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

Afsaneh Alavi¹,², Eran Shavit¹, Jeannine Archer² and Christian Pagnoux³

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 coexistence 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: autoimmune inflammatory 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;
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. 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. 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.

Discussion

HS is an uncommon disease, with uncertain prevalence between <0.5% and 4% in different studies. Vasculitides are an uncommon heterogeneous group of rare diseases. 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.

There is clearly a role for the pro-inflammatory tumor necrosis factor (TNF)-α, IL-1 beta and IL-17 pathways in HS. 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. L-selectin and E-selectin have been reported to be higher in patients with PG, acne and suppurative hidradenitis (PASH) syndrome. 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.

More than 200 cases of syndromic HS (i.e. secondary or associated with a systemic condition), have been reported in the literature, mainly with inflammatory bowel disease (IBD), spondyloarthropathies, familial Mediterranean fever, as well as with PG in PASH and PAPASH (pyogenic arthritis, PG, acne and HS). 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. 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. Pathergy (characterized by development of PG at the site of trauma) has been reported in 20%–30% of patients with PG. 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. Successful treatment of both PG and HS usually requires multiple modalities, including treating associated disease and emerging evidence suggest potential for targeted therapies.
### 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 |
|------|-----------|------------------|-------------------------------|-----------------------|-------------------------------|--------------------------------------------|------------|
| 1    | Takayasu  | 36/F/Caucasian    | 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 | Colchicine, Oral CS, AZA, MTX, LEF Adalimumab (after HS diagnosis) |
|      |           | (white)          |                               |                       |                               | Non-smoker ANCA negative Hb:10.7 g/dL (L) | | |
| 2    | GPA       | 53/F/ Caucasian  | 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 |
|      |           | (white)          |                               |                       |                               | Non-smoker | S/P VZV (shingles) Non-smoker CRP: 86 (H) C-ANCA: positive Creatinine: 215 μmol/L (H) | | |
| 3    | GPA       | 25/M/ Caucasian  | 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 | | | Systemic CS orally, CS in IV pulse therapy, Cyclophosphamide, Rituximab Doxycycline (for HS) |
|      |           | (middle eastern—Arabic descent) |                               |                       |                               | | | |
| 4    | GPA       | 27/F/ Caucasian  | Pulmonary nodules (necrotizing granuloma on biopsy) DVT | Perianal abscess and inguinal, axillary involvement Severe fibrosis and scar requiring ileostomy | Acneform 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) |
|      |           | (white)          |                               |                       |                               | Non-smoker | | |
| 5    | BD        | 27/F/Hispanic descent | Recurrent genital ulcers Oral ulcers Bilateral sacroiliitis | Perianal abscess and nodules | Erythema nodosum Psoriasis Nodular vasculitis Acneform eruption | Asthma Atopic diathesis Non-smokerANA: negative ANCA: negative HLA-B27 negative | NSAID’s, Colchicine, sulfasalazine, AZA, infliximab, adalimumab (for HS) Etanercept (for HS) Ustekinumab (for HS) |

**Note:** 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.
Declaration of conflicting interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship and/or publication of this article.

