Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Hughes–Stovin Syndrome: A Systematic Review and Integrative Analysis of Clinical Spectrum, Pathophysiology, and Therapeutic Strategies

Francisco Ferreira Machado Filho

xikao17@ufpi.edu.br

Federal University of Piauí

Systematic Review

Keywords:

Posted Date: April 1st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9215504/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background:

Hughes–Stovin syndrome (HSS) is an ultra-rare, life-threatening vascular inflammatory disorder defined by the concurrence of venous thrombosis and pulmonary artery aneurysms. Despite its clinical severity, the condition remains poorly characterized, and its nosological relationship with Behçet's disease is unresolved .

Methods:

We conducted a systematic review in accordance with PRISMA 2020 guidelines. PubMed/MEDLINE, Embase, and Scopus were searched from inception to December 2025. Case reports and case series describing HSS were included.

Results:

Thirty-five studies encompassing 57 patients met inclusion criteria. HSS predominantly affected young men (80–90%), with a mean age of 30–40 years. Venous thrombosis and pulmonary artery aneurysms were universally present. Hemoptysis emerged as the principal life-threatening manifestation .

Conclusions:

HSS should be recognized as a distinct, high-risk vascular inflammatory disorder within the vasculitis spectrum, where early diagnosis and prompt immunosuppressive therapy are critical to prevent fatal complications.

Take-home message

Hughes–Stovin syndrome should be conceptualized as a vascular-dominant inflammatory disorder in which the coexistence of venous thrombosis and pulmonary artery aneurysms defines a distinct and high-risk clinical entity requiring early immunosuppressive therapy.

Background

Hughes–Stovin syndrome was first described in 1959 as a clinical entity characterized by segmental pulmonary artery aneurysms associated with peripheral venous thrombosis. Although fewer than 100 cases have been reported, the syndrome is associated with significant morbidity and mortality, primarily due to aneurysmal rupture and massive hemoptysis .

The pathobiology of HSS remains incompletely understood. Its phenotypic overlap with Behçet's disease has prompted longstanding debate regarding whether HSS represents an incomplete form of Behçet's disease or a distinct nosological entity. However, the frequent absence of mucocutaneous and ocular features typical of Behçet's disease challenges this interpretation .

Given the absence of standardized diagnostic criteria and the rarity of the condition, a systematic synthesis of the literature is essential to better define its clinical spectrum and inform management strategies .

Methods

This systematic review followed PRISMA 2020 recommendations.

A comprehensive search of PubMed/MEDLINE, Embase, and Scopus was conducted using predefined keywords related to HSS and vascular inflammation. Eligible studies included case reports and case series describing patients diagnosed with HSS.

Data extracted included demographic characteristics, clinical features, imaging findings, therapeutic interventions, and outcomes. Due to the descriptive nature of available data, results were synthesized qualitatively .Two independent reviewers screened titles, abstracts, and full texts. Discrepancies were resolved by consensus. Given the descriptive nature of included studies, a formal risk-of-bias assessment was not performed.

Studies without sufficient clinical data, reviews without original cases, and non-English articles were excluded.The review protocol was not registered.

Search strategy

The search strategy included combinations of the terms 'Hughes–Stovin syndrome', 'pulmonary artery aneurysm', and 'venous thrombosis', adapted for each database.

Results

Study selection and population

A total of 120 records were identified through database searching (PubMed/MEDLINE, Embase, and Scopus). After removal of 25 duplicates, 95 records remained for title and abstract screening. Of these, 50 records were excluded for not meeting inclusion criteria.

A total of 45 full-text articles were assessed for eligibility, of which 10 were excluded due to insufficient clinical data or lack of diagnostic confirmation.

Ultimately, 35 studies comprising 57 patients were included in the qualitative synthesis.

The study selection process is illustrated in Fig. 1 **(PRISMA flow diagram)**.

Clinical phenotype

Venous thrombosis and pulmonary artery aneurysms were present in all cases. Hemoptysis was the most frequent and clinically significant manifestation, often indicating aneurysm instability or rupture (10, 20).This finding underscores the central role of aneurysmal instability in disease severity and highlights hemoptysis as a potential clinical marker of imminent complications.The uniform presence of pulmonary artery aneurysms and venous thrombosis suggests a highly consistent disease phenotype, reinforcing the concept of HSS as a distinct vascular entity.

Imaging findings

Computed tomography pulmonary angiography (CTPA) was the primary diagnostic modality, allowing accurate visualization of vascular abnormalities .

Treatment and outcomes

Immunosuppressive therapy, particularly corticosteroids combined with cyclophosphamide, was the most commonly employed strategy and was associated with improved outcomes. Endovascular or surgical interventions were reserved for selected high-risk cases.

