

World Journal of *Clinical Cases*

World J Clin Cases 2020 April 26; 8(8): 1343-1560



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Semimonthly Volume 8 Number 8 April 26, 2020

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Responsible Electronic Editor: *Ji-Hong Liu*

Proofing Production Department Director: *Xiang Li*

Responsible Editorial Office Director: *Jin-Lei Wang*

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Semimonthly

EDITORS-IN-CHIEF

Dennis A Bloomfield, Bao-Gan Peng, Sandro Vento

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

April 26, 2020

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PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Primary cutaneous mantle cell lymphoma: Report of a rare case

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Author contributions: Zheng XD collected the data, reviewed the literature, and drafted the manuscript; Xie JL analyzed and interpreted the imaging findings; Zhang YL and Zhou XG were responsible for the revision of the manuscript for important intellectual content; all authors issued final approval for the version to be submitted.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: All authors declare that they have no conflict of interest.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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Abstract

BACKGROUND

We describe the case of a 74-year-old man diagnosed with primary cutaneous mantle cell lymphoma (MCL), an extremely rare and controversial condition that is not included in the World Health Organization-European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas.

CASE SUMMARY

The patient presented diffuse cutaneous erythematous plaques and nodules throughout the body. Skin lesions were biopsied and histopathological examination showed diffuse monomorphic lymphocyte infiltration in the dermal and subcutaneous layers, sparing the epidermis. Immunohistochemical staining revealed CD20, cyclin-D1, CD5, and SOX-11 expression. Fluorescence *in situ* hybridization showed *CCND1/IGH* gene rearrangement. Correct diagnosis of primary cutaneous MCL requires ensuring that no other parts are involved; these cases require close follow-up to monitor their possible progression to systemic disease and for treating relapsed cutaneous disease. In this case, positron emission tomography scanning and clinical staging revealed no systemic involvement, and follow-up examination at 20 mo after diagnosis showed no evidence of systemic disease. The prognosis of primary cutaneous MCL is relatively good. Our patient received six cycles of chemotherapy, and the cutaneous manifestations presented almost complete remission.

CONCLUSION

Primary cutaneous MCL is rare, and its prognosis is relatively favorable. However, correct diagnosis is a prerequisite for proper treatment.

Key words: Primary; Cutaneous; Mantle cell lymphoma; Diagnosis; Treatment; Prognosis; Case report

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Core tip: Primary cutaneous mantle cell lymphoma (MCL) is rare and has been the subject of isolated case reports. To correctly diagnose primary cutaneous MCL, it must

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Manuscript source: Unsolicited Manuscript

Received: January 18, 2020

Peer-review started: January 18, 2020

First decision: February 26, 2020

Revised: April 3, 2020

Accepted: April 8, 2020

Article in press: April 8, 2020

Published online: April 26, 2020

P-Reviewer: Cerwenka H, Saito M

S-Editor: Wang YQ

L-Editor: Wang TQ

E-Editor: Liu JH



be ensured that no other parts are involved, and these cases require close follow-up to monitor the possible progression to systemic disease and treat relapsed cutaneous disease. Correct diagnosis is crucial for clinical treatment and prognosis. The prognosis of primary cutaneous MCL is relatively favorable, and treatment options should comply with the clinical condition of the patient.

Citation: Zheng XD, Zhang YL, Xie JL, Zhou XG. Primary cutaneous mantle cell lymphoma: Report of a rare case. *World J Clin Cases* 2020; 8(8): 1507-1514

URL: <https://www.wjgnet.com/2307-8960/full/v8/i8/1507.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v8.i8.1507>

INTRODUCTION

Mantle cell lymphoma (MCL) is a mature B-cell neoplasm characterized by uncontrolled proliferation of small to medium-sized lymphoid cells within the mantle zone^[1]. More than 95% of cases of MCL show the CCND1 chromosomal translocation t(11;14)(q13;q32), which triggers cyclin D1 overexpression^[2,3]. Lymph nodes are the most frequently involved sites. The spleen and bone marrow, with or without peripheral blood involvement, are also important sites of the disease. Other frequently involved extra-nodal sites include the gastrointestinal tract and Waldeyer's ring. However, skin involvement in MCL is rare, and most cases occur due to secondary cutaneous dissemination by widespread disease^[4-8]. Primary cutaneous MCL is even rarer, and mostly isolated cases have been documented previously and the majority of such patients typically present with systemic lymphoma in later stages^[4,9-13]. The World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC) does not classify primary cutaneous MCL as a cutaneous lymphoma^[14]. Here, we report a rare case of primary cutaneous MCL and describe its clinical, histopathological, immunohistochemical, and genetic features, as well as its treatment and prognosis.

CASE PRESENTATION

Chief complaints

Diffuse cutaneous erythematous plaques and nodules (Figure 1).

History of present illness

In May 2018, a 74-year-old man showed diffuse cutaneous erythematous plaques and nodules with irregular borders on the chest; the effect of anti-allergy treatment was not prominent.

History of past illness

The patient's history of past illness was not remarkable.

Personal and family history

The patient's father had a history of hypertension, and his mother had a history of breast cancer.

Physical examination upon admission

After the first examination, the number of cutaneous lesions increased progressively and involved the entire body, with diameters ranging from 0.5 to 1 cm. The patient's overall physical condition was good, without B symptoms.

Laboratory examinations

Skin lesions on the trunk and scrotum were biopsied. Histopathological examination showed diffuse monomorphic lymphocyte infiltration in the dermal and subcutaneous layers, but not in the epidermis (Figure 2A and B). The lymphoid cells were mostly small to medium in size, with irregular nuclear contours (Figure 2C).

Immunohistochemistry (Figure 3) showed the following phenotypic characteristics: CD21 and CD23 staining displayed a broken follicular dendritic cell network; staining for other markers was as follows: Cyclin D1⁺, SOX11⁺, CD5⁺, CD20⁺, CD43⁺, BCL2⁺, BCL-6 scattered⁺, CD10⁺, LEF1⁺, CD56⁻, CD30⁻, CD2⁻, TIA1⁻, CD4⁻, CD8⁻, and Ki-67⁺.

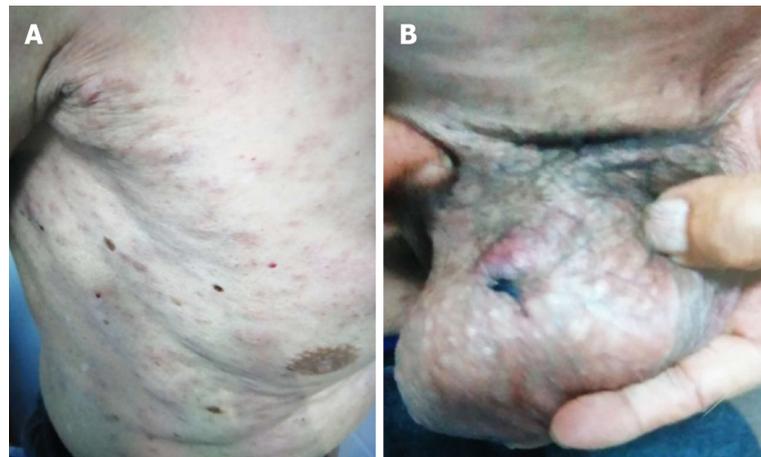


Figure 1 Clinical cutaneous features of this case. A: Diffuse, irregular cutaneous erythematous nodules and plaques on the trunk; B: Diffuse, irregular cutaneous erythematous nodules and plaques on the scrotum.

Tumor cells showed a proliferation index of approximately 20%. *In situ* hybridization revealed the absence of EBER⁺ tumor cells. Fluorescence *in situ* hybridization (FISH) revealed *CCND1/IGH* gene rearrangement, a distinctive feature of the t(11;14) (q13;q32) chromosomal translocation (Figure 4). Altogether, these clinical phenotypes were consistent with the diagnosis of cutaneous MCL. The clinical data revealed no lymphadenopathy, bone marrow biopsy and peripheral blood examination were normal, and there was no spleen or liver involvement.

Imaging examinations

Positron emission tomography did not reveal systemic involvement.

FINAL DIAGNOSIS

Primary cutaneous MCL was the ultimate diagnosis.

TREATMENT

The patient received six cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) chemotherapy.

OUTCOME AND FOLLOW-UP

The cutaneous manifestations presented almost complete remission without recurrence and progression.

The patient underwent a follow-up examination in January 2020, 20 mo after diagnosis, and no evidence of systemic disease was observed. The peripheral blood test results and bone marrow biopsy at this time were normal.

DISCUSSION

Skin involvement in MCL is very uncommon, accounting for 2%-6% of all cases^[6]. Cutaneous manifestations in MCL occur primarily in cases with systemic disease. Secondary skin involvement in MCL has been described in several studies, but primary cutaneous MCL has seldom been reported^[4-13]. Indeed, the presence of primary cutaneous MCL is controversial. It is not included in the WHO-EORTC classification^[14] and in the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues^[2] for cutaneous lymphomas. A primary cutaneous lymphoma following the WHO-EORTC definition^[14], refers to a lymphoma that presents in the skin without extracutaneous disease during the process of diagnosis. Some studies^[11,15] have pointed out that a conclusive diagnosis of primary cutaneous MCL can only be achieved if there are no extracutaneous lesions during 6 mo of clinical follow-up with

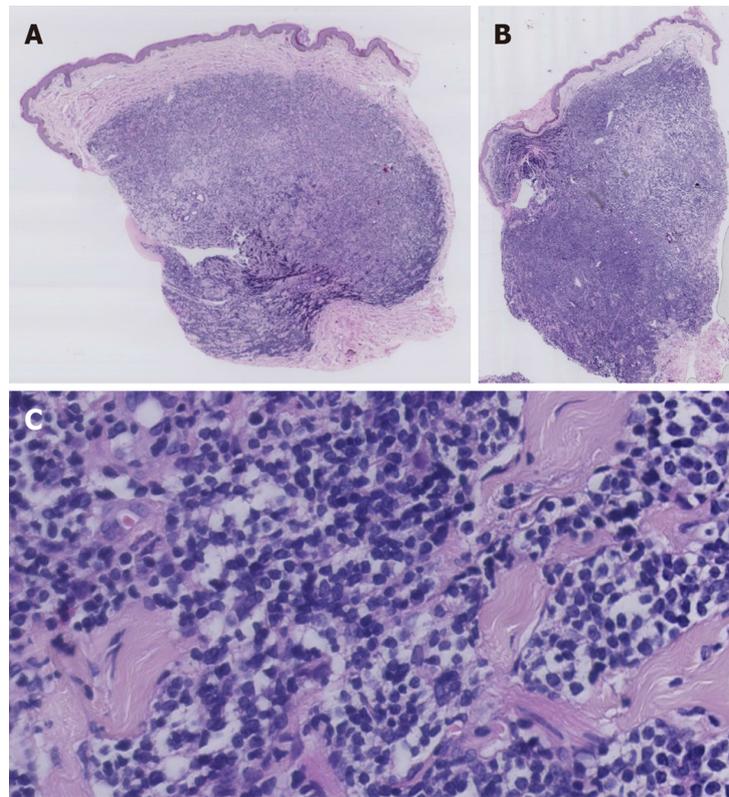


Figure 2 Histopathological changes of this case. A: A diffuse superficial and deep dermal monomorphic lymphoid infiltrate with a Grenz-zone was observed, sparing the epidermis of biopsy of skin lesions on the trunk (HE staining, $\times 20$); B: A diffuse superficial and deep dermal monomorphic lymphoid infiltrate with a Grenz-zone was observed, sparing the epidermis of biopsy of skin lesions on the scrotum (HE staining, $\times 20$); C: The lymphoid cells were small to medium-sized with mildly irregular nuclei, interspersed through the collagen fibers (HE staining, $\times 400$).

adequate staging. Our patient showed no signs of extracutaneous lesions during the process of diagnosis and up to 20 mo after diagnosis.

A review of the literature reveals less than 50 reported cases of cutaneous MCL. Sen *et al*^[4] reported five cases of cutaneous MCL in 2002, Motegi *et al*^[5] reviewed 17 cases of skin involvement in MCL in 2006, Wehkamp *et al*^[6] reported 14 cases in 2015, and Gru *et al*^[7] reviewed ten cases in 2016. In addition, several case reports are available in literature^[9,12,13]. Of these cases, only eight were thought to be primary cutaneous MCL, of which only five were found as clear cases of this condition^[4,10-13]. The clinical features and follow-up information of these cases are summarized in Table 1. The lesions of the described cases were limited to the skin without systemic involvement. Our 74-year-old male patient presented diffuse cutaneous erythematous plaques and nodules.

Gru *et al*^[7] reported that among the cases studied, they observed tumor cell infiltration into the dermis and subcutaneous tissue, with cell-free infiltration zone between the dermis and epidermis. The lymphocytes were mostly small to intermediate in size, with two of ten cases belonging to the blastoid variant. A previous study by Sen *et al*^[4] reported that most cases of cutaneous MCL had blastoid morphology and should be classified as blastoid variants. Recently, the largest case study on cutaneous MCL was conducted by Wehkamp *et al*^[6], who also found that all of their analyzed cases, except two, had blastoid morphology, and this type was considered extensively aggressive. The median survival of patients with classic histological features was 50 mo, whereas that for patients with blastoid morphology was 18 mo^[16]. The five previously reported cases of primary cutaneous MCL showed that the tumor cell sizes were predominantly intermediate to large. However, our case showed a diffuse monomorphic small to medium-sized lymphocyte infiltration, which did not belong to the blastoid variant.

MCL refers to a B-cell lymphoma with characteristic immunohistochemical and molecular features such as the expression of cyclin D1 and t(11;14)(q13;q32) translocation. More than 95% of MCL cases express cyclin D1, whereas only a few cases are negative^[17]. In MCL cases, SOX11 has emerged as an effective marker for diagnosis, with approximately 93%-95% of MCL cases being SOX11-positive. Combined immunohistochemistry tests for cyclin D1 and SOX11 exhibited a

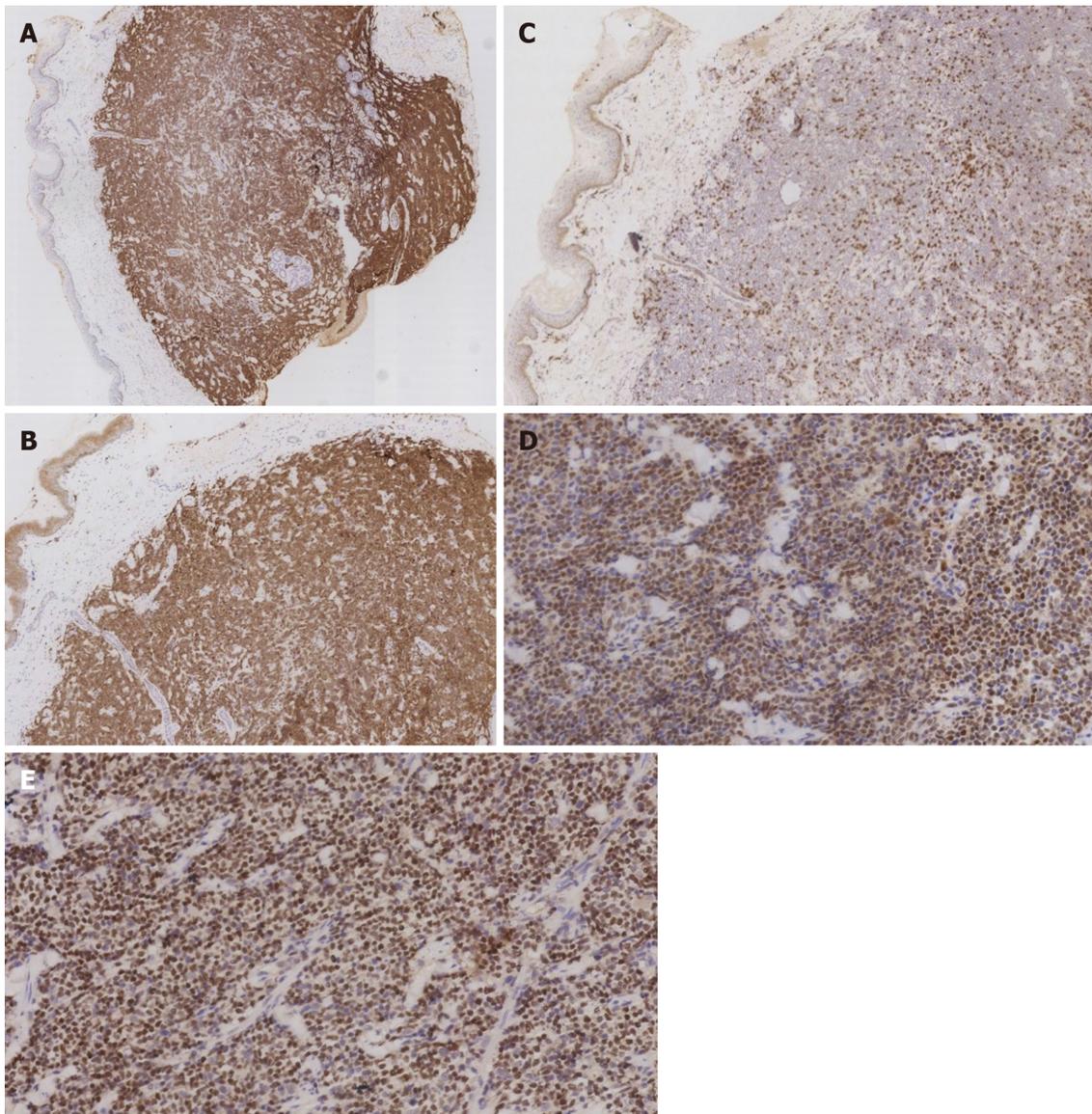


Figure 3 Immunohistochemical features of this case. A: Positivity for CD20 ($\times 25$); B: Positivity for CD5 ($\times 50$); C: Negativity for CD3 ($\times 50$); D: Positivity for cyclin D1 ($\times 200$); E: Positivity for SOX-11 ($\times 200$).

specificity and sensitivity of both 100% for diagnosing MCL^[18]. Accurate differentiation of MCL from other cutaneous lymphomas is thus possible by using the characteristic immunohistochemical and genetic features. Our case was positive for both cyclin D1 and SOX11 and showed CCND1 translocation.

Skin involvement in MCL mainly appears in cases with systemic disease, which show invasive clinical progression and poor prognosis because of a high recurrence rate. According to previous studies^[19,20], systemic chemotherapy is the standard treatment for MCL. However, the therapy of choice for primary cutaneous MCL is difficult to confirm as this condition has been not reported frequently; it is thus unclear whether the standard treatment for systemic disease can be applicable to a localized manifestation. Of the five previously reported cases of primary cutaneous MCL in addition to the current case, four patients received chemotherapy, whereas the remaining two showed isolated skin nodules and were treated with local radiotherapy or surgery. The prognoses of all six patients were relatively good, with nearly complete remission of the skin lesions after 6–31 mo of follow-up.

CONCLUSION

In conclusion, primary cutaneous MCL is rare and has been the subject of isolated case reports. Correct diagnosis of primary cutaneous MCL requires ensuring that no other parts are involved, and these cases require close follow-up to monitor the

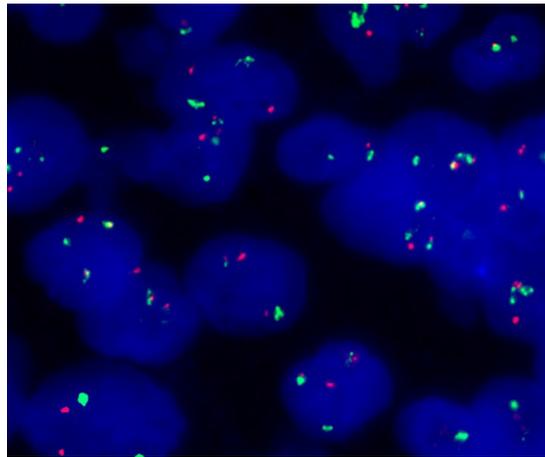


Figure 4 Fluorescence *in situ* hybridization analysis of this case. Fluorescence *in situ* hybridization analysis demonstrated fusion of the *CCND1* gene locus (orange) and the immunoglobulin heavy chain gene locus (green).

possible progression to systemic disease and for the treatment of relapsed cutaneous disease. The prognosis of primary cutaneous MCL is relatively favorable, provided that the diagnosis is conclusive, and treatment options should comply with the clinical condition of the patient. For localized disease, radiotherapy or surgical resection followed by frequent observation should be the treatment of choice; however, chemotherapy should be considered efficient for prolonged survival.

Table 1 Clinical features of five cases of primary cutaneous mantle cell lymphoma reported previously

Case	Ref.	Age (yr)	Sex	Site	Clinical presentation	Treatment	Outcome (mo)
1	Sen <i>et al.</i> ^[4] , 2004	76	Male	Thigh	A single nodule	Hyper-CVAD	30
2	Estrozi <i>et al.</i> ^[11] , 2009	72	Male	Temporal region	Cutaneous nodule	Surgical resection and radiotherapy	6
3	Zattra <i>et al.</i> ^[10] , 2010	77	Male	The whole body	Diffuse erythematous nodules and plaques	Chemotherapy (refer to note)	28
4	Mazzuocolo <i>et al.</i> ^[12] , 2013	72	Female	Back	Erythematous nodule	Surgical resection	24
5	Hamad <i>et al.</i> ^[13] , 2015	68	Female	Legs	Cutaneous erythema	Chemotherapy (R-CHOP)	31

Note: Etoposide 100 mg/d and prednisone 25 mg/d for 5 d per mo for 11 mo, then maintained on 5 mg prednisone daily.

ACKNOWLEDGEMENTS

The authors would like to thank Lan Sun from our department for performing and providing the FISH results and corresponding images.

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