

Case Report

Vitiligo as a possible manifestation of infective endocarditis complicated with ischaemic stroke: A case reportD. S. Satharasinghe¹, D. H. Hettige¹, P. Weerawansa², N. Lokunarangoda², H. M. S. Senanayake^{2*}¹Professorial Medical Unit, Teaching Hospital, Anuradhapura, Sri Lanka.²Department of Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka, Saliyapura, Sri Lanka**Abstract**

We report a case of young stroke sequel to sub-acute infective endocarditis with simultaneous occurrence of vitiligo. Since the early days of medical practice, identifying peripheral stigmata of infective endocarditis was highlighted as a way of early diagnosis of infective endocarditis. The literature describes several cutaneous manifestations of infective endocarditis. This is possibly the first that reports an association between vitiligo with infective endocarditis and stroke.

The patient was a thirty-four-year-old previously well female who had an intermittent fever for one month with a gradual development of vitiligo involving both hands, feet, and lips. She presented with the development of a left-sided ischaemic stroke one month after the onset of fever. She was diagnosed with having mitral valve infective endocarditis and underwent a six-week course of intravenous antibiotics until regression of the mitral valve vegetation.

Vitiligo may occur possibly as an immunological phenomenon of infective endocarditis. Additionally, it may correlate with the occurrence of ischaemic stroke in patients with infective endocarditis.

Keywords: Infective endocarditis, Ischaemic stroke, Vitiligo**Copyright:** © 2021 Satharasinghe D. S. *et al.*  This is an open-access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.**Funding:** None**Competing interest:** None**Received:** 23.06.2021**Accepted revised version:** 17.07.2021**Published:** 31.12.2021***✉ Correspondence:** Senanayakehms@gmail.com,  <https://orcid.org/0000-0001-5739-1979>

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Introduction

Infective endocarditis is an uncommon clinical entity that, if unrecognized, leads to serious morbidity [1]. Identifying extra-cardiac manifestations is of paramount importance for early suspicion of infective endocarditis in primary care, as a delay in referral to initiate treatment would result in grave permanent consequences. Splinter haemorrhages, Osler's nodes, purpura, and Janeway lesions are well-known cutaneous manifestations of infective endocarditis. To the best of

our knowledge, this is the first time vitiligo has been described as a cutaneous manifestation of infective endocarditis complicated with a stroke.

Case report

A previously-well, 34-year-old female, presented with right-sided face-arm-leg weakness. This had been preceded by intermittent low-grade fever for four weeks. With the onset of fever, she had developed vitiligo involving bilateral hands (Figure 1), feet, and lips. She

had no history of thyroid disease, diabetes, hypertension, or cardiac problems. Also, there were no joint symptoms, other skin rashes, mouth ulcers, or constitutional symptoms that would suggest an underlying inflammatory disorder.

She had taken medical advice for fever and had been prescribed antibiotics on two occasions during the course. Two weeks before admission, she had an episode of mild slurring of speech with right-sided face-arm-leg weakness noted upon waking up, which lasted eight hours and resolved completely. This episode had not been further evaluated.

On examination, her pulse rate was 80 beats per minute and regular with a blood pressure of 110/70 mmHg. She had a changing pan-systolic murmur at the apex. Neurological examination revealed right side upper motor type facial nerve palsy with right upper limb and lower limb weakness of power (3/5). Fundi were normal, and other cranial nerves were intact.

Her white cell count was $7.9 \times 10^9/L$, haemoglobin 114 g/L, and platelets $286 \times 10^9/L$. The inflammatory markers were elevated with CRP of 193 mg/dL and ESR of 36 mm/hour. All three pairs of blood cultures were negative, possibly due to prior treatment with antibiotics. Tests for the HACEK group of organisms were not carried out as the tests were not available in the hospital. Her non-contrast-CT Brain showed a lacunar infarction involving the left thalamus (Figure 2).

She underwent a 2D echocardiogram, which revealed a large mobile mass attached to the posterior mitral valve leaflet (PMVL), measuring 16x17 mm. Both anterior and posterior mitral valve leaflets were prolapsing, giving rise to a grade II mitral regurgitation. There was no evidence of rheumatic valvular disease.

Her blood picture revealed prominent rouleaux formation. Her antinuclear antibody test (ANA) was negative, and homocysteine and vitamin B 12 levels were normal. A skin biopsy from the hypopigmented lesions showed a reduced number of melanocytes and the absence of melanin pigment in keratocytes compatible with vitiligo. Direct immunofluorescence staining for IgA, IgG, and C3 was negative.

The diagnoses of native mitral valve infective endocarditis complicated with left-sided motor lacunar stroke and new-onset vitiligo were made. Considering her sub-acute presentation and the occurrence of vitiligo,

Carney complex, and atrial myxoma were considered as other possible differential diagnoses before performing the echocardiogram.

She was started on intravenous ceftriaxone 2 g daily and intravenous gentamicin 80 mg eight hourly for two weeks. A repeat 2D echocardiogram showed poor resolution of the vegetation. Intravenous ceftriaxone was continued for another two weeks, and the repeat echocardiogram showed persistent vegetation measuring 13x11 mm. After another two weeks of antibiotics, the echocardiogram showed a healed vegetation attached to PMVL measuring 7x7 mm with grade II mitral regurgitation.

Stroke rehabilitation was instituted with regular physiotherapy from admission. Over time, her vitiligo partially resolved. The patient and her family were briefed about the risk of further embolic strokes during the treatment period. This helped them face the unexpected chain of events and to cooperate during the prolonged course of treatment.

The patient had an uneventful recovery during the ward stay. Her inflammatory markers returned to normal, and the modified Barthel index improved from 10/20 to 18/20. On discharge, the patient was advised on lifelong infective endocarditis prophylaxis. She remained well at the three-month evaluation.



Figure 1: Vitiligo involving the fingertips of both hands

Discussion

In this patient with infective endocarditis, vitiligo started to appear soon after the onset of fever. She had no preceding history of autoimmune thyroid disease, type I



Figure 2: Non-contrast CT brain with a lacunar stroke in left thalamus (arrow)

diabetes mellitus, rheumatological diseases, medication use, or exposure to chemicals such as phenols suggesting an alternative aetiology for the development of vitiligo; hence is likely that the vitiligo was a manifestation of infective endocarditis.

The story of this patient shows how challenging it is to diagnose infective endocarditis at the early stages of the disease. Sir William Osler stated that "Few diseases present greater difficulties in the way of diagnosis than infective endocarditis. Difficulties in many cases are practically insurmountable" [2]. Back in the era when the diagnostic facilities were not readily available, diagnosing infective endocarditis was mostly a post-mortem process. Yet, over the past thirty years, neither the incidence nor the mortality of infective endocarditis has reduced [3]. While several factors like elderly age, female sex, underlying heart disease are non-modifiable, delay in diagnosis [4] is a key element that can be modified.

Thus, the importance of identifying extra-cardiac manifestations is highlighted as a surrogate marker of underlying infective endocarditis, especially in the primary care setting at the onset of the disease.

Infective endocarditis can involve multiple organ systems. Depending on the infecting organism and its virulence, a spectrum of extra-cardiac manifestations has been described. Based on the Association for the Study and Prevention of Infectious Endocarditis prospective population study of patients with infective endocarditis, 11.9% had dermatological manifestations [3]. These included splinter haemorrhages, Osler's nodes, purpura, and Janeway lesions. The pathogenesis of Janeway lesions and Osler nodes includes micro-embolization and immune-mediated vasculitis [5,6].

The autoimmunity which targets melanocytes for destruction is considered the main mechanism of vitiligo [7]. In endocarditis, circulating immune complexes mediated complement activation is responsible for some of the extra-cardiac manifestations and tissue damage. The importance of being aware of dermatological manifestations of infective endocarditis is also heightened by the fact that they are significantly associated with symptomatic and asymptomatic strokes [8]. It is even recommended to perform routine brain magnetic resonance imaging (MRI) to see evidence of clinically silent infarctions. In this patient, given the nature and the location (thalamic lacunar stroke) of the stroke, immunological phenomenon such as vasculitis or micro-embolization are possible mechanisms.

While there is no direct evidence of increased risk of stroke in patients with vitiligo, few case reports describe the co-occurrence of ischaemic stroke and vitiligo in homocystinuria, mitochondrial encephalo-myopathy, lactic acidosis, and stroke-like episodes (MELAS syndrome) [9-11]. Further studies are warranted to ascertain whether there is an increased risk of stroke in patients with infective endocarditis who develop vitiligo, as observed in our patient. It is equally important to explore the underlying mechanisms. This may have prognostic value and potentially open up pathways for new therapeutic options such as anti-inflammatory agents or anticoagulants to be considered for stroke prophylaxis in selected patients with infective endocarditis who are suspected of having a disproportionate systemic inflammatory response, identified early by clinical features such as vitiligo.

The patient was aware that she developed the stroke as a consequence of infective endocarditis and was well satisfied with the complete recovery of her neurological deficit and resolution of vegetation. She is hopeful that her vitiligo, too, would fully resolve with time.

Conclusion

Vitiligo may occur as an early cutaneous manifestation of infective endocarditis and may be a predictor of vascular phenomena such as ischaemic stroke. Therefore, clinicians may consider the

possibility of subacute infective endocarditis in a patient who presents with prolonged fever accompanied by new-onset vitiligo. Further studies are warranted to identify the causal relationship between infective endocarditis, vitiligo, and ischaemic stroke.

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