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Case Report

Granulomatous Mycosis Fungoides Associated with Knee Prostheses: A Case Report and Literature Review

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Abstract

Background: Granulomatous Mycosis Fungoides (MF) is a rare subtype of cutaneous T-cell lymphoma characterized by granulomatous inflammation. While MF is relatively well-known in dermatological practice, its association with prosthetic implants, particularly knee prostheses, is exceedingly rare. This case presents a novel instance of granulomatous MF potentially triggered by the chronic inflammation associated with a metallic knee prosthesis.

Case description: We report the case of an 87-year-old female patient with ischemic heart disease and a total knee prosthesis, who presented with erythematous arcuate rash and nodules confined to the area around her right knee. Histopathological findings revealed non-necrotizing granulomas with epidermotropism, and immunohistochemistry confirmed the presence of CD4+/CD8+ T-cell infiltration, consistent with a diagnosis of granulomatous MF. The association between her prosthetic knee and the development of this condition is discussed.

Conclusion: This case represents one of the first documented instances of granulomatous MF potentially linked to knee prosthesis. It highlights the need for vigilance in monitoring patients with prosthetic implants for rare, chronic inflammatory responses that may lead to lymphoproliferative disorders.

Abbreviations

MF: Mycosis Fungoides; CTCL: Cutaneous T-Cell Lymphoma; DLBCL: Diffuse Large B-Cell Lymphoma; ALCL: Anaplastic Large Cell Lymphoma; BIA-ALCL: Breast Implant-Associated Anaplastic Large Cell Lymphoma; TNF: Tumor Necrosis Factor; IL: Interleukin; PCR: Polymerase Chain Reaction; MRI: Magnetic Resonance Imaging; TCR: T-Cell Receptor; AFB: Acid-fast Bacilli; CD: Cluster of Differentiation; IgH: Immunoglobulin Heavy Chain; PJI: Prosthetic Joint Infection; ACD: Allergic Contact Dermatitis; RAE: Reactive Angioendotheliomatosis; SKINTED: Surgery-Associated Chronic Dermatitis

Introduction

Cutaneous T-cell lymphomas (CTCL), of which Mycosis Fungoides (MF) is the most common subtype, typically present with patches, plaques, and tumors on the skin [1,2]. Granulomatous MF is an unusual histological variant characterized by granulomatous inflammation within the skin. While the causes of MF are not fully understood, it has been associated with chronic inflammation, genetic predisposition, and immune system dysregulation [1,2].

Lymphomas associated with prosthetic implants, particularly metallic knee prostheses, are an emerging but poorly understood phenomenon [3–5]. Prosthetic implants

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can induce chronic inflammatory responses [3,6], which in rare cases, can lead to lymphoproliferative disorders such as lymphoma. Most cases reported in the literature are large B-cell lymphomas associated with prosthetic joints [7,8], while reports of T-cell lymphomas, including MF, linked to prosthetic materials are scarce [4,9].

This article presents a novel case of granulomatous MF in an 87-year-old woman, potentially triggered by her right knee prosthesis. This case emphasizes the need for heightened clinical awareness and a multidisciplinary approach to the diagnosis and management of similar conditions. Additionally, we review the existing literature on prosthetic-associated lymphomas and discuss possible pathophysiological mechanisms

Case presentation

Clinical data

An 87-year-old female patient with a history of ischemic heart disease, hypertension, and a right knee total arthroplasty (Triathlon CS type knee prosthesis) in September 2020, presented with an erythematous arcuate rash and small nodules localized around her right knee (Figure 1). The rash appeared almost two years later after her knee replacement surgery, though there were no immediate postoperative complications.

Histopathological examination

histopathological examination (Figures 2-5)revealed a dense dermal lymphoid infiltrate with non-



Figure 1: Skin lesions in the right popliteal fossa and the outer aspect of the right

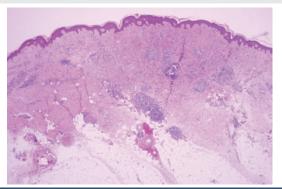


Figure 2: Low-power view showing a dense dermal infiltrate with a nodular and band-like pattern extending into the deep dermis. The epidermis is largely preserved, with mild acanthosis and focal interface changes. Hematoxylin-eosin stain (H&E), original magnification ×40.

