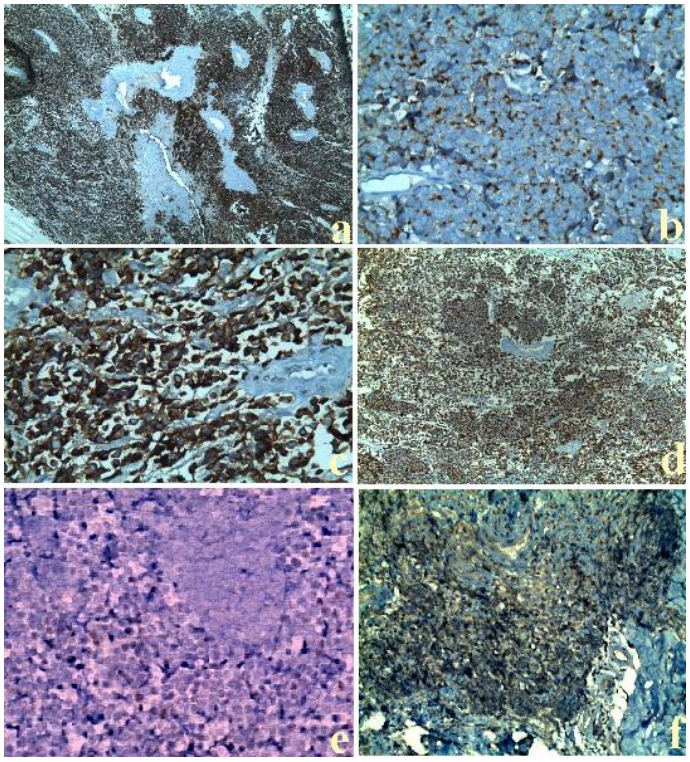

Figure 2a. Tumor cells showed reactivity with EMA. b. Dot like Cytokeratin 20 staining. c. Synaptophysin. d. Chromogranin A. e. CD99. f. Nuclear immunreactivity with TdT (X200).

Discussion

Merkel cell carcinoma (MCC) shares many histological and immunohistochemical features with small cell neuroendocrine carcinoma from other locations [6]. Although, CK20 has been reported to be occasionally positive in small cell carcinoma of the lung, it is considered to be a fairly specific and sensitive marker for MCC, showing membranous and paranuclear dot-like positivity in the neoplastic cells [7, 8]. In our case, the crushing artefact and the small cell morphology made us to thought metastatic small cell carcinoma, but paranuclear dot-like positivity for CK20 and clinical findings helped us to rule out the diagnosis of metastatic neuroendocrine carcinomas. TdT is expressed in most cases of acute lymphoblastic lymphoma (ALL), a small subset of acute myeloid leukemia (AML), occasional cases of CD56(+)/CD4(+) hematodermic neoplasm and some pediatric non-hematopoietic small round cell solid tumors [9]. A few cases of MCC expressing TdT has been published although the functional role of TdT in MCC remains unclear. The gene coding for TdT protein has been mapped to chromosome 10q. Interestingly, comperative genomic hybridization studies in MCC have revealed aberration of chromosome 10 in 33% of the cases [10]. It's tempting to speculate that this frequent aberration might be casually related to aberrant TdT protein expression. Future molecular analyses are needed to elucidate this issue. TdT expression in MCC may serve as an additional immunohistochemical discriminator in the differential diagnosis of non-cutaneous neuroendocrine tumours. On the other hand, TdT expression in MCC may elicit difficulty on the differential diagnosis from hematolymphoid neoplasms. When faced with a cutaneous or soft tissue lesion showing blastic morphology, the immunohistochemical panel should include epithelial markers (AE1/AE3, CAM5.2, CK7, CK20), neuroendocrine markers (NSE, Synaptophysin and CGA), and CD56, TTF-1, and first line hematolymphoid markers (CD45, CD34, TdT, CD10, CD3, CD20, myeloperoxidase and CD117) [11]. CD34 is a hematopoietic progenitor marker, which is positive in most cases of ALL along with TdT and CD10, and some cases of AML, but negative in MCC. CD99 positivity in MCC should be interpreted in conjunction with

other markers for small round cell tumors. CD56 and BCL2 are sensitive but not spesific markers, and can be used in combined with epithelial markers, CK20 and neuroendocrine markers in the diagnosis of MCC. Although CK7 expression has been reported in MCC, TTF-1 negativity can differentiate MCC from cutaneous metastasis of small cell carcinoma from other sites [11].

In conclusion, TdT expression can be seen in a subset of MCC. This finding may help to differentiate MCC from metastatic non-cutaneous neuroendocrine carcinomas, on the other side this may cause erroneous diagnosis of acute leukemia/lymphoma.

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