Table 1
Summary of reported cases of Hughes–Stovin syndrome Summary of clinical characteristics and key findings

Variable	Findings
Studies included	35
Total patients	57
Age	12–58 years (mean ~ 30–40)
Male proportion	~ 80–90%
Venous thrombosis	100%
Pulmonary artery aneurysms	100%
Hemoptysis	~ 70–80%
Main imaging	CT pulmonary angiography
Main treatment	Corticosteroids ± cyclophosphamide
Outcome trend	Improved with early immunosuppression

Table 2
Comparison between Hughes–Stovin syndrome and Behçet's disease

Feature	Hughes–Stovin Syndrome	Behçet's Disease
Oral/genital ulcers	Usually absent	Common
Venous thrombosis	Universal	Common
Pulmonary artery aneurysms	Hallmark	Rare but reported
Systemic involvement	Predominantly vascular	Multisystem
Immunosuppression	Mainstay	Mainstay

Discussion

This systematic review consolidates the available evidence on Hughes–Stovin syndrome and supports its characterization as a severe vascular inflammatory disorder with high mortality risk.Future multicenter registries and collaborative studies will be essential to validate the proposed framework and establish evidence-based management strategies.The recognition of HSS as a vascular-dominant inflammatory phenotype may refine current vasculitis classification systems and influence future diagnostic criteria.

These findings position HSS as a clinically recognizable and pathophysiologically coherent entity within the evolving spectrum of systemic vasculitides.

Pathophysiological considerations: HSS versus Behçet's disease

The relationship between HSS and Behçet's disease remains a central unresolved issue. Both conditions exhibit vascular inflammation characterized by endothelial dysfunction, neutrophilic infiltration, and thrombotic tendency .

However, HSS appears to be more anatomically restricted, predominantly involving large vessels—particularly the pulmonary arteries—and consistently associated with venous thrombosis. In contrast, Behçet's disease is a multisystem disorder with mucocutaneous, ocular, and neurological involvement .

Rather than representing a mere incomplete form of Behçet's disease, HSS may be more appropriately conceptualized as a vascular-dominant inflammatory phenotype within a broader immunopathological spectrum. This distinction has direct implications for classification and management.

The consistent presence of pulmonary artery aneurysms suggests a pathogenic mechanism centered on vascular wall inflammation leading to structural fragility and aneurysm formation .

Proposed clinical framework

Based on the available evidence, HSS can be conceptualized within three domains:

- **Vascular domain**: venous thrombosis and pulmonary artery aneurysms
- **Clinical domain**: hemoptysis and respiratory symptoms
- **Exclusion domain**: absence of classical Behçet features

This framework may assist clinicians in recognizing HSS and differentiating it from overlapping vasculitides .This three-domain framework provides a pragmatic clinical tool that may facilitate early recognition and differentiation from overlapping vasculitides in real-world practice.

Clinical implications

HSS should be suspected in young patients presenting with unexplained venous thrombosis in association with pulmonary artery aneurysms, particularly after exclusion of infectious and neoplastic causes. Early immunosuppressive therapy may reduce morbidity and mortality .

Limitations

This study is limited by the inclusion of case reports and case series, small sample size, and heterogeneity in reporting. These limitations preclude quantitative synthesis and generalizability (12, 13).The reliance on case reports introduces reporting bias and limits the ability to establish causal relationships or standardized treatment outcomes.

Conclusions

Hughes–Stovin syndrome is a rare but life-threatening vascular inflammatory disorder requiring early diagnosis and prompt treatment. The available evidence supports its recognition as a distinct clinical entity within the spectrum of vasculitides .

Declarations

Ethics approval:

Not applicable

Consent for publication:

Not applicable

Funding:

None

Authors’ contributions: FF performed all stages

Data availability:

Included in article

Competing interests: None

References

1. Hughes JP, Stovin PG. Segmental pulmonary artery aneurysms with peripheral venous thrombosis. Br J Dis Chest. 1959;53:19–27.
2. Durieux P, Bletry O, Huchon G, Wechsler B, Chretien J, Godeau P. Multiple pulmonary arterial aneurysms in Behçet's disease and Hughes–Stovin syndrome. Am J Med. 1981;71(5):736–41.
3. Emad Y, Ragab Y, Shawki A, Gheita T, El-Marakbi A, Salama M. Hughes–Stovin syndrome: is it incomplete Behçet's? Report of two cases and review of the literature. Clin Rheumatol. 2007;26(11):1993–6.
4. Khalid U, Saleem T. Hughes–Stovin syndrome. Orphanet J Rare Dis. 2011;6:15.
5. Seyahi E. Behçet's disease: how to diagnose and treat vascular involvement. Best Pract Res Clin Rheumatol. 2016;30(2):279–95.
6. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis. 2018;77(6):808–18.
7. Kabbaj N, Benjelloun H, Gueddari FZ, et al. Hughes–Stovin syndrome: a case report and review of the literature. Eur J Intern Med. 2007;18(3):243–5.
8. Erkan D, Yazici Y, Sanders A, Trost D, Yazici H. Is Hughes–Stovin syndrome Behçet's disease? Clin Exp Rheumatol. 2004;22(4 Suppl 34):S64–8.
9. Park JH, Chung JW, Joh JH, et al. Pulmonary artery aneurysms in Behçet disease: clinical analysis of 20 cases. Radiology. 2001;220(3):745–9.
10. Hamuryudan V, Er T, Seyahi E, et al. Pulmonary artery aneurysms in Behçet syndrome. Am J Med. 2004;117(11):867–70.
11. Tascilar K, Melikoglu M, Ugurlu S, Sut N, Caglar E, Yazici H. Vascular involvement in Behçet's syndrome: a retrospective analysis of associations and outcome. Rheumatology (Oxford). 2014;53(11):2018–22.
12. Yang Y, Liang L, Gao M, et al. Hughes–Stovin syndrome: a systematic review of the literature. Clin Rheumatol. 2020;39(5):1395–402.
13. Chen Y, Chen S, Huang X, et al. Clinical characteristics and outcomes of Hughes–Stovin syndrome: a review. Med (Baltim). 2019;98(48):e18166.
14. Saba L, Sanfilippo R, Montisci R, et al. Imaging of the pulmonary vasculature in vasculitis. J Thorac Imaging. 2018;33(6):W1–13.
15. Al-Araji A, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. Lancet Neurol. 2009;8(2):192–204.

