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Venous thromboembolic events in systemic vasculitis

In a population-base study published in the *Annals of Rheumatic Disease*, Aviña-Zubieta *et al*[1] showed that there is almost 2.5-fold increase in risk of venous thromboembolism (VTE) in patients with giant cell arteritis (GCA) compared with that in the general population. Higher incidence of VTE is apparently not unique for GCA as a similar increase in risk of deep vein thrombosis (DVT) and pulmonary embolism was recently found in a meta-analysis of studies in patients with different inflammatory rheumatic diseases.[2]

We detected only two cases of venous thrombosis (orbital and retinal veins) in our series of 76 patients with GCA, though at least two-thirds of them have been followed for 2 years. At the same time, there were 30 cases of VTE and other vein thrombosis in a cohort of 357 patients with antineutrophil cytoplasmic autoantibodies (ANCA)-associated vasculitides between 2006 and 2014 (table 1). The frequency of VTE in eosinophilic granulomatosis with polyangiitis was higher (10.1%) than in granulomatosis with polyangiitis (8.2%) and microscopic polyangiitis (6.7%) probably due to thrombogenic effect of eosinophilia.[3] It is known that eosinophils release tissue factor as well as other cationic proteins. The former initiates coagulation while the latter inhibit natural anticoagulant activity and activate platelets, eventually leading to excessive thrombin generation.[4] The majority of our patients were relatively young, developed VTE during first year after diagnosis and had no other known risk factors for thromboembolic events. These data confirm the potential contribution of vasculitis-associated factors (eg, hypercoagulability, endothelial damage, stasis of blood, etc) and/or high-dose glucocorticoids to the development of VTE. Our data agree with a French Vasculitis Study Group retrospective study that established high frequency of VTE (around 8%) in patients with ANCA-associated vasculitides.[5] The significantly lower risk of VTE in polyarteritis nodosa in the latter study suggests that ANCA themselves may contribute to a higher incidence of venous thrombosis in systemic vasculitis. Patients with ANCA-associated vasculitis can harbour antibodies with dual reactivity to plasminogen and complementary proteinase 3 (PR3), a recombinant protein translated from the antisense strand of PR3 cDNA.[6] Antiplasminogen antibodies delay the conversion of plasminogen to plasmin and increase the dissolution time of fibrin clots and, therefore, can probably promote thrombotic complications.

What is a cost-effective strategy of prevention of VTE in systemic vasculitides? Using compression ultrasound in a pilot study, we have found asymptomatic DVT in four (9.5%) of 42 patients with ANCA-associated vasculitides. Therefore, its prevalence may be higher than expected and can justify wider screening though obviously we need more data. Low-dose aspirin is frequently used in patients with GCA to prevent ischaemic events. It should be probably administered more often in patients with ANCA-associated vasculitides as in our previous study more than half of 102 patients with granulomatosis with polyangiitis had high or very high predicted 10-year risk of fatal cardiovascular diseases calculated using SCORE charts.[7] Aspirin significantly reduces the risk of arterial thrombosis, but it is less effective in the prevention of VTE and, therefore, cannot replace anticoagulants. Aviña-Zubieta *et al* suggested anticoagulation in a high-risk GCA population. But who is in high risk? All patients? In our cohort, there were no fatal VTE events. Therefore, we cannot recommend routine anticoagulation for all patients with GCA or ANCA-associated vasculitides. We agree with the authors that the risk of VTE should not be ignored in patients with GCA and other vasculitides. And we need more studies to evaluate the role of vasculitis-associated thrombogenic risk factors and to develop a strategy of screening to identify patients who really require prolonged anticoagulation.

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Competing interests None.

Table 1 Characteristic of patients with VTE events

	GPA (n=243)	MPA (n=45)	EGPA (n=69)	Total (n=357)
VTE, n (%)	20 (8.2)	3 (6.7)	7 (10.1)	30 (8.4)
Men, n	11	2	3	16
Median age, year (range)	51 (25–78)	49 (46–64)	53 (30–65)	52 (25–78)
Traditional VTE risk factors*	5	1	2	8
VTE events	14	2	5	21
DVT	12	2	5	19
DVT+PE	2	0	0	2
Other vein thrombosis†	8	1	2	11
Time to VTE after diagnosis				
First 6 months	5/16	3/3	2/5	10/24
First 12 months	8/16	3/3	3/5	13/24
Death from any cause	2	0	0	2
Death from PE	0	0	0	0

*Metabolic syndrome, type 2 diabetes mellitus, multiple intravenous injections, chronic venous insufficiency.
†Orbital vein (2), jugular vein (1), renal vein (1), testicular vein (1), superficial veins (6).
DVT, deep vein thrombosis; EGPA, eosinophilic granulomatosis with polyangiitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; PE, pulmonary embolism; VTE, venous thromboembolism.

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