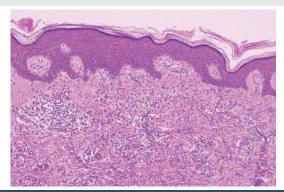


Figure 3: Higher magnification revealing an atypical lymphocytic infiltrate with epidermotropism and focal Pautrier microabscesses. The lymphocytes display irregular, hyperchromatic nuclei, and are dispersed within the superficial dermis and epidermis. H&E, original magnification ×100.

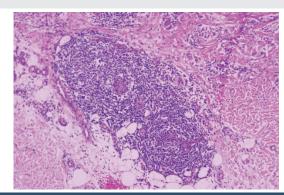


Figure 4: Deep dermal focus of granulomatous inflammation characterized by well-formed granulomas composed of epithelioid histiocytes and scattered multinucleated giant cells, surrounded by atypical lymphocytes. H&E, original magnification ×200.

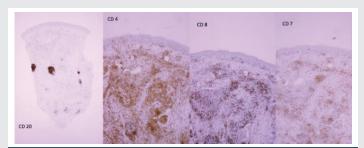


Figure 5: Immunohistochemical profile of the dermal infiltrate in granulomatous mycosis fungoides. Immunostaining shows a predominant T-cell phenotype. (A) CD20 highlights isolated reactive B-cell aggregates. (B) CD4 shows strong and diffuse positivity in most dermal lymphocytes. (C) CD8 expression is scattered and limited to a minority of cells. (D) CD7 demonstrates partial loss of expression, a common finding in mycosis fungoides, supporting the diagnosis of a clonal T-cell proliferation. Immunohistochemistry, original magnification ×100.

necrotizing granulomas, characterized by aggregates of epithelioid histiocytes interspersed with atypical lymphocytes exhibiting hyperchromatic, cerebriform nuclei. These atypical lymphocytes showed focal epidermotropism, and scattered Pautrier microabscesses were identified. The granulomatous component was well-demarcated, with multinucleated giant cells occasionally noted. PCR for mycobacteria was negative and sarcoidosis was also ruled out.

Immunohistochemical staining confirmed the T-cell lineage of the atypical lymphocytes, with strong positivity

for CD4 and weak for CD8, partial loss of CD7 expression, and negativity for CD30. This immunophenotypic profile supported the diagnosis of granulomatous MF and excluded other differential diagnoses such as cutaneous sarcoidosis, leprosy, or granulomatous drug reactions.

Moreover, we found positive rearrangement of TCR b and g chains but negative for IgH (blood and skin).

Imaging

CT and MRI scans showed no significant abnormalities aside from the prosthesis (Figure 6).

Magnetic resonance imaging reveals the presence of a knee prosthesis without evidence of surrounding soft tissue abnormalities, joint effusion, or signs of local infiltration. The examination shows no pathological findings apart from the expected artifact and signal void related to the metallic implant.

Diagnosis

The diagnosis was established based on the integration of clinical presentation, histopathological findings, and immunophenotypic features, in accordance with the WHO-EORTC criteria for primary cutaneous lymphomas. The granulomatous variant of MF is an uncommon and diagnostically challenging subtype, differing from classic MF in the predominance of a granulomatous inflammatory milieu, which may mask the atypical epidermotropic lymphocytes and delay recognition. Highlighting these distinctive microscopic and immunological features is essential for accurate diagnosis, particularly in cases arising adjacent to prosthetic implants where chronic inflammation may confound the histological picture.

In this patient, the proximity of the lesion to the metallic knee prosthesis raises the possibility that chronic immune stimulation induced by prosthetic wear particles could have contributed to the granulomatous inflammatory response, potentially acting as a cofactor in the development of this rare lymphoma variant.

Patient evolution

Conservative treatment was initiated with a high-potency corticosteroid (Clobetasol 0.5 mg/g) applied once daily, resulting in significant improvement of the lesions (Figure 7).

Discussion

The association between lymphomas and prosthetic implants is rare but significant, particularly in the context of breast implants, where the relationship with anaplastic large cell lymphoma (ALCL) is the most well-documented [10,11]. While most prosthetic-related lymphomas involve B-cell origins, particularly diffuse large B-cell lymphoma (DLBCL) this case presents a rare instance of a T-cell lymphoma, specifically granulomatous Mycosis Fungoides (MF), associated with a knee prosthesis. Such a link underscores the complexity of the immune responses elicited by foreign materials in the human body, ranging from allergic reactions to lymphoproliferative disorders.



Figure 6: Axial T1-weighted MRI of the right knee.



Figure 7: Clinical photographs showing marked improvement after treatment. The Papulonodular lesions have resolved completely, with significant reduction of inflammation and post-inflammatory hyperpigmentation remaining in the affected

Breast Implant-Associated Anaplastic Large Cell Lymphoma (BIA-ALCL) is by far the most recognized form of lymphoma associated with implants, predominantly affecting women who have undergone breast reconstruction or augmentation [12]. BIA-ALCL typically arises in the fibrous capsule surrounding the breast implant, and its pathogenesis is thought to involve a combination of chronic inflammation, genetic susceptibility, and immune system dysregulation. This condition presents with symptoms such as late-onset seroma, mass formation, or pain around the implant site, often occurring years after the initial surgery.

BIA-ALCL is a type of T-cell lymphoma that expresses CD30, similar to systemic ALCL, but is generally negative for the anaplastic lymphoma kinase (ALK) gene. Its relatively indolent nature allows for localized treatment in many cases, often involving complete surgical excision of the implant and surrounding fibrous capsule. In cases where the disease is more advanced, chemotherapy may be employed [10-12].

The occurrence of BIA-ALCL has led to increased awareness of the potential oncogenic risks associated with prosthetic implants. The U.S. Food and Drug Administration (FDA) has monitored the incidence of BIA-ALCL and, in certain cases, has recalled textured breast implants, which seem to have a higher

association with the disease. While the exact mechanisms remain under investigation, chronic bacterial contamination, biofilm formation, and the activation of the immune system have all been proposed as contributing factors

Outside of breast implants [11,13,14], lymphomas linked to orthopedic prostheses such as those used in joint replacements are extremely rare. In a review of the literature, only a handful of cases have been reported involving knee, hip, or other orthopedic prostheses. Most of these lymphomas are of B-cell origin, particularly diffuse large B-cell lymphoma (DLBCL), and are often diagnosed years after the implant surgery. In contrast, the current case of granulomatous MF represents a rare instance of a T-cell lymphoma associated with a knee prosthesis, further expanding the spectrum of prostheticassociated lymphoproliferative disorders.

Granulomatous MF, as seen in this patient, is an especially rare subtype of MF characterized by the presence of granulomas within the malignant T-cell infiltrates [2]. The pathogenesis of this form of MF is not fully understood, but it is thought that chronic inflammation plays a central role [3,6]. The prosthetic knee implant, which is made of metal alloys, may act as a continuous source of localized inflammation, potentially triggering or exacerbating the immune dysregulation that leads to lymphoma

The pathogenesis of lymphomas associated with prosthetic implants likely involves chronic immune stimulation. In the

case of breast implants, chronic bacterial biofilm formation has been implicated as a possible trigger for immune activation, leading to the proliferation of T-cells, which in some cases results in ALCL. For orthopedic implants, such as knee and hip prostheses, wear particles from metallic components may lead to local tissue damage and a persistent inflammatory response. This inflammatory milieu can promote the clonal expansion of B or T-cells, eventually leading to lymphoma in predisposed individuals. Metallic implants, in particular, are known to generate wear particles over time, which are not biologically inert [15,16]. These microparticles may stimulate the release of pro-inflammatory cytokines such as tumor necrosis factor (TNF)- α , interleukin (IL)-6, and IL-1 β from macrophages. The chronic release of these cytokines may result in ongoing tissue inflammation, and in rare cases, the chronic immune stimulation may lead to genetic mutations within lymphocytes, promoting malignant transformation. Similar to BIA-ALCL, which can develop in the context of chronic inflammation from breast implants, prosthetic-related T-cell lymphomas like MF may arise from a similar mechanism, although this remains speculative in the absence of more extensive research.

The diagnosis of prosthetic-associated lymphomas can be challenging due to their rarity and the nonspecific nature of their initial presentation. In cases involving knee prostheses, patients may present with localized pain, swelling or cutaneous lesions. All this symptoms raise several differential diagnoses listed in Table 1.

Table 1: Differential Diagnoses of Pain, Inflammation, and Erythema Post-Knee Prosthesis.

Diagnosis	Clinical Features	Histopathology	Immunohistochemistry / Microbiology	Timing / Context	Reference
Prosthetic Joint Infection (PJI)	Pain, erythema, swelling, joint effusion, fever.	Neutrophilic infiltrate, tissue necrosis.	Positive culture (Staph aureus, coagulase-negative staph, etc).	Early or late post- surgery.	[17]
Allergic Contact Dermatitis (ACD)	Localized erythematous plaques or vesicles near the prosthesis.	Spongiosis, superficial perivascular lymphocytic infiltrate with eosinophils.	Negative culture, positive patch testing (nickel, cobalt, chromium).	Weeks to months after implantation.	[18]
Lymphoma	Persistent erythematous plaques, papules or nodules around the prosthesis site.	Atypical lymphocytes with cerebriform nuclei	CD4+, CD30+ - ALCL CD20+ - DLCBCL CD3+, CD4+, CD7 loss, TCR clonality- MF	Delayed presentation.	[4,5,7-11,13,14].
Sarcoidosis	Papules, plaques or nodules; systemic symptoms may be present.	Non-caseating granulomas without necrosis.	Negative AFB/fungal stains. CD4+ predominance.	May be systemic; variable timing.	[19]
SKINTED (Surgery-Associated Chronic Dermatitis)	Chronic eczematous dermatitis localized over prosthetic area.	Acanthosis, hyperkeratosis, mild spongiosis.	No infectious organisms; negative microbiology.	Months to years after surgery.	[20,21]
Intralymphatic Histiocytosis	Erythematous plaques or bands; associated with prosthetic joints or arthritis.	Clusters of histiocytes within dilated lymphatic vessels.	CD68, multiple dilated lymphatic vessels with intraluminal histiocytic aggregates; negative culture.	Delayed onset (months to years).	[22,23]
Reactive Angioendotheliomatosis (RAE)	Livedoid, violaceous plaques or nodules; sometimes ulceration.	Proliferation of endothelial cells in dermal vessels.	CD31+, CD34+, Factor VIII+; rule out intravascular lymphoma.	Variable; often associated with vascular disease or prosthesis.	[24]
Soft Tissue Sarcoma	Firm, often painless subcutaneous masses; may show inflammation if ulcerated or infected.	Atypical spindle or pleomorphic cells; high mitotic activity; possible necrosis.	Variable; may express vimentin, desmin, or other lineage-specific markers. Culture negative.	Months to years post-surgery; may be unrelated or triggered by prosthetic irritation.	[25,26]

ALCL- Anaplastic large cell lymphoma, DLBCL- Diffuse Large B-cell lymphoma, MF- mycosis fungoides, AFB- Acid-Fast Bacilli



In the current case, the patient's presentation with nodules and erythematous rash around the knee prosthesis initially raised suspicion of a localized inflammatory or infectious process. However, biopsy and histopathological examination revealed the diagnosis of granulomatous MF, a rare but significant finding.

Histopathological examination remains the gold standard for diagnosis, with immunohistochemical staining helping to differentiate between various types of lymphomas. In the case of T-cell lymphomas such as granulomatous MF, markers such as CD4, CD8, and CD30 can be used to identify the clonal proliferation of malignant T-cells.

This case highlights the importance of considering lymphoma in the differential diagnosis of patients presenting with unusual skin lesions or nodules around prosthetic implants. Although rare, prosthetic-associated lymphomas are a serious complication that may require surgical intervention, chemotherapy, or radiation therapy. For orthopedic surgeons and dermatologists, early recognition and appropriate referral for biopsy and further diagnostic testing are essential for ensuring timely diagnosis and treatment.

Given the rarity of prosthetic-associated lymphomas, further research is needed to better understand their pathogenesis and to establish clear guidelines for the monitoring and management of patients with prosthetic implants. In the meantime, a multidisciplinary approach involving dermatologists, oncologists, and orthopedic surgeons is crucial for optimizing patient outcomes.

Conclusion

This case represents one of the first documented instances of granulomatous MF associated with a knee prosthesis, highlighting the potential role of chronic inflammation in lymphomagenesis. Our case highlights that, although B-cell lymphomas predominate among prosthetic-associated lymphoproliferative disorders, rare T-cell variants such as granulomatous Mycosis Fungoides may also occur, potentially driven by chronic immune activation from prosthetic wear particles within a granulomatous inflammatory milieu. Recognition of this association underscores the need for heightened clinical suspicion, interdisciplinary management, and further research to elucidate the underlying pathogenic mechanisms and optimize surveillance strategies for patients with prosthetic implants.

Ethics

The patient provided informed consent for the publication of the clinical case, thus meeting the required ethical standards for the dissemination of medical information and ensuring respect for her privacy and autonomy.

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