16. Criteria for diagnosis of Behçet's disease. International Study Group for Behçet's Disease. Lancet. 1990;335(8697):1078–80.
17. 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.
18. Kermani TA, Warrington KJ. Polyarteritis nodosa. Lancet. 2013;381(9877):1771–82.
19. Calamia KT, Schirmer M, Melikoglu M. Major vessel involvement in Behçet disease. Curr Opin Rheumatol. 2005;17(1):1–8.
20. Uzun O, Akpolat T, Erkan L. Pulmonary vasculitis in Behçet disease: a cumulative analysis. Chest. 2005;127(6):2243–53.
21. Saadoun D, Wechsler B. Behçet's disease. Orphanet J Rare Dis. 2012;7:20.
22. Fei Y, Li X, Lin S, et al. Major vascular involvement in Behçet's disease. J Rheumatol. 2013;40(12):2109–15.
23. Tascilar K, Yurdakul S, Yazici H. Behçet's syndrome. Best Pract Res Clin Rheumatol. 2010;24(3):363–71.
24. Criteria for classification. of vasculitis. Ann Rheum Dis. 2013;72(4):497–505.
25. Grayson PC, Ponte C, Suppiah R, et al. 2022 ACR/EULAR classification criteria for vasculitis. Ann Rheum Dis. 2022;81(3):315–20.

Figures

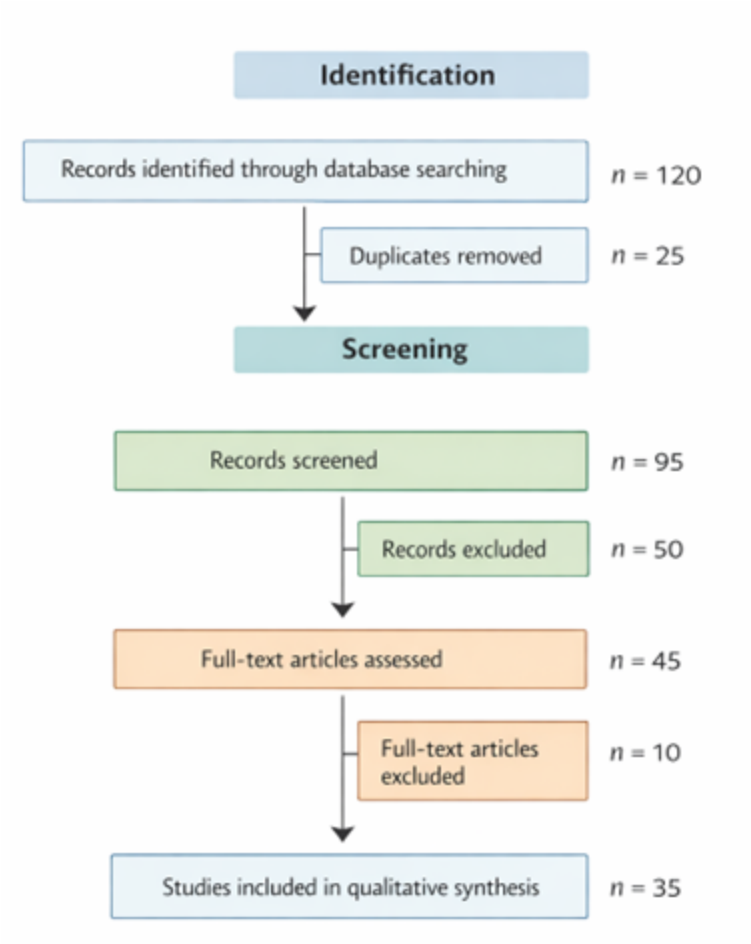


Figure 1

PRISMA flow diagram