

Complete Aortic Endograft Occlusion in a Patient with Psoriasis: A Case Report and Systematic Review of the Literature Seeking for a Potential Causal Association

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Abstract

Background: We report a case of a patient with complete aortic endograft occlusion and no morphological characteristic that could explain this event, other than the hypercoagulant status associated with psoriasis. The patient had severe intertriginous psoriasis complicated with cellulitis and sepsis and was treated with endograft excision and replacement with an aortic tube graft.

Purpose: We sought to identify a potential causal association by performing a systematic literature review on psoriasis related thrombosis.

Main findings: Seven case-control studies between patients with psoriasis and healthy controls examined various aspects of platelet function and morphology. Seven large epidemiological studies provide solid evidence that patients with psoriasis are at high risk for venous thromboembolism. In total, 19 studies were identified associating psoriasis with significant platelet activation, aortic and systemic inflammation, faster arterial thrombotic occlusion, and plaque formation.

Conclusions: It may be reasonable to hypothesize a connection between severe psoriasis and graft thrombosis. This should be taken under consideration when performing major vascular surgery in patients with psoriasis and physicians may need to consider managing these patients as high risk for arterial thrombosis.

Keywords: Psoriasis; Arterial thrombosis; Ischemia; Platelet activation; Thromboembolism; Aortic aneurysm

Introduction

Psoriasis has been involved in the development of Deep Venous Thrombosis (DVT) [1] and has been linked with elevated levels of various cytokines, and interleukins that dramatically promote the platelet aggregation rate [2]. Furthermore, patients with psoriasis are at increased risk for aortic aneurysms [3,4], Acute Coronary Syndrome (ACS) [5], and have global arterial inflammation [6]. However, there has been no report of arterial thrombosis or graft thrombosis associated with psoriasis.

Complete aortic endograft occlusion after Endovascular Aortic Repair (EVAR) is rare and in most cases an apparent cause e.g. iliac artery angulations, iliac perimeter calcification, floating thrombus, severe peripheral arterial disease, or incomplete deployment is present to justify this serious complication [7]. Having recently treated a patient with complete aortic endograft occlusion and no

morphological characteristic that could explain the acute thrombosis, other than the hypercoagulant status associated with psoriasis, we decided to report our case and seek a potential causal association by performing a systematic literature review on psoriasis related thrombosis.

Methods

Case report

Medical notes, including emergency department admission notes, operative notes, medical charts, imaging, lab tests, microbiological testing, drug charts, and follow up notes were retrieved and studied to describe the case in detail.

Systematic literature review

Search strategy: To identify relevant studies, we systematically searched PubMed (until November 2020) using the following search

pattern: psoriasis and (thrombosis or DVT or platelets or thrombus or clotting or thromboembolism or acute ischemia or graft thrombosis or aortic inflammation). No limitation on the year of publication or language was set. Furthermore, the references in the relevant articles, including review studies, were checked to identify additional resources. Abstracts of conference proceedings were not sought.

Inclusion criteria: Two of the authors (VGA and DC) independently performed the literature search to locate potentially eligible studies. All studies, including reviews, epidemiological and laboratory studies, case reports and case series, reporting on the relation of psoriasis with venous or arterial thrombosis and coagulation disorders were retrieved.

Data extraction: The following data were extracted from all eligible articles: first author, year of publication, type of study, main outcomes and conclusions. The most important findings were tabulated.

The study adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [8].

Case Report

A 62 year old male patient was transferred to our department from a small rural hospital with acute bilateral lower limb ischemia. Six months prior to this admission the patient had been submitted to Endovascular Aortic Repair (EVAR) for a 5.5cm infrarenal abdominal aortic aneurysm. There was endograft thrombosis and occlusion extending from the main body to both limbs of the endograft (Cook Zenith AAA Endovascular Graft). It should be noted that both on the CT scan that was performed on admission (Image 1) and the one month post-EVAR follow-up CT scan, there was no morphological

characteristic that could explain the acute thrombosis eg., iliac artery angulations, iliac perimeter calcification, floating thrombus, severe peripheral arterial disease, or incomplete deployment.

Unfortunately, this was a late presentation as the time taken by the referring doctors to establish diagnosis was more than 15 days. The patient had already developed wet gangrene and severe neurological deficit of his right foot with ischemic skin extending to mid-calf. The left lower limb was also ischemic with rest pain but viable.

The patient had a history of psoriasis and his right groin area had developed inverse (intertriginous) psoriasis. The groin skin fold on the right had acutely developed a 5 by 15cm ulceration complicated with fungal infection and exacerbated by ischemia. There was cellulitis and local sepsis, white cells count (WCC) was 17.5 10⁹/L (normal range 4-11 10⁹/L) and Neutrophils 13.3 10⁹/L (normal range 2.0-7.5 10⁹/L). This did not involve the femoral incision that was performed for EVAR deployment but restricted the surgical option for an extranatomical bypass (axillofemoral bypass) to revascularise the limb. The patient was afebrile. Dermatology consultation and advice was sought and treatment with broad spectrum antimicrobial (4g piperacillin/0.5g Tazobactam administered IV every 6 hours and Vancomycin 1g administered IV every 12hours) and antifungal (400mg IV Fluconazole administered IV once daily) was immediately initiated. The cultures taken from the groin ulceration grew dermatophytes. Coagulation tests including prothrombin time, platelet count, activated partial thromboplastin time, and fibrinogen were within normal range. However, tests that are associated with platelet activation were higher than normal; Platelet Distribution Width (PDW) was 19.4% (normal range 9-17%) and Mean Platelet Volume (MPV) was 13.2 fL

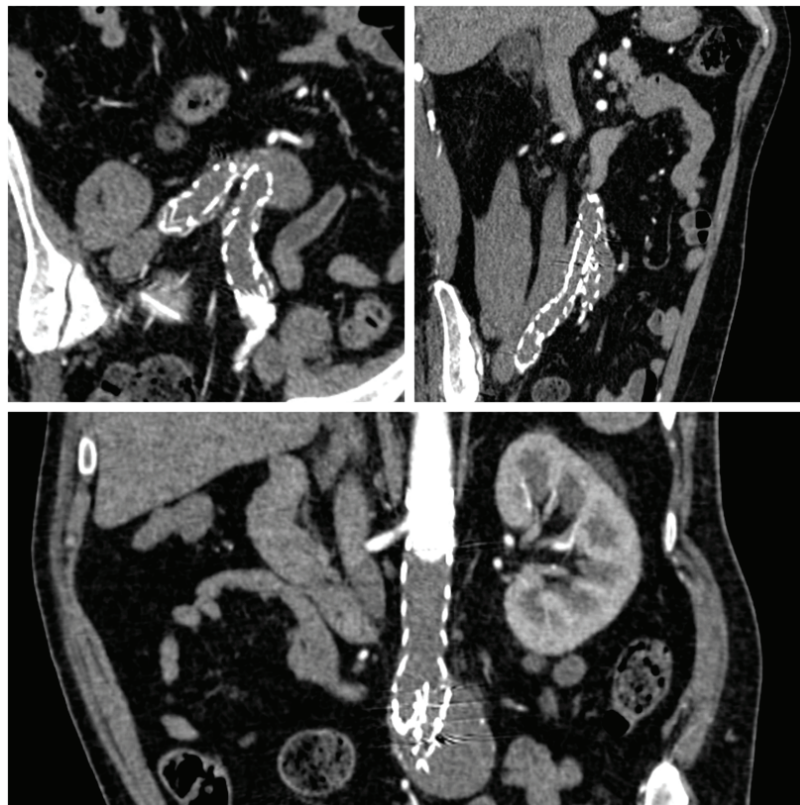


Image 1: Endograft thrombosis and occlusion extending from the main body to both limbs of the endograft (Cook Zenith AAA Endovascular Graft).

(normal range 7-11 Fl). The patient was not on any active treatment for the psoriasis, including Disease-Modifying Antirheumatic Drugs (DMARDs). The Psoriasis Area Severity Index (PASI) was 13.8. He was on Aspirin 100mg once daily, was a smoker, and had nothing else of note in his past medical history.

The surgical plan involved above knee amputation of the right limb, excision of the endograft and replacement with a tube graft. The patient was informed in detail about the risks and benefits of the procedure and refused amputation despite having been explained the detrimental effects of revascularising a potentially non-viable limb. He was also informed and consented to include the details of his case in scientific research and publication.

A middle line abdominal incision was performed and the aortic neck was dissected to obtain control both below and above the renal arteries. The iliac arteries were also dissected to the level of their bifurcation. The aneurysm sac was opened and the endograft limbs were forcefully retracted (Image 2a) and detached from their anchoring points in the common iliac arteries. Thrombectomies were performed distally and back flow from both limbs was successfully established. The endograft main body was cut and removed leaving intact the suprarenal fixation and a 2cm length of the endograft fabric to permit a safe anastomosis. Impressively, the thrombus plug in the part of the graft that was left behind could withhold the force of the aortic pulsation without the need to clamp the aorta at a higher level (Image 2b). Proximal aortic thrombectomy was performed and an aortic clamp was applied on the endograft fixation points just below the renal arteries. A 20mm

tube graft was placed proximally oversewing the endograft fabric and native aortic neck wall and distally on the aortic bifurcation (Image 2c). Initial attempt to restore blood flow ended in acute thrombosis of the new tube graft and iliac arteries. Incomplete thrombectomies and/or a hypercoagulable state associated with psoriasis maybe have been the reason for this. Thrombectomies were performed again proximally and distally in the aorta and iliac vessels. Flow was successfully restored this time with pulsation present at the level of both femoral arteries. Additional distal thrombectomies were done *via* a femoral cut-down on the left. The operation was otherwise uneventful with minimal blood loss and, at closure, the small bowel and colon appeared healthy and well perfused. The patient was transferred to the Intensive Care Unit (ICU). Unfortunately, within few hours the patient deteriorated developing lactate acidosis and severe haemodynamic instability and died 24 hours after the operation. This outcome may be largely attributed to a severe revascularisation syndrome caused by restoring blood flow to the non-viable right limb.

Systematic literature review

Literature review: In figure 1, we present a flow diagram describing the selection process followed to identify reports included in this systematic review. The PubMed search yielded 433 potentially relevant articles; after studying the title, abstracts, and full texts, 19 studies fulfilled the inclusion criteria for this systematic review

In table 1, we present the characteristics and outcomes of the reviewed papers. Seven case-control studies between patients with

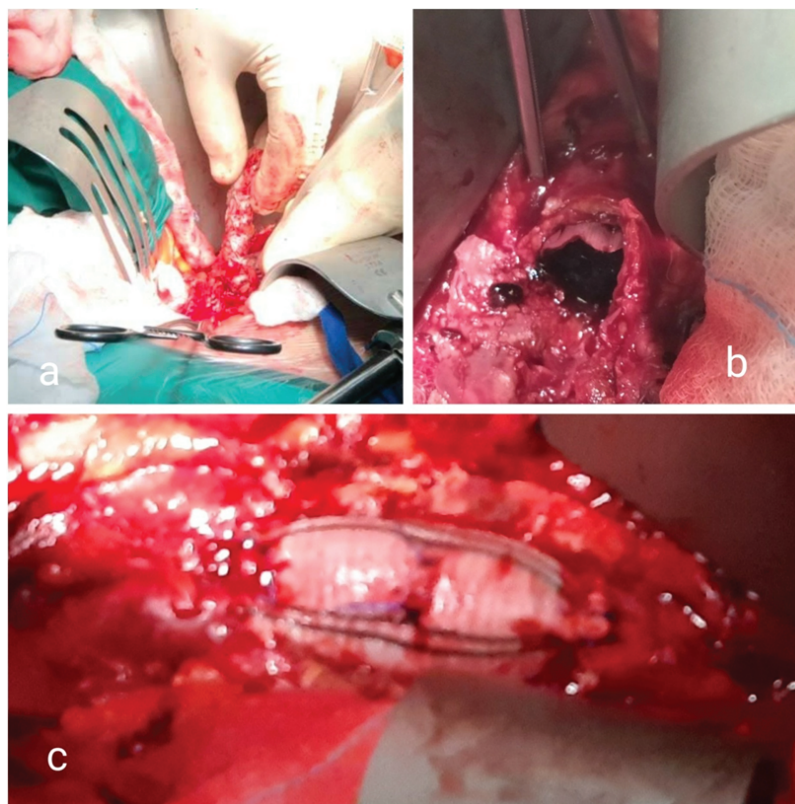
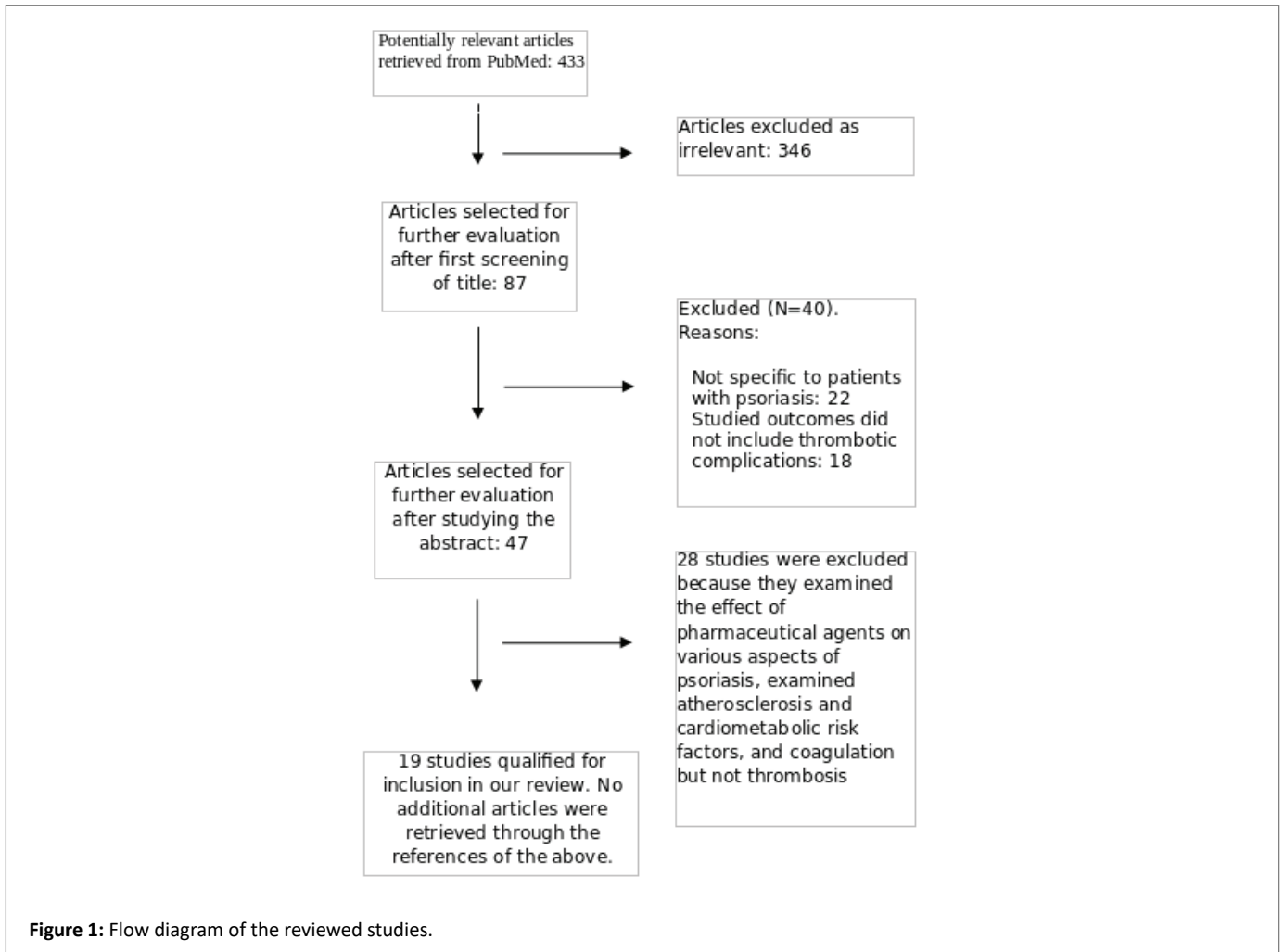


Image 2a: Detached endograft limbs.

2b: Endograft main body cut and removed leaving intact the suprarenal fixation and a 2cm length of the endograft fabric. The thrombus plug can withhold the force of the aortic pulsation without the need to clamp the aorta.

2c: 20mm tube graft was placed proximally over sewing the endograft fabric and native aortic neck wall and distally on the aortic bifurcation.



psoriasis and healthy controls examined various aspects of platelet function and morphology including Mean Platelet Volume (MPV), Platelet Mass Index (PMI) [9,10], distribution width, p-selectin concentrations [2,11], platelet aggregation [2], light transmission aggregometry as index of platelet reactivity [12], plasma levels of beta-thromboglobulin (beta-TG), Platelet Factor 4 (PF4) [13], and Platelet-Derived Microparticles (PDMPs) [11] as markers of platelet activation. All of the above studies concluded that there is evidence of platelet activation in psoriasis causing higher plaque formation [9], global arterial inflammation [2,6], and abnormally high platelet reactivity [12]. Mean platelet volume levels are increased in patients with psoriasis [10] and this may be a marker of the severity. Patients with extensive disease are at higher risk of having platelet dysfunction [11].

Seven large epidemiological studies from Korea [14], Taiwan [15], Sweden [5], USA [16,17], Denmark [18,19], and a meta-analysis [1] of some of the above studies provide solid evidence that patients with psoriasis are at high risk for VTE. Furthermore, we have identified 2 experimental mouse model studies that have associated psoriasis with arterial thrombotic occlusion [20] and with aortic root inflammation and thrombosis [21]. Finally, 2 cases-reports [22,23] were also included in this systematic review pointing to the need of clinical awareness of occurrence of thrombosis and pulmonary embolism in patients with psoriasis.

Discussion and Conclusion

This case of aortic endograft occlusion is, to our knowledge, the first report of arterial graft thrombosis in patients with psoriasis. It should be noted that it was impossible to identify any other known cause of endograft occlusion including more than 15% oversized endograft in iliac arteries with iliac artery angulation $\geq 60^\circ$ and iliac perimeter calcification $\geq 50\%$. The patient had at the time of presentation severe (intertriginous) psoriasis complicated with cellulitis and local sepsis. The iliac artery occlusion caused ischemia of the groin area and may have exacerbated the desquamation of the inguinal crease leading to infection and severe tissue loss. The fact that the right iliofemoral area was heavily contaminated precluded the option of an axillofemoral bypass. We had to keep the new graft away from the infected area and thus, decided to replace the endograft with a straight tube graft.

Patients with extensive psoriasis are at higher risk of acute thrombotic events [13] and this may have happened in this case. Impressively, the new aortic graft also thrombosed few seconds after restoring circulation indicating that the patient was in a hypercoagulable state. In retrospect, the choice to revascularise a potentially non-viable limb should have been avoided. Furthermore, a more aggressive treatment for psoriasis prior to the operation may have been of benefit including DMARDs. There is evidence that patients with well controlled psoriasis have lower risk for thrombotic events compared to patients with poorly controlled disease [16]. In fact, the risk for VTE in patients

Table 1: Main characteristics, outcomes, and results of studies included in the systematic review.

First Author/ Reference	Year of publication	Country	Study design and population	Studied Outcomes	Results/conclusions
Unal M [8]	2016	Turkey	Comparative study between 320 patients with psoriasis and 200 healthy controls	Mean platelet volume (MPV), Platelet mass index (PMI), ESR and CRP	Higher PMI and MPV values, which mean higher plaque formation capacity and more active platelets, in psoriasis may make psoriasis patients more sensitive to atherosclerotic plaque formation and complications.
Rhee TM, et al. [13]	2017	Korea	Cross-sectional study with data from National Insurance service registry. 13,385 psoriasis patients (1,947 with severe psoriasis)	Risk of atrial fibrillation (AF) and thromboembolic events (TE)	Severe, but not mild, psoriasis significantly increased AF and TE risk.
Chung WS, et al. [15]	2017	Taiwan	Matched case-control study with data drawn from National Health Database. 8945 patients with psoriasis and 8945 controls	Incidence of venous thromboembolism (VTE)	After adjustment for covariates, the patients with psoriasis presented a 2.02-fold risk of VTE
Bengtsson K, et al. [5]	2017	Sweden	Prospective nationwide cohort study that included 16,063 patients with psoriatic arthritis and 266,435 general population controls	Risk for acute coronary syndrome (ACS), stroke and VTE	Patients with psoriatic arthritis are at increased risk for ACS, stroke events, and VTE. For VTE the age- and sex-adjusted HRs were increased about 50% compared to GP.
Ogdie A, et al. [16]	2018	USA	Cohort study in a primary care medical record database. 12,084 patients with psoriatic arthritis, and 194,288 with psoriasis and controls (n = 1 225 571).	VTE defined as the combined endpoint of Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE). Interaction with Disease Modifying Anti-Rheumatic Drugs (DMARD)	Patients with RA (with and without a DMARD prescription) and patients with mild psoriasis had significantly elevated risks of VTE (HR 1.35, 1.29, and 1.07, respectively). Severe psoriasis and PsA prescribed a DMARD had an elevated but not statistically significant risk for VTE.
Hjuler KF, et al. [6]	2017	Denmark	Observational, controlled clinical study including patients with psoriasis (n=12) and matched controls (n=23)	Arterial inflammation assessed by 18 F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography	Global arterial inflammation and subcutaneous inflammation were significantly increased in patients with moderate-to-severe psoriasis compared with controls. (mean ± SD whole vessel TBR max 2.46 ± 0.31 vs. 2.09 ± 0.36; P=0.005)
Chandrashekar L, et al. [2]	2015	India	Cross-sectional matched case control study-62 patients with psoriasis and 62 controls.	Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW)], P-selectin and Platelet Derived Microparticle (PDMP), high sensitivity C-reactive Protein (hs-CRP), Interleukin (IL)-6	Significant platelet activation and systemic inflammation were observed in patients with psoriasis, especially when associated with severe disease.
Ahlehoff O, et al. [19]	2015	USA	Experimental mouse model study to determine whether chronic skin-specific inflammation was sufficient to promote thrombosis. Case control study between mice with acute (C57Bl/6 n=25) and chronic (K5-IL-17C n=14) skin inflammation and controls (n=21 for both groups)	Arterial thrombosis was induced using carotid artery photochemical injury and carotid artery diameters were measured post-clot formation. Measures of clot formation including Prothrombin (PT) and activated Partial Thromboplastin Time (aPTT)	Chronic, but not acute, skin-specific inflammation was associated with faster arterial thrombotic occlusion

Yudhishdran JM, et al. [22]	2015	Sri Lanka	Case report	Clinical report of a patient psoriasis and chronic portal vein thrombosis with cavernous transformation	Clinical awareness of occurrence of thrombosis in patients with psoriasis.
Ahlehoff O, et al. [19]	2015	Denmark	Nationwide cohort study. Danish patients hospitalized with nonvalvular atrial fibrillation in the period 1997-2011 (n=99,357) excluded subjects treated with anticoagulation	Hospitalization or death from thromboembolism in patients with psoriasis	In patients with nonvalvular atrial fibrillation not treated with oral anticoagulation, severe psoriasis was associated with increased risk of thromboembolism.
Ungprasert P, et al. [1]	2014	USA	Meta-analysis of observational studies that reported VTE risk in patients with psoriasis vs. non-psoriasis participants.	Odds ratio, relative risk, hazard ratio or standardized incidence ratio for VTE	Pooled results from 4 studies and patients. The risk ratio of VTE in patients with psoriasis was 1.46 (95% CI, 1.29-1.66).
Wang Y, et al. [20]	2012	USA	Murine model of psoriasiform skin disease (n=18) compared to controls (n=19)	Accumulation of macrophages, T lymphocytes, and B lymphocytes, necrosis factor- α , IL-17A, vascular endothelial growth factor, IL-12, monocyte chemoattractant protein-1, and S100A8/A9, as well as splenic and circulating CD11b(+)Ly-6C(hi) pro-inflammatory monocytes	Skin-specific inflammation promotes aortic root inflammation and thrombosis
Ko JH, et al. [21]	2011	Taiwan	Case report	Clinical report of a 42y old patient with psoriasis and acute pulmonary embolism	Severe psoriasis can be associated with eosinophilia and metabolic syndrome, acute pulmonary embolism
Lutsey PL, et al. [16]	2012	USA	Cohort drawn from The Iowa Women's Health Study (38,608 women who were followed for a median of 11.3 years)	Incidence of VTE events and age-adjusted hazard ratio (HR) for VTE. HR 1.40 (95% CI: 1.00, 1.94) patients with psoriasis versus controls	There is a relation between chronic, systemic inflammation and risk of VTE, and suggests that patients with even mild-to-moderate psoriasis may be at elevated risk of a VTE event.
Di Minno MN, et al. [11]	2012	Italy	Case control study. Individuals with psoriatic arthritis receiving tumor necrosis factor- α (TNF- α) blockers (n=114) and healthy controls (n=114) matched for age, sex, and cardiovascular risk factors	Light transmission aggregometry	Subjects with active psoriatic arthritis had abnormally high platelet reactivity
Ahlehoff O, et al. [18]	2011	Denmark	National cohort study with 35,138 patients with mild and 3,526 patients with severe psoriasis were identified and compared with 4,126,075 controls	Risk for VTE	Patients with psoriasis are at increased risk of VTE. The risk was highest in young patients with severe psoriasis. The rate ratio (RR) of VTE was elevated in all patients with psoriasis with RR 1.35 (95% confidence interval [CI] 1.21-1.49) and RR 2.06 (CI 1.63-2.61) for mild and severe psoriasis, respectively.
Canpolat F, et al. [9]	2010	Turkey	Case-control study comparing 106 patients with psoriasis (48 with psoriatic arthritis and 58 without) and 95 healthy controls.	Mean platelet volume	MPV in patients with psoriasis 8.7 ± 0.9 fL was significantly higher than that of control subjects 7.3 ± 0.8 fL ($p < 0.001$). There was also statistical difference between MPV levels of patients with (9.5 ± 0.8) and without (8.0 ± 0.7) arthritis ($p < 0.001$). MPV levels are increased in patients with psoriasis and PsA. MPV may be a marker for the severity of psoriasis.

Tamagawa-Mineoka R, et al. [10]	2010	Japan	Case-control study in 21 patients with psoriasis and 22 healthy control subjects	Plasma Levels of Platelet-Derived Microparticles (PDMPs) and soluble P-selectin	Plasma PDMPs and soluble P-selectin levels were markedly higher in patients with psoriasis compared with those in healthy control subjects. Blood platelets are activated in patients with psoriasis, especially in those with extensive disease
Tamagawa-Mineoka R, et al. [13]	2008	Japan	Case control study with 22 healthy control and 16 patients with psoriasis	Plasma levels of beta-thromboglobulin (beta-TG) and Platelet Factor 4 (PF4) as platelet activation markers	Blood platelets are activated in patients with psoriasis

with severe psoriasis and Psoriatic Arthritis (PsA) who are prescribed a DMARD, does not differ significantly to healthy controls [16].

The systematic literature review provides evidence to support that patients with psoriasis are at increased risk for ACS, stroke events, and VTE. Furthermore, the reviewed studies have associated psoriasis with significant platelet activation, aortic and systemic inflammation, faster arterial thrombotic occlusion in mouse models, and plaque formation. The major limitation of this systematic review is that the available studies have methodological heterogeneity that does not permit any meaningful statistical analysis. In our patient MPV and PDW that are associated with platelet activation were abnormally high. Based on the above evidence, it is reasonable in our case; to at least hypothesize that there may be a causal association between severe psoriasis and the event of complete aortic endograft occlusion. One should take this under consideration when performing major vascular surgery in patients with psoriasis and consider managing these patients as high risk for arterial thrombosis; including administering oral anticoagulation and/or double antiplatelet therapy, and performing more frequent duplex ultrasound follow-up for patency issues.

Disclosure Statement

All authors have no conflict of interest to disclose.

Authors Contribution

VGA conceived and drafted the manuscript. VGA and DC performed the systematic review. KGM, SG, MM, DC, and SK contributed to the final version of the manuscript. SK and KGM supervised the project. SK passed away after completion and submission of this manuscript.

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