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Title

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Journal

Dermatology Online Journal, 25(10)

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Publication Date

2019

DOI

10.5070/D32510045822

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Peer reviewed

Follicular spicules of multiple myeloma

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Abstract

Follicular spicules are a very rare but highly characteristic cutaneous manifestation of multiple myeloma. The spicules typically appear as hyperkeratotic horns in the follicular openings of the face, most commonly on or around the nose and forehead. The pathophysiology of this condition has not been fully elucidated and remains an active area of research and debate. Herein we describe a patient who presented with follicular spicules in the context of unintentional weight loss, anemia, and elevated inflammatory markers. We discuss the diagnostic work-up for such a presentation, review the classification of follicular spicules of multiple myeloma, and describe approaches to manage this uncommon skin condition.

Keywords: hyperkeratosis, follicular spicules, multiple myeloma, paraneoplastic, malignancy

Introduction

Multiple myeloma (MM) is a hematologic cancer characterized by monoclonal proliferation of plasma cells that results in excess production of abnormal proteins called immunoglobulins. Signs and symptoms of MM tend to be variable and non-specific, including fatigue, anorexia, constipation, polydipsia, and weight loss. Some patients with MM have no symptoms. Dermatologic manifestations of MM are rare, but the most common cutaneous manifestation is follicular spicules of multiple myeloma. Herein, we present a patient with constitutional symptoms concerning for MM who

presented with rare but distinct skin signs that are consistent with this hematologic malignancy.

Case Synopsis

A 50-year-old man presented with progressive skin lesions and unexplained continued weight loss of 35 pounds with a normal appetite over one year. He initially presented to his primary physician for an itchy facial rash of the face and ears that developed gradually over several months. A dermatology consultation was recommended for evaluation of his skin findings.

Initial physical examination revealed diffuse xerosis with a rough, gritty texture affecting the scalp, face, and neck. He had no personal history of such symptoms and no other significant medical conditions. Exposures included regular use of cleaning products (e.g. bleach) in his occupation, but no recent travel or sick contacts. At this time, laboratory work revealed an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and low hemoglobin with elevated mean corpuscular volume (MCV) consistent with anemia of chronic disease as presented in **Table 1** (April 2018). A rheumatology consultation was recommended for evaluation of a possible autoimmune process.

The rheumatology consultant believed that the skin changes were likely related to the abnormal laboratory results but that there were no symptoms or other findings concerning for a primary rheumatologic disease. Since the skin changes were progressing, the patient was re-referred for a dermatology consultation. At follow-up, the

eruption had extended to include keratotic spicules (some perifollicular) on the patient's scalp, face, ears, neck, upper back, and fingertips. In addition, a few scattered, small papules were observed on the forehead and several fingertips exhibited hyperkeratosis (**Figures 1, 2**). No other concerning skin lesions were identified and no skin changes were observed on the lower body. Furthermore, the patient also complained of continued weight loss as well as fatigue. As reported in **Table 1** (August 2018), an extensive infectious work up did not reveal any abnormalities and repeated measurements of CRP and hemoglobin showed further deviation from normal reference ranges whereas ESR and MCV remained stable but persistently abnormal. The patient also underwent age-appropriate colon cancer screening with a colonoscopy that was normal, followed by a malignancy workup that included CT imaging of the chest, abdomen, and pelvis that were all normal.

At this point, concern for a hematologic malignancy required a medical oncology consultation and additional workup with results detailed in **Table 1** (September 2018). In addition, a representative skin lesion was biopsied; findings are seen in **Figure 3**. In summary, laboratory studies revealed abnormal serum protein electrophoresis (SPEP) with immunofixation showing a markedly elevated M-band with a spike in the gamma region and an elevated kappa to lambda free light chain ratio. The



Figure 1. Keratotic spicules on face/nose.



Figure 2. Hyperkeratosis of several fingertips.

skin biopsy revealed a dilated follicular infundibulum with exophytic keratotic plug, which was read in combination with the serological findings to support a diagnosis of follicular spicules of multiple myeloma (FSMM). This diagnosis was subsequently supported by bone marrow biopsy.

At the time of publication, the patient is undergoing chemotherapy with bortezomib and lenalidomide plus dexamethasone, followed by plans to perform an autologous stem cell transplant.

Case Discussion

We present a patient with FSMM, a highly characteristic manifestation of MM that is exceptionally rare, with less than a dozen reports in the literature [1-6]. Dermatologic manifestations of MM are classified as specific and non-specific. Specific lesions are very rare and include extramedullary plasmacytomas (cutaneous or mucosal) as well as secondary skin involvement from underlying bone tumors [1]. These usually occur in late stages of MM. Conversely, non-specific signs occur early in MM and are the result of hematologic alterations related to abnormal serum protein levels [2]. Non-specific signs include spicules and papules, as seen in this case, as well as ulcers, hair casts on the scalp and lash line, and unusual nail changes [1-6]. Since non-specific lesions can be the first sign of MM development or recurrence, early recognition (often

Table 1. Key laboratory results with values outside of reference range indicates as high (H) or low (L).

| | April 2018 | August 2018 | September 2018 |
|--------------------------------------|------------|--------------|---------------------------------|
| Erythrocyte sedimentation rate (ESR) | >120 (H) | >120 (H) | |
| C-reactive protein (CRP) | 0.6 (H) | 3.0 (H) | |
| Hemoglobin | 10.7 (L) | 9.1 (L) | |
| Mean corpuscular volume (MCV) | 98 | 98 | |
| HIV 1+2 Antibody/Antigen | | Non-reactive | |
| HSV 1 IgG Enzyme-Linked Immunoassay | | Negative | |
| HSV 2 IgG Enzyme-Linked Immunoassay | | Negative | |
| T pallidum IgG+IgM | | Non-reactive | |
| HCV Antibody | | Negative | |
| HIV-1 RNA | | | Negative |
| Alanine transaminase (ALT) | | | 114 |
| Aspartate aminotransferase (AST) | | | 16 |
| Alkaline phosphatase | | | 44 |
| Thyroid stimulating hormone (TSH) | | | 0.89 |
| T4 free | | | 1.2 |
| Protein urine | | | 31.8 |
| Lactate dehydrogenase (LDH) | | | 1.2 |
| Albumin | | | 3.7 (L) |
| Vitamin A | | | 32 (L) |
| Kappa/Lambda free | | | 51.32 (H) |
| Kappa light chain free | | | 417.4 (H) |
| Serum protein electrophoresis (SPEP) | | | Abnormal |
| M-band-1 | | | 45.5 (H), spike in Gamma region |

by a dermatologist) can facilitate early diagnosis and prompt treatment.

The pathogenesis of FSMM has not been fully characterized [1-6]. Hypotheses range from an alteration in normal keratinization resulting from underlying hematologic malignancy to an autoantibody that modifies the keratinization

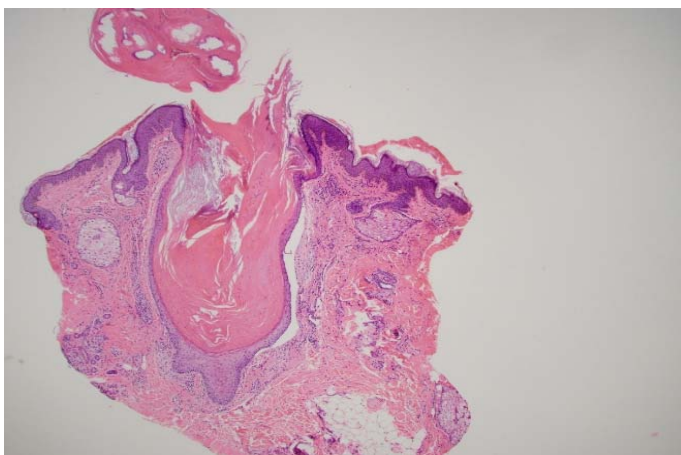


Figure 3. Dilated follicular infundibulum with exophytic keratotic plug. H&E, 40x.

process [2]. In several of the reported cases, the spicules were histologically proven to be composed of precipitates of the monoclonal dysproteins identical to the serum protein, but this testing is not performed in all cases since characteristic skin findings in the setting of confirmed MM is considered sufficient for diagnosis [1-6]. Nevertheless, immunofluorescence can help to differentiate FSMM from other etiologies of hyperkeratotic spicules such as hypovitaminosis A, chronic renal failure, human immunodeficiency virus/acquired immunodeficiency syndrome, or trichodysplasia spinulosa (TS), [1].

TS is particularly interesting to consider because of its many clinical features in common with FSMM [7, 8]. TS is caused by a virus called trichodysplasia-associated polyomavirus (TSPyV), [9, 10]. TSPyV circulates widely in the population, with as many as 70% of healthy adults exhibiting seroconversion, but clinical manifestations of TSPyV are extremely rare, with only a few dozen cases of TS reported and in primarily immunocompromised patients [5, 11]. In

these cases, cutaneous papules and hyperkeratotic spicules typically involve the face, ears, trunk, and extremities [10]. Histopathology characteristically reveals dilated follicles with protruding spicules and hyperkeratosis [10, 12]. Therefore, TS and FSMM both occur in the setting of immunocompromise and have very similar clinical and histopathological findings. However, in a patient with follicular spicules and a confirmed diagnosis of MM as in the case presented here, the most likely diagnosis remains FSMM. In fact, the majority of existing literature does not provide compelling evidence for any viral cause of FSMM, including TSPyV, but rather supports an immunoglobulin-mediated cause of the skin changes as described above [5, 8].

Conclusion

Follicular spicules of multiple myeloma is a rare but highly characteristic dermatologic manifestation of

MM. Patients presenting with cutaneous symptoms concerning for MM should be evaluated for constitutional symptoms and referred to an oncologist. The most effective management of FSMM is treatment of the underlying malignancy with chemotherapy and, if indicated, autologous bone marrow transplantation. For symptomatic relief, dermatologists can be helpful by prescribing topical keratolytics that contain retinoids, urea, or salicylic acid to help normalize skin appearance until chemotherapy takes effect [2, 5]. In most cases, the natural course of follicular spicules and other non-specific cutaneous manifestations of MM is complete resolution with successful treatment and remission of the hematologic malignancy.

Potential conflicts of interest

The authors declare no conflicts of interests.

References

1. Satta R, Casu G, Dore F, et al. Follicular spicules and multiple ulcers: cutaneous manifestations of multiple myeloma. *J Am Acad Dermatol*. 2003;49:736-40. [PMID: 14512931].
2. Tay LK, Lim FL, Ng HJ, et al. Cutaneous follicular hyperkeratotic spicules--the first clinical sign of multiple myeloma progression or relapse. *Int J Dermatol*. 2010;49:934-6. [PMID: 21128919].
3. Bork K, Bockers M, Pfeifle J. Pathogenesis of paraneoplastic follicular hyperkeratotic spicules in multiple myeloma. Follicular and epidermal accumulation of IgG dysprotein and cryoglobulin. *Arch Dermatol*. 1990;126:509-13. [PMID: 2108615].
4. Miller JJ, Anderson BE, Ioffreda MD, et al. Hair casts and cutaneous spicules in multiple myeloma. *Arch Dermatol*. 2006;142:1665-6. [PMID: 17179013].
5. Hosler GA, Weibel L, Wang RC. The cause of follicular spicules in multiple myeloma. *JAMA Dermatol*. 2015;151:457-8. [PMID: 25471315].
6. Mazzeo M, Di Raimondo C, Gurnari C, et al. Early detection of IgH monoclonal rearrangement in follicular spicules of the nose preceding multiple myeloma diagnosis. Case report and review of the literature. *G Ital Dermatol Venereol*. 2018. [PMID: 30249084].
7. Linke M, Geraud C, Sauer C, et al. Follicular erythematous papules with keratotic spicules: a quiz. Trichodysplasia spinulosa. *Acta Derm Venereol*. 2014;94:492-6. [PMID: 24322674].
8. van Boheemen S, Fouchier RA, Hajdarbegovic E. The cause of follicular spicules in multiple myeloma-reply. *JAMA Dermatol*. 2015;151:458. [PMID: 25471521].
9. DeCrescenzo AJ, Philips RC, Wilkerson MG. Trichodysplasia spinulosa: A rare complication of immunosuppression. *JAAD Case Rep*. 2016;2:307-9. [PMID: 27536719].
10. Kazem S, van der Meijden E, Kooijman S, et al. Trichodysplasia spinulosa is characterized by active polyomavirus infection. *J Clin Virol*. 2012;53:225-30. [PMID: 22196870].
11. Chen T, Mattila PS, Jartti T, et al. Seroepidemiology of the newly found trichodysplasia spinulosa-associated polyomavirus. *J Infect Dis*. 2011;204:1523-6. [PMID: 21926381].
12. van Boheemen S, Jones T, Muhlemann B, et al. Cidofovir gel as treatment of follicular spicules in multiple myeloma. *JAMA Dermatol*. 2015;151:82-4. [PMID: 25188537].