

IMPACT OF DENGUE-INDUCED THROMBOCYTOPENIA ON MANDATORY ANTICOAGULATION FOR PATIENTS WITH PROSTHETIC HEART VALVES ON WARFARIN

Singapore Med J 2015; 56(4): 235-236 doi: 10.11622/smedj.2015066

Dear Sir,

We report two patients on anticoagulation with warfarin for congenital heart disease, who developed dengue-related thrombocytopenia.

Patient 1 is a 26-year-old man who was anticoagulated with warfarin 4.5 mg because of St Jude mechanical aortic valve for severe congenital aortic stenosis. He presented with four days of fever and generalised myalgia. His vital signs were stable, but he developed thrombocytopenia and subtherapeutic international normalised ratio (INR) due to noncompliance. He tested positive for dengue NS1 antigen and became increasingly thrombocytopenic. Warfarin was held off on Day 6 of illness (Table I). He responded to intravenous hydration and was restarted on warfarin on Day 10 of illness. INR checked a week later was therapeutic.

Patient 2, an 18-year-old man with Loey-Dietz syndrome, had a Bentall procedure (aortic valve replacement with conduit) at 14 years of age for aortic root dilatation, followed by Dacron graft repair of his ascending aorta at 16 years of age for aortic dissection. He was anticoagulated with oral warfarin 6 mg daily with a targeted INR of 2. He was admitted for dengue fever on Day 5 of illness, with fever, blood pressure of 109/63 mmHg, thrombocytopenia of $107 \times 10^9/L$ and INR of 1.69 on admission. He tested positive for dengue NS1 antigen and dengue IgM. His platelet count continued to fall and reached a nadir on Day 7 of illness (Table I). He was continued on his regular warfarin dose with close monitoring. He remained haemodynamically stable without bleeding or valve thrombosis throughout.

Currently, there are no guidelines on how warfarin administration affects thrombocytopenia in patients with prosthetic valves and concurrent dengue. The risks of bleeding both from anticoagulation and severe dengue need to be balanced against the risks of valve thrombosis from withholding warfarin. A major bleeding rate of 4% per patient-year has been reported for patients on warfarin for prosthetic valves.⁽¹⁾ Although reportedly anticoagulation can be safely withheld for less than seven days without valve complications in the setting of intracranial haemorrhage,⁽²⁾ subtherapeutic INR values for 16.3 ± 9.0 days have been associated with a 1% risk of thromboembolism.⁽³⁾ Apart from a single case report where warfarin was withheld for a woman with a mitral prosthesis who had dengue haemorrhagic fever,⁽⁴⁾ there are no guidelines on management of anticoagulation in the face of dengue-induced thrombocytopenia. We withheld anticoagulation in one patient and continued anticoagulation in the other based on close clinical and laboratory monitoring. We did not use low-molecular-weight heparin as a bridging therapy, as there is a paucity of evidence to support this.⁽⁵⁾

In conclusion, our patients had favourable outcomes with careful adjustment of warfarin dosing for their prosthetic valves in the setting of acute dengue fever with thrombocytopenia. Future studies should be undertaken to develop clinical guidelines for patients on mandatory anticoagulation who have dengue with warning signs or are at risk of bleeding, especially for those residing in endemic countries.

Table I. Clinical and laboratory details of Patients 1 and 2.

Patient no./date	Day of illness	Platelet ($\times 10^9/L$)	Haematocrit (%)	INR	Warfarin dose (mg)	Clinical features
Patient 1						
17/6	4	58	51.1	1.3	4.5	
18/6	5	43	48.8	1.45	4.5	
19/6	6	44	48.9	1.85	0	
20/6	7	37	50.7	1.61	0	Hypotensive and flushed
21/6	8	32	45.9	1.5	0	
22/6	9	39	46.5	1.27	0	
23/6	10	56	48.9	1.08	3	
24/6	11	74	47.4	1.11	3	
25/6	12	122	47.6	1.14	3	
01/7	18	182	47.9	2.23	4.5	
Patient 2						
23/6	5	107	43.7	1.69	Continued on the regular warfarin dose	None
24/6	6	112	43.3	2.03		
25/6	7	90	43.4	2.41		
26/6	8	112	40.5	2.65		
01/7	13	271	41.4	3.06		

INR: International normalised ratio

ACKNOWLEDGEMENT

We thank Dr Dimple Rajgor for her assistance in editing, formatting and submission of the manuscript for publication.

Yours sincerely,

Tammy SH [Lim](#)^{1,2}, Robert T [Grignani](#)^{1,2}, Paul A [Tambyah](#)³, Swee-Chye [Quek](#)^{1,2}

¹Khoo Teck Puat-National University Children's Medical Institute, National University Health System, ²Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, ³Department of Medicine, National University Health System, Singapore. paul_anantharajah_tambyah@nuhs.edu.sg

REFERENCES

1. Wong CS, Batchelor K, Bua J, Newall F. Safety and efficacy of warfarin in paediatric patients with prosthetic cardiac valves: a retrospective audit. *Thromb Res* 2011; 128:331-4.
2. Krittalak K, Sawanyawisuth K, Tiamkao S. Safety of withholding anticoagulation in patients with mechanical prosthetic valves and intracranial haemorrhage. *Intern Med J* 2011; 41:750-4.
3. Dentali F, Pignatelli P, Malato A, et al. Incidence of thromboembolic complications in patients with atrial fibrillation or mechanical heart valves with a subtherapeutic international normalized ratio: a prospective multicenter cohort study. *Am J Hematol* 2012; 87:384-7.
4. Gamakaranage C, Rodrigo C, Samarawickrama S, et al. Dengue hemorrhagic fever and severe thrombocytopenia in a patient on mandatory anticoagulation: balancing two life threatening conditions: a case report. *BMC Infect Dis* 2012; 12:272.
5. Tufano A, Guida A, Di Minno MN, et al. Prevention of venous thromboembolism in medical patients with thrombocytopenia or with platelet dysfunction: a review of the literature. *Semin Thromb Hemost* 2011; 37:267-74.