CASE REPORT

Dengue haemorrhagic fever, during the immediate postoperative period in a patient who had undergone mechanical aortic valve replacement

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INTRODUCTION

Dengue fever is an endemic disease in Sri Lanka. In the past, it had high mortality. Patients with severe dengue have a higher risk of bleeding tendency. When a patient is on mandatory anticoagulation, they have a higher chance of bleeding. We are reporting a case of dengue fever during the immediate postoperative period in a patient who had undergone a mechanical aortic valve replacement. Balancing bleeding and thromboembolic risks were challenging when managing such a patient.

Keywords: Dengue, aortic valve replacement, anticoagulant

CASE

A 47-year-old female with severe aortic regurgitation was admitted to National Hospital, Kandy for aortic valve replacement as an elective procedure. She was not a known patient with chronic medical illnesses or bleeding disorders. She had undergone aortic valve replacement with a 21mm on-X mechanical bi-leaflet valve. Her initial postoperative recovery was uneventful, and she was extubated on day one. She was started on low molecular weight heparin 1mg per kg and warfarin 5 mg from day one as a bridging regime. On postoperative day 7, she developed a moderate pleural effusion, which was haemorrhagic. We stopped both warfarin and enoxaparin at this point. During this period, the platelet count and INR were 314 000/µl and 2.32, respectively. We restarted heparin 1mg per kg and warfarin 5 mg on day 11. The pleural effusion settled, and INR was 1.4 at this time.

While awaiting INR correction, she developed dengue, confirmed by NSI antigen though IgG and IgM antibodies for dengue were negative. The patient developed suprapubic pain on day five of dengue fever (15×7.5×7.2 cm). In addition, she developed hypotension, and the haemoglobin dropped to 5.2 g/dL. She was managed with blood transfusions and stoppage of antiplatelets and anticoagulants (Table 1). Meantime platelet count, haematocrit and haematoma (with USS abdomen) were closely monitored.

Ultimately, the patient recovered well, and the haematoma started to regress. We discharged the patient on postoperative day 36 with an INR of 2.02 and a platelet count of 441000/ µl.

DISCUSSION

Dengue fever has a wide range of clinical manifestations. It can vary from asymptomatic individuals to patients with severe dengue, which presents as vascular leakage and shock or severe haemorrhage and organ failure. Thrombocytopenia, platelet dysfunction, dysfunction of coagulation factors and vascular endothelium are demonstrated in severe dengue[1]. This is due to the activation of various inflammatory cytokines such as C3a, C5a, tumour necrosis factor (TNF)-α, interleukin (IL)-2, IL-4, IL-6, IL-8, IL-10, interferon (INF)-γ, monocyte chemotactic protein (MCP)-1 and histamines which are released during the dengue[1]. It results in a high haemorrhagic tendency.

In the first postoperative month, the risk of thromboembolism in post-valve replacement patients is high[2]. It is recommended to start oral anticoagulation from the postoperative day one. Enoxaparin is used to bridge until the target INR is achieved[2]. On-X mechanical aortic valve has a low thrombogenic profile. The PROACT trial shows a safe INR range of 1.5 to 2 for the On-X mechanical valve[3].

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TABLE 1. Patient's clinical, laboratory parameters and treatment of our patient during the period of dengue infection

Day of illness	D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12
WBC ($\times 10^9$/L)	8.24	3.11	3.43	2.36	2.21	4.4	6.9	10.53	11.06	12.62	9.26	7.83
Hb (g/dl)	9	8.4	8.6	7.5	8.1	8.6	7.9	5.2	8.2	8.5	8.2	10.1
Platelet ($\times 10^9$/L)	97	73	90	105	80	80	86	220	232	272	225	267
HCT%	27.8	26	25.9	23.2	24.6	26.9	24.7	16.6	29.8	32.6		
INR	1.4	1.31	1.08		1.09	1.11		1.05	1.06	0.98	0.94	1.01
APTT (Sec)			49.4					45.9		30.3		
Clinical events	headache, myalgia, retro-orbital pain				supra-pubic pain	8.5×6.2cm pelvic haematoma	9.2×14×8.3 cm(563ml) haematoma	15×7.2 ×7.5cm size haematoma		Pelvic haematoma-stable in size		
Aspirin										75mg daily	75mg daily	75mg daily
Enoxaparin	60 mg bd	30mg daily	30mg daily	30mg daily	30mg daily	W/H	W/H	W/H	W/H	W/H	W/H	30mg bd
Warfarin	5 mg daily	1mg daily	1mg daily	1mg daily	1mg daily	W/H	W/H	W/H	W/H	W/H	W/H	2.5mg daily

WBC, white blood cell count; Hb, haemoglobin; HCT, haematocrit; INR, international normalized ratio; APTT, activated partial thromboplastin time; W/H, withhold

There is no definitive evidence in the literature that suggests an ideal target INR when we treat the mechanical valve-replaced patient with dengue fever. We decided to reduce the warfarin dose and enoxaparin when the platelet count dropped below 100000/ µl. Our patient developed a large pelvic haematoma which led to hypotension. Despite the INR level being 1.11 at the time of the pelvic bleed, the APTT was 49.5, which is elevated. The reason for this would have been dengue-associated coagulation abnormalities.

A couple of case reports regarding patients with mechanical valves developing dengue fever are available in the literature. Firstly, a Sri Lankan patient with a mechanical mitral valve replacement was affected with severe dengue. Warfarin was stopped when the platelet count became below 100000/µl and restarted again when the count started to rise above 50000/µl. Though the patient was off anticoagulation for ten days, she did not develop thromboembolic complications[4].

Secondly, there was a Chinese patient with mitral valve replacement who was treated by withholding the warfarin during the critical period and restarted when he was clinically stable and platelet and coagulation profile started to stabilize. He did not develop bleeding manifestations or thromboembolic complications[5].

Both of above mentioned patients had a platelet count of less than 20000/µl and an INR greater than two during the critical periods.

Our patient's platelet count was greater than 80000/µl, and INR was less than 1.5 throughout the illness. One of our primary concerns was valve thrombosis. The risk of valve thrombosis is high in the first month of replacement, and she had low INR values consistently, making us give a low dose of anticoa-gulants during the critical period and initial recovery period.

Despