Cutaneous lesions as presentation form of mantle cell lymphoma

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Abstract

Mantle cell lymphoma is a type of non-Hodgkin lymphoma that affects extranodal areas, especially, bone narrow, digestive tract and Waldeyer ring. Here we report a case of mantle cell lymphoma IV Ann Arbor stage with cutaneous lesions on nasal dorsum and glans penis as the first manifestations. Skin involvement is a very rare manifestation and less than 20 cases have been reported in the literature. The importance of establishing multidisciplinary relationships for a global approach has been shown by this clinical case.

Introduction

Mantle cell lymphoma (MCL) is a type of non-Hodgkin lymphoma that frequently affects extranodal areas, especially, bone narrow, digestive tract and Waldeyer ring. Other areas can also be affected too, however skin involvement is very rare.[1,2] MCL is characterized by specific morphologic, inmunophenotypic and cytogenetic features [t(11;14)(q13;q32)] and cyclin D1 overexpression.[3]

Case Report

We report a 73-years-old man with a personal history of bilateral cataracts, facial right paralysis, vertiginous syndrome treated with trimetazidin and teleangiectasic rosacea without treatment. He was referred to our Department from Otolaryngology (ORL) where he was assessed for presenting nasal obstruction three months ago. No fever, asthenia or anorexia were reported. Physical examination revealed: i) papular erythematous, infiltrated, 2.5 × 2 cm of diameter lesion on nasal dorsum; ii) exulcerative, exudative lesion with an erythematous edge about 3×4 cm of diameter in glans penis were observed (Figure 1). Blood test and cutaneous biopsies were performed.

Histological examination of cutaneous lesions on face and penis showed diffuse lymphocytic proliferation with middle size cells with irregular and clefted nucleous (Figure 2). Moderate mitotic activity was observed. Immunochemistry was positive for CD-20 and D1-Cyclin and negative for CD3 and CD10. Ki-67 showed a high proliferation rate (Figure 3). These results were consistent with mantle cell lymphoma (MCL). Blood tests, including hemogram, biochemistry and hepatic profile were in normal ranges. ORL study included a turbinate biopsy. Diffuse lymphocytic tumoral proliferation infiltrates with middle size tumoral cells were observed. Tumoral cells showed clefted and irregular nucleous with granular chromatin, moderate mitotic rate and apoptotic bodies. Bone narrow biopsy, thorax Rx, CT scan, MRI, PET and cytogenetic study were performed. Limphocytic infiltrates showing features of MCL were observed in bone narrow. Multiple adenopathies and heterogeneous high intensity sings in both lungs were observed in PET studies (Figure 4). Cytogenetic studies were performed and t(11;14) was observed by FISH.

After hematologic and dermatologic assessment MCL IVA Ann Arbor stage and intermediate-high IPI diagnosis was established.

Four cycles of R-CHOP were administered every 21 days. A clear improvement after two cycles was observed (Figure 3). Two years later, the patient is still alive with Hematological, ORL and Dermatological periodical controls.

Discussion

The MCL represents around 10% of non-Hodgkin lymphomas (NHL). It usually affects medium or elder people. Skin involvement is rare, nevertheless, it can be the first manifestation of MCL. Only 19 cases of cutaneous MCL have been reported in the literature. It represents 2-6% of all NHL and the 17% are in stage IV. Men are more frequently affected than women (13:4) with a mean age of 63-years-old. Lesions usually appear in trunk, in contrast with our patient that presented the lesions first in face and genital area. A high variety in clinical appearence has been described. Nodular lesions are the most frequent clinical presentation, but macules, papules or plaques have been described too.

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Our patient presented two diferent clinical forms; nasal dorsum with papular presentation and ulcerative clinical appearence in glans penis. Genital ulcerative form of cutaneous MCL is uncommon. Up to 82% of patients with skin lesions present coexisting extracutaneous involvement, so extension studies are necessary to find other affected organs including blood tests, Rx, CT scan, MRI and PET. MCL has a median survival of 3-5 years, with a better prognosis in patients with non-nodal disease. MCL is associated to a poor prognosis.[3,4] The median survival time

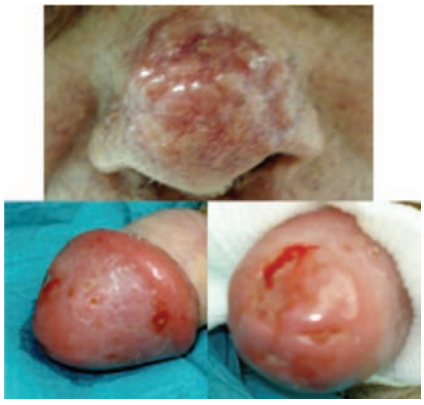

Figure 1. Clinical appearance of cutaneous lesions on face and glans penis.

