Letter to the Editor (Case report)

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Systemic lupus erythematosus mimicry caused by viral infection with Coxsackie B4**Rheumatology key message**

- Coxsackie B4 can cause systemic lupus erythematosus mimicry.

DEAR EDITOR, cases of viral infection with clinical and biochemical features mimicking those of SLE have been described. Both may cause fever, rash, lymphadenopathy and production of ANA. As such, differentiating viral infections from SLE can be challenging and requires a thorough interpretation of medical history, clinical presentation, biochemical results and disease progression. EBV, Parvovirus B19 (B19) and CMV are known to initiate abnormal immune responses, triggering and mimicking SLE [1]. Coxsackie B4 (CB4) virus has been associated with autoimmune diseases, such as type 1 diabetes [2, 3], but to date no cases link CB4 to SLE.

Herein, we present a case of a 25-year-old Caucasian female that developed a transient SLE mimic caused by an acute CB4 infection. During the course of a common

cold, she developed pain and stiffness of the knee and a cutaneous annular papulovesicular rash on both arms and legs (Fig. 1A). Anatomopathological examination showed a lymphohistiocytic dermatitis with interphase pathology. Within several days, her articular symptoms worsened into a symmetrical polyarthritis of the hands, elbows, feet and knees. The patient did not recall photosensitivity, Raynaud phenomenon, alopecia or thrombosis. One week after symptom onset, laboratory testing showed mildly elevated inflammatory markers. ANA was positive at a titre of 1:160, with a nucleolar and speckled pattern. Screening for specific autoantibodies was negative (Thermofischer CTD screen) and anti-double stranded DNA (dsDNA) antibodies, assessed using the Farr radioimmunoassay, were negative (Fig. 1B). Treatment was initiated with non-steroidal anti-inflammatory drugs and glucocorticoids (methylprednisolone 16 mg qd) by the general practitioner, prior to the rheumatology consultation. While the arthritis initially responded well to the therapy, the rash did not. Three weeks later, after discontinuation of glucocorticoids, the rash deteriorated, and the arthritis recurred. At rheumatology consultation, laboratory testing showed a positive ANA titre at 1:80, positive lupus anticoagulant (LAC) and negative IgM and IgG anticardiolipin antibodies. Complement levels were normal (Fig. 1B). Based on the symptoms of a common cold, preceding the onset of

Fig. 1 Clinical (A) and biochemical (B) evolution over time

A		B		
		At general practitioner (week 1)	At rheumatology consultation (week 4)	After therapy (week 20)
CRP (mg/L)*	18.6	26.3	1.8
	ESR (mm/h)**	19	NA	8
	ANA***	1:160	1:80	negative
	dsDNA, ENA	Negative	Negative	Negative
	LAC	NA	Positive	Negative
	Anticardiolipin IgG	NA	Negative	Negative
	Complement levels	Normal	Normal	Normal
	RF	Negative	Negative	NA
	PB19 IgG/IgM	NA	Negative	NA
	CMV IgG/IgM	NA	Negative	NA
	EBV IgG	NA	Positive	NA
	CB4 IgM	NA	1:256	NA

*Reference range ≤ 5 mg/L; **Reference range 1–15 mm/h; ***Reference range $< 1:80$. NA: not available.

the rash and the arthritis, the absence of complement usage and the low ANA titre without specific autoantibodies, we considered a viral infection as causative agent. CMV and B19 serology were negative. EBV serology was compatible with previous, non-recent infection. Based on the cutaneous phenotype, a Coxsackie infection was suspected. CB4 serology confirmed an IgM titre increase from 1:64–1:256 over a 2-week period, compatible with an acute CB4 infection. Treatment with glucocorticoids (prednisone at 20 mg qd) was restarted and tapered over the course of 15 weeks. Cutaneous lesions healed with central hypopigmentation and scarring. Inflammatory markers and LAC normalized, and ANA titre returned to negative (Fig. 1B). As the patient remained clinically asymptomatic, prednisone treatment was permanently withdrawn. Nine months after disease onset, ANA returned to positive at 1:80, in an asymptomatic patient.

Parvovirus B19, CMV and EBV are notorious mimickers of SLE with ANA production, arthritis and cutaneous manifestations [1]. To our knowledge, our case is the first to describe SLE mimicry in the context of an acute CB4 infection. CB4 belongs to the family of the enteroviruses, which are commonly associated with a non-pruritic, non-desquamating maculopapular skin eruption [4]. Our patient presented with a subacute cutaneous lupus erythematosus (SCLE)-like rash. Anatomopathological examination showed perivascular and perifollicular lymphohistiocytic dermatitis with interphase pathology and interstitial deposition of mucin, resembling, but not pathognomonic for SCLE [5]. Additional direct immunofluorescence to supplement the non-definitive histology was not performed [6].

Our case highlights the necessity to remain attentive towards SLE mimickers, including a number of viral infections. According to the latest 2019 classification criteria of SLE, our case could easily be misclassified [7]. Therefore, a critical view on a low-positive ANA titre [8] and absent specific autoantibodies in association with atypical clinical manifestations is crucial. Our case adds CB4 to the list of viral infections that could cause a possible clinical picture strongly resembling SLE.

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Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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References

- Chasset F, Richez C, Martin T *et al.* Rare diseases that mimic systemic lupus erythematosus (lupus mimickers). *Joint Bone Spine* 2019;86:165–71.
- Akatsuka H, Yano Y, Gabazza EC *et al.* A case of fulminant type 1 diabetes with coxsackie B4 virus infection diagnosed by elevated serum levels of neutralizing antibody. *Diabetes Res Clin Pract* 2009;84:e50–2–e52.
- el-Reshaid K, al-Mofti S, Stepic NR. Induction of insulin resistance by autoantibodies to insulin receptors following on an acute Coxsackie B4 infection. *Diabetes Res Clin Pract* 1994;25:207–10.
- Horstmann DM. Enterovirus infections: etiologic, epidemiologic and clinical aspects. *Calif Med* 1965;103:1–8.
- Ribero S, Sciascia S, Borradori L, Lipsker D. The cutaneous spectrum of lupus erythematosus. *Clin Rev Allergy Immunol* 2017;53:291–305.
- Okon LG, Werth VP. Cutaneous lupus erythematosus: diagnosis and treatment. *Best Pract Res Clin Rheumatol* 2013;27:391–404.
- Aringer M, Costenbader K, Daikh D *et al.* 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol* 2019;71:1400–12.
- Willems P, De Langhe E, Westhovens R *et al.* Antinuclear antibody as entry criterion for classification of systemic lupus erythematosus: pitfalls and opportunities. *Ann Rheum Dis* 2019;78:e76.