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

References
1. Revuz JE, Canoui-Poitrine F, Wolkenstein P, et al. Prevalence and factors associated with hidradenitis suppurativa: results from two case-control studies. J Am Acad Dermatol 2008; 59(4): 596–601.
2. Jemec GB. Clinical practice. Hidradenitis suppurativa. N Engl J Med 2012; 366(2): 158–164.
3. Kurayev A, Ashkar H, Saraiya A, et al. Hidradenitis suppurativa: review of the pathogenesis and treatment. J Drugs Dermatol 2016; 15(8): 1017–1022.
4. Gasparic J, Theut Riis P and Jemec GB. Recognizing syndromic hidradenitis suppurativa: a review of the literature. J Eur Acad Dermatol Venereol 2017; 31: 1809–1816.
5. Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides. Arthritis Rheum 2013; 65(1): 1–11.
6. Zouboulis CC, Del Marmol V, Mrowietz U, et al. Hidradenitis suppurativa/acne inversa: criteria for diagnosis, severity assessment, classification and disease evaluation. Dermatology 2015; 231(2): 184–190.
7. Niv D, Ramirez JA and Fivenson DP. Pyoderma gangrenosum, acne, and hidradenitis suppurativa (PASH) syndrome with recurrent vasculitis. JAAD Case Rep 2017; 3(1): 70–73.
8. Marzano AV, Ceccherini I, Gattorno M, et al. Association of pyoderma gangrenosum, acne, and suppurative hidradenitis (PASH) shares genetic and cytokine profiles with other autoinflammatory diseases. Medicine 2014; 93(27): e187.
9. Sahin MT, Oztürkcan S, Türel-Ermertcan A, et al. Behçet’s disease associated with hidradenitis suppurativa. *J Eur Acad Dermatol Venereol* 2007; 21(3): 428–429.
10. Baerveldt EM, Kappen JH, Thio HB, et al. Successful long-term triple disease control by ustekinumab in a patient with Behçet’s disease, psoriasis and hidradenitis suppurativa. *Ann Rheum Dis* 2013; 72(4): 626–627.
11. Vinding GR, Miller IM, Zarchi K, et al. The prevalence of inverse recurrent suppuration: a population-based study of possible hidradenitis suppurativa. *Br J Dermatol* 2014; 170(4): 884–889.
12. Jemec GB, Heidenheim M and Nielsen NH. The prevalence of hidradenitis suppurativa and its potential precursor lesions. *J Am Acad Dermatol* 1996; 35(2 Pt 1): 191–194.
13. Shi L. Anti-neutrophil cytoplasmic antibody-associated vasculitis: prevalence, treatment, and outcomes. *Rheumatol Int* 2017; 37: 1779–1788.
14. Watts RA, Mahr A, Mohammad AJ, et al. Classification, epidemiology and clinical subgrouping of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis. *Nephrol Dial Transplant* 2015; 30(Suppl. 1): i14–i22.
15. Wang B, Yang W, Wen W, et al. Gamma-secretase gene mutations in familial acne inversa. *Science* 2010; 330: 1065.
16. Radtke F, Fasnacht N and Macdonald HR. Notch signaling in the immune system. *Immunity* 2010; 32: 14–27.
17. Wolk K, Warszawska K, Hoeﬂich C, et al. Deﬁciency of IL-22 contributes to a chronic inﬂammatory disease: pathogenic mechanisms in acne inversa. *J Immunol* 2011; 186: 1282–1289.
18. Ah-Weng A, Langtry JA, Velangi S, et al. Pyoderma gangrenosum associated with hidradenitis suppurativa. *Clin Exp Dermatol* 2005; 30: 669–671.
19. Carlson JA, Ng BT and Chen KR. Cutaneous vasculitis update: diagnostic criteria, classiﬁcation, epidemiology, etiology, pathogenesis, evaluation and prognosis. *Am J Dermatopathol* 2005; 27(6): 504–528.
20. Marzano AV, Borghi A, Meroni PL, et al. Pyoderma gangrenosum and its syndromic forms: evidence for a link with autoinflammation. *Br J Dermatol* 2016; 175(5): 882–891.
21. Sakane T, Takeno M, Suzuki N, et al. Behçet’s disease. *N Engl J Med* 1999; 341: 1284–1291.
22. Ring HC, Thorsen J, Saunte DM, et al. The follicular skin microbiome in patients with hidradenitis suppurativa and healthy controls. *JAMA Dermatol* 2017; 153(9): 897–905.
23. Marzano AV, Damiani G, Ceccherini I, et al. Autoinflammation in pyoderma gangrenosum and its syndromic form (pyoderma gangrenosum, acne and suppurative hidradenitis). *Br J Dermatol* 2017; 176(6): 1588–1598.
24. Hodak E, Atzmony L, Pavlovsky L, et al. Hidradenitis suppurativa is associated with familial Mediterranean fever—a population-based study. *J Invest Dermatol* 2017; 137(9): 2019–2021.
25. Deckers IE, Benhadou F, Koldijk MJ, et al. Inflammatory bowel disease is associated with hidradenitis suppurativa: result from a multicenter cross-sectional study. *J Am Acad Dermatol* 2017; 76(1): 49–53.
26. Shlyankevich J, Chen AJ, Kim GE, et al. Hidradenitis suppurativa is a systemic disease with substantial comorbidity burden. *J Am Acad Dermatol* 2014; 71(6): 1144–1150.
27. Richette P, Molto A, Viguier M, et al. Hidradenitis suppurativa associated with spondyloarthritis—results from a multicenter national prospective study. *J Rheumatol* 2014; 41(3): 490–494.
28. Loetscher J, Fistarol S and Walker UA. Pyoderma gangrenosum and erythema nodosum revealing Takayasu’s arteritis. *Case Rep Dermatol* 2016; 8(3): 354–357.
29. Domnez S, Pamuk ON, Gedik M, et al. A case of granulomatosis with polyangiitis and pyoderma gangrenosum successfully treated with infliximab and rituximab. *Int J Rheum Dis* 2014; 17(4): 471–475.
30. Ujiie H, Sawamura D, Yokota K, et al. Pyoderma gangrenosum associated with Takayasu’s arteritis. *Clin Exp Dermatol* 2004; 29(4): 357–359.
31. Alavi A, French LE, Davis MD, et al. Pyoderma gangrenosum: an update on pathophysiology, diagnosis and treatment. *Clin Exp Dermatol* 2004; 29(4): 357–359.
32. Boer J. Should hidradenitis suppurativa be included in dermatoses showing koebnerization? Is it friction or fiction? *Dermatology* 2017; 233(1): 47–52.
33. Napolitano M, Megna M, Timoshchuk EA, et al. Hidradenitis suppurativa: from pathogenesis to diagnosis and treatment. *Clin Cosmet Investig Dermatol* 2017; 10: 105–115.
34. Kimball AB, Okun MM, Williams DA, et al. Two phase 3 trials of adalimumab for hidradenitis suppurativa. *N Engl J Med* 2016; 375(5): 422–434.
35. Vinkel C and Thomsen SF. Autoinflammatory syndromes associated with hidradenitis suppurativa and/or acne. *Int J Dermatol* 2017; 56(8): 811–818.