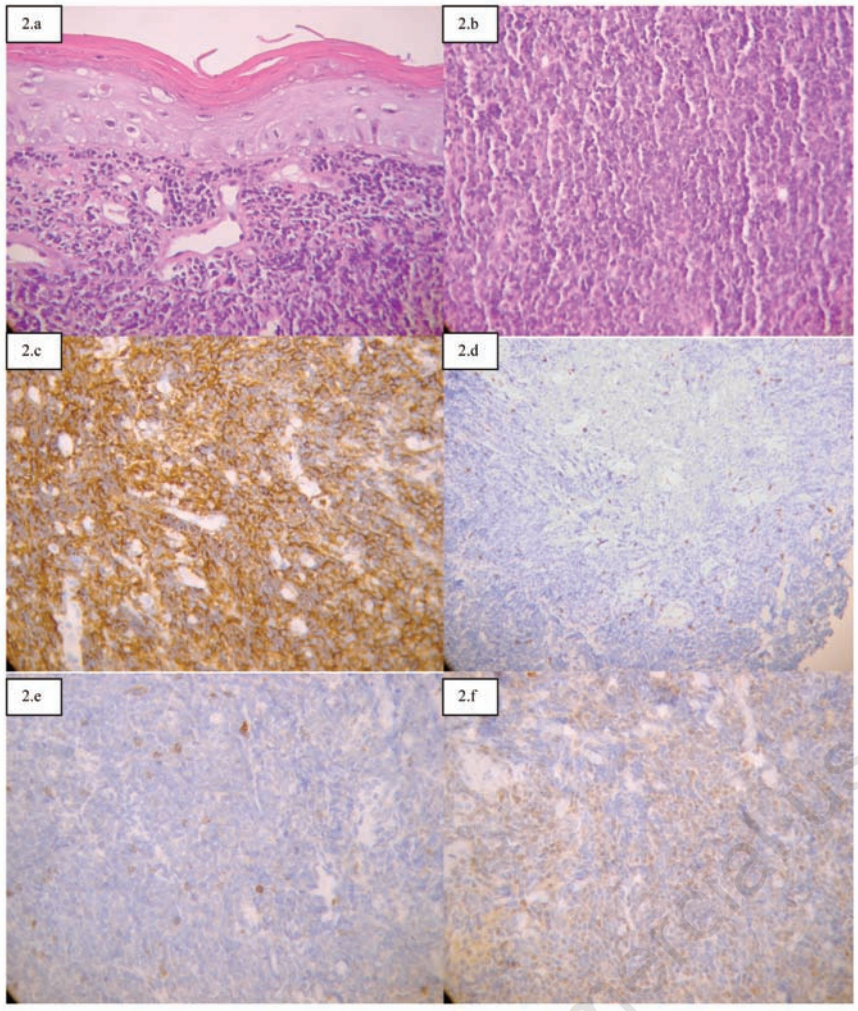

Figure 2. Histological finding: a, b) Hema-toxylin and Eosin; c) CD20; d) CD3; e) CD10 and f) D1-Cyclin stains.

Table 1. Skin manifestation of mantle cell lymphoma.

N	Author	Age/Gender	Extracutaneous involvement	Stage	Prognosis
1	Ellison	66M	Yes	IV	D (55 days after hospitalizazion)
2	Geerts	65F	Yes	IVA	D (1.5 years after diagnosis)
3	Geerts	77F	Yes	IVA	
4	Bertero	51M	Yes	IVA	A (17 years after diagnosis)
5	Bertero	78F	No	IE	D (3 years after diagnosis)
6	Bertero	43M	Yes	IVA	A
7	Bertero	22M	No	IE	A
8	Marti	61F	Yes	IVA	D (15 months after diagnosis)
9	Moody	47M	Yes	IVA	A (3 years after onset)
10	Dubus	56M	Yes	IVA	D (1 year after treatment)
11	Dubus	89M	Yes	IVA	D (5 days after diagnosis)
12	Dubus	72M	Yes	IVA	A (1 year after treatment)
13	Sen	85M	Yes	IVB	D (20 months after onset)
14	Sen	76M	No	IE	A (30 months after onset)
15	Sen	56M	Yes	IVA	A (21 months after onset)
16	Sen	57M	Yes	IVB	D (19 months after onset)
17	Sen	61M	Yes	IVB	D (17 months after onset)
18	Motegi	62M	Yes		A (4 months after diagnosis)
19	Estrozi	72M	Yes	IVA	A (6 months after diagnosis)
20	Merino	73M	Yes	IVA	A (2 years after diagnosis)

Most of data adapted from Motegi S, Okada E, Nagai Y, Tamura A, Ishikawa O. Skin manifestation of mantle cell lymphoma. Eur J Dermatol. 2006 Jul-Aug; 16(4):435-8. D, dead; A, alive.

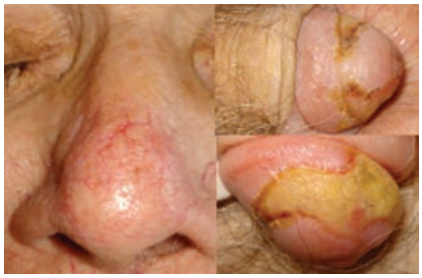

Figure 3. Clinical appearance after treatment.

is aproximately 3 years (range 2-5 years). The ten year survival rate is only 5-10%. Younger age and limited diseases are favorable prognostic features. Survival behavior of patients with cutaneous involvement is showed in Table 1. The skin involvement is considerer as independent prognostic factor, but it is uncertain.[3,5,6] Treatment is difficult. First-line treatments for solitary lesions include surgical excision, antibiotics, and radiotherapy. Systemic involvement needs an aggressive management. Only 30% of patients experienced a complete response. It is based in single akylating agents, CVP (cyclophosphamide, vincristine and prednisone) and CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) regimens, Hyper-CVAD (hyperfractionated cyclophosphamide, doxorubicin, vincristine, and dexamethasone) with or without rituximab, R-CHOP (CHOP plus rituximab) or Hyper-CVAD with autologous stem cell transplantation. Our patient was treated with R-CHOP with a complete response. R-CHOP have showed a higher complete response rate than CHOP. Complications from chemotherapy may include infection, neutropenia, anemia, and thrombocytopenia, fatigue, neuropathy, dehydration after diarrhea or vomiting and cardiac toxicity from doxorubicin.[6,7] Only ORL area involvement is also rare. So, our patient presented with a very unique clinical picture. In fact, sinonasal lymphomas are relatively uncommon and represent less than 1% of all head and neck malignancies. T/NK cell lymphoma is the most frequent in nasal cavity, however B-cell lymphoma is the main type in paranasal sinuses.[8,9] So, here we present a rare case of MCL with cutaneous and nasal cavity lesions as presentation signs. The role of dermatologists is very important, in establishing an early diagnosis. We have to consider this entity in the dermatologic differential diagnosis of tumours and we have to be aware about the importance of multidisciplinary approach.

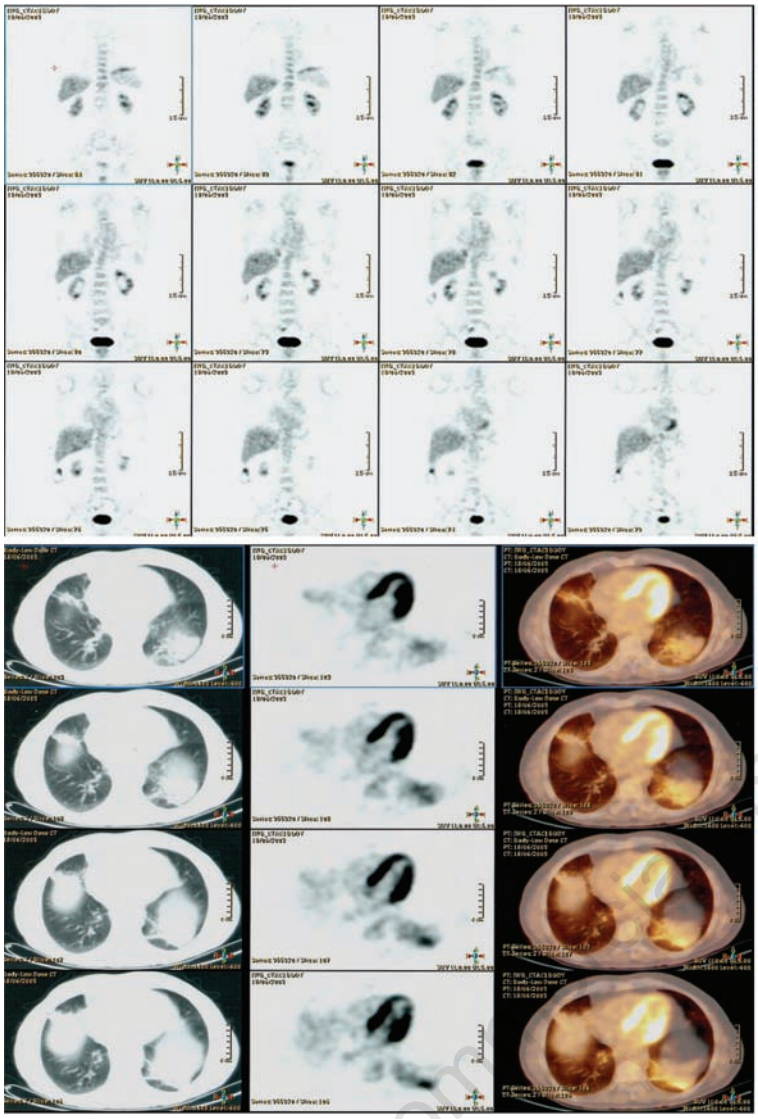

Figure 4. Upper side: Preauricular, retroauricular, occipital, submandibular, subcarinal, right hilum and groin lymphadenopathies, heterogeneuos. Lower side: High intesity sings in both lungs were observed in PET studies.

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