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Hidradenitis suppurativa and vasculitis: A case series and literature review of a rare association

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Abstract

Hidradenitis suppurativa is a chronic inflammatory skin disease with dysregulation of the immune system. Its pathophysiology is not clear, and it has been reported in association with various inflammatory disorders such as pyoderma gangrenosum, arthritis, familial Mediterranean fever and inflammatory bowel diseases. However, the co-existence of HS and vasculitis is exceptional and has not been investigated. We report on five patients with vasculitis that are followed in our centers: one with Takayasu's arteritis, three with granulomatosis with polyangiitis and one with Behcet's disease and compare them with those previously reported in the literature. A case series and literature review with key words of "vasculitis," "hidradenitis suppurativa," and "acne inversa" found only one previous report of hidradenitis suppurativa and cutaneous vasculitis and two with Behcet's disease. Whereas the association of pyoderma gangrenosum and vasculitis is well-known, that with hidradenitis suppurativa is rarer. There may be some pathogenic continuum between hidradenitis suppurativa, pyoderma gangrenosum and vasculitis.

Keywords

Hidradenitis suppurativa, vasculitis

Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease, characterized by recurrent painful nodules and abscesses, commonly in apocrine bearing areas, such as the axilla and groin.[1,2] HS is not common and has been reported mainly with two groups of disorders: autoinflammatory disorders, such as pyogenic arthritis, pyoderma gangrenosum (PG) and acne (PAPA syndrome); synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO syndrome); and a group with folliculopilosebaceous structural disorders and hyperkeratosis, such as follicular occlusion syndromes, keratitis–ichthyosis–deafness (KID) syndrome or Dowling-Degos disease (DDD).[3,4]

Vasculitis is due to inflammation of the blood vessel wall and can affect the skin and/or any other organ system of the body. Vasculitis can be easily divided according to the caliber of the vessels predominantly involved: (1) large-aorta and arterial branches, (2) medium-sized vessels and (3) small vessels that include arterioles, capillaries and post-capillary venules.[5] To the best of our knowledge, vasculitis has only been reported in one case of syndromic HS thus far, and two cases have been reported with HS and Behcet's disease (BD). In the current paper, we are reporting a series of five new patients with HS associated with vasculitis, along with a literature review.

Methods

We describe the five patients with HS and vasculitis one with Takayasu's arteritis (TAK), one with Behcet's disease (BD;

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variable vessel vasculitis subset) and three with granulomatosis with polyangiitis (GPA)) co-managed at the vasculitis clinic at Mount Sinai Hospital, Toronto and the wound clinic at Women's College Hospital, Toronto. All vasculitis diagnoses were confirmed by a rheumatologist and satisfied the 2012 Chapel Hill Consensus Conference criteria.[5] The diagnosis of HS was confirmed by a dermatologist using modified Dessau diagnostic criteria, which require typical morphology and location of the lesions and at least two flares in the past 6 months.[6] A literature review was conducted through a MEDLINE, EMBASE and PubMed search using keywords "hidradenitis suppurativa," "acne inversa," "vasculitis," "Behcet's disease," "granulomatous vasculitis," and "ANCA-vasculitis." Informed consent was obtained for the patients, as part of the Vasculitis clinic cohort database study.

Results

Table 1 outlines a summary of all five cases and their comorbidities. Case 1 was a young female with TAK vasculitis and erythema nodosum. Her HS presented with a combination of classic HS topography plus more than 50 inflammatory skin nodules (Figures 1 and 2). Our two cases of HS and GPA presented with purpuric rash, lung manifestations and positive anti-proteinase 3 (PR3)-ANCA. One case of GPA presented with hemoptysis and classic lung involvement, with asthma. HS in all the latter three cases was presented with involvement of the axilla and groin (Figures 3 and 4) with multiple tracks and nodules with predominant inflammatory components. In our fifth case, HS and BD, HS mainly presented as recurrent abscesses in the perianal area with no fistula and no associated inflammatory bowel disease (IBD). She also had associated erythema nodosum. In case number 2, the vasculitis presentations precede the HS lesions, while in others they started after initial presentation of HS. In the rest of the cases, HS lesions presented at least 3 years prior to the clinical presentation of vasculitis. Our HS patients were not treated with antibiotic medications that may have triggered the appearance of vasculitis.

Niv et al.[7] have reported a patient with PG, acne and hidradenitis suppurativa (PASH) syndrome and recurrent leukocytoclastic vasculitis, who was the only reported case with HS and clear vasculitis. Previously, another patient with pyogenic arthritis, PG, acne and hidradenitis suppurativa (PAPASH) overlapping with another syndrome of PG, acne and ulcerative colitis (PAC) was found to have positive ANCA serology and specifically anti-PR-3, but no evidence of clinical vasculitis.[8] The co-existence of HS and BD has been reported in two other cases, including one with both BD and psoriasis, successfully managed with Ustekinumab.[9,10]

Discussion

HS is an uncommon disease, with uncertain prevalence between $<0.5\%$ and 4% in different studies.[11,12] Vasculitides are an uncommon heterogeneous group of rare diseases.[13,14] The association of both conditions is exceptional.

The pathogenesis of HS is not completely understood, although it appears that there are two key pathogenic components: abnormalities in the follicular-apocrine apparatus as well as an immune response dysregulation. It has been proposed that a primary abnormality in the pilosebaceous-apocrine unit leads to follicular occlusion, cyst development and rupture into the dermis. This can trigger an exaggerated response of the cutaneous innate immune system, while ongoing intermittent disease activity can lead to recurrent flares.[12]

There is clearly a role for the pro-inflammatory tumor necrosis factor (TNF)-α, IL-1 beta and IL-17 pathways in HS.[15–18] The pathogenesis of vasculitides is variable and may involve immune complex formation via circulating antigens (e.g. infectious agents, medications, neoplasms) or the production of auto-antibodies, such as anti-proteinase 3 or anti-myeloperoxidase antibodies.[19] L-selectin and E-selectin have been reported to be higher in patients with PG, acne and suppurative hidradenitis (PASH) syndrome.[20] This latter finding might also be a clue to the link between HS and vasculitis. Microorganisms might also play a role in the pathogenesis of HS and BD.[21,22]

More than 200 cases of syndromic HS (i.e. secondary or associated with a systemic condition), have been reported in the literature,[20,23] mainly with inflammatory bowel disease (IBD), spondyloarthropathies, familial Mediterranean fever,[24–27] as well as with PG in PASH and PAPASH (pyogenic arthritis, PG, acne and HS).[20,22] Both PG and HS share a common inflammatory pathway, dysregulation of immune system, neutrophil predominance, pathergy and response to anti-TNF or anti-IL-1 agents. The association between PG and vasculitis has been reported in multiple cases in the literature.[7,28,29] In a study from Japan, 35 cases of PG associated with TAK have been reported with the most common location for PG lesions being upper arms.[30]

Pathergy (characterized by development of PG at the site of trauma) has been reported in 20%–30% of patients with PG.[31] There is a case report of 14 patients with active HS developing typical HS lesions at the site of external trauma related to isomorphic phenomena or pathergy in patients with HS.[32] Successful treatment of both PG and HS usually requires multiple modalities, including treating associated disease and emerging evidence suggest potential for targeted therapies.[33,34,35]

Table 1. Summary of all five cases and their characteristics.

Case	Diagnosis	Age/sex/ethnicity	Characteristics of vasculitis	Characteristics of HS	Dermatological manifestations	Medical Hx/smoking status and lab results	Treatment
Case 1	Takayasu	36/F/Caucasian (white)	Aortitis with aneurysmal dilation requiring surgery	Inflammatory nodules, abscesses, tunnels, scars located to her right axilla, trunk and groin	Erythema nodosum	Ascending aortic aneurysm diagnosed on routine CXR aortic arch replacement Non-smoker ANCA negative Hb:10.7 g/dL (L)	Colchicine, Oral CS, AZA, MTX, LEF Adalimumab (after HS diagnosis)
Case 2	GPA	53/ F/ Caucasian (white)	Hemoptysis (alveolar hemorrhage), respiratory distress, epistaxis, oral ulceration	Abscesses and draining tunnels in bilateral axilla, lower abdomen and inframammary area	Purpuric rash of lower legs	DM type II Hypertension S/P Cholecystectomy S/P Pancreatitis S/P post-op PE Uterus fibroids Non-smoker CRP: 289 (H) ESR: 82 (H) C-ANCA (anti PR3 positive)	corticosteroid in IV pulses, Plasma exchange cyclophosphamide, AZA, MTX Rituximab
Case 3	GPA	25/M/ Caucasian (middle eastern—Arabic descent)	Recurrent bilateral iritis Migratory arthralgia Acute renal failure (pauci-immune glomerulonephritis crescentic GN with little sclerosis on renal biopsy) Nasal congestion/mucosal erythema	Involvement of both axilla		S/P VZV (shingles) Non-smoker CRP: 86 (H) C_ANCA: positive Creatinine: 215 μmol/L (H)	Systemic CS orally, CS in IV pulse therapy, Cyclophosphamide, Rituximab Doxycycline (for HS)
Case 4	GPA	27/F/ Caucasian (white)	Pulmonary nodules (necrotizing granuloma on biopsy) DVT	Perianal abscess and inguinal, axillary involvement Severe fibrosis and scar requiring ileostomy	Acneiform eruption	PCOS Non-smoker CRP: 179 (H) P-ANCA: positive (MPO) Hb: 7.9 g/dL (L)	Oral corticosteroids, AZA, rituximab and infliximab (for HS)
Case 5	BD	27/F/Hispanic decscent	Recurrent genital ulcers Oral ulcers Bilateral sacroiliitis	Perianal abscess and nodules	Erythema nodosum Psoriasis Nodular vasculitis Acneiform eruption	Asthma Atopic diathesis Non-smoker ANA: negative ANCA: negative HLA-B27 negative	NSAID's, Colchicine, sulfasalazine, AZA, infliximab, adalimumab (for HS) Etanercept (for HS) Ustekinumab (for HS)

HS: hidradenitis suppurativa; CXR: chest X-ray; ANCA: anti-neutrophilic cytoplasmic antibody; L: low; CS: corticosteroids; AZA: azathioprine; MTX: methotrexate; LEF: leflunomide; GPA: granulomatous polyangiitis; DM: diabetes mellitus; S/P: status post; post op: post operative; PE: pulmonary embolism; CRP: C-reactive protein; H: high; ESR: erythrocyte sedimentation rate; anti-PR3: anti-proteinase 3; IV: intravenous; VZV: varicella zoster virus; DVT: deep vein thrombosis; PCOS: polycystic ovarian syndrome; MPO: myeloperoxidase; BD: Behcet's disease; NSAID's: nonsteroidal anti-inflammatory drugs; GN: glomerulonephritis; ANA: antinuclear antibody.

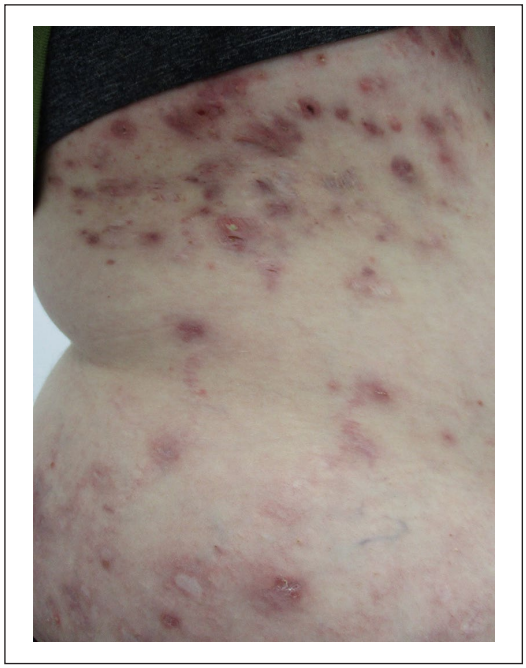

Figure 1. The trunk showing multiple inflammatory nodules and scars.

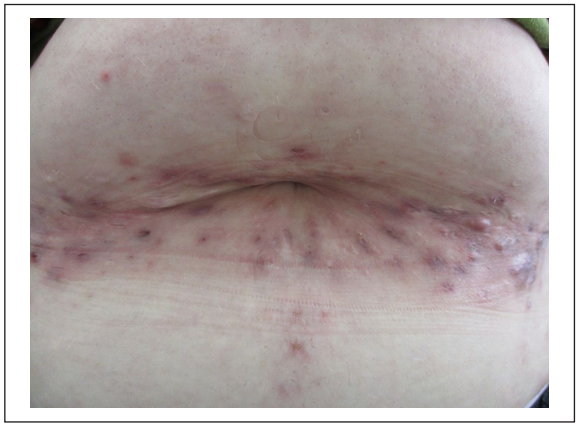

Figure 2. The anterior trunk (periumbilical) showing multiple inflammatory nodules and scars.

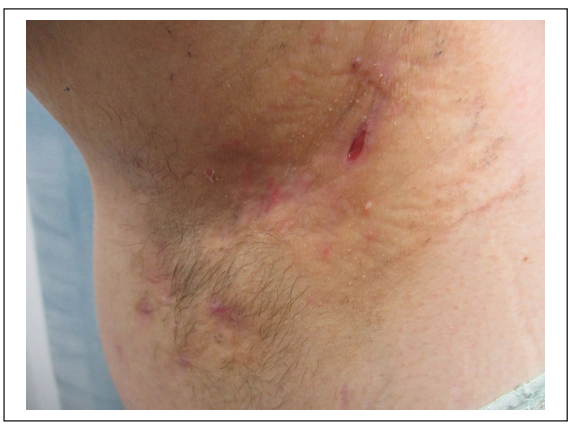

Figure 3. Axillary lesions, with ulceration and Hurley Stage II.

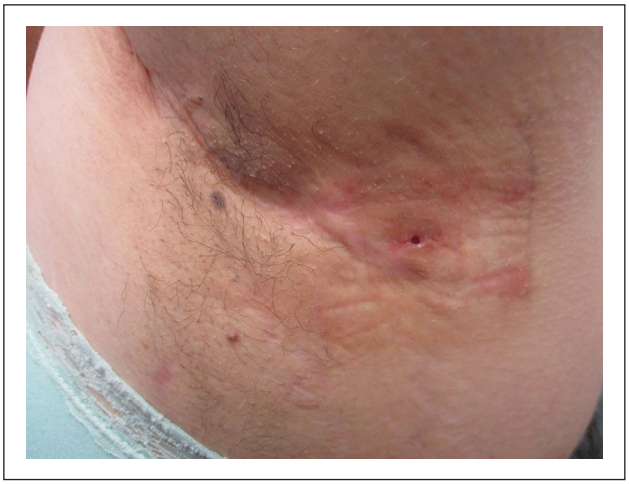

Figure 4. Axillary lesions; active nodule, small sinus tract and scar lesions are depicted.

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Informed consent

All patients have provided written consent for publication of the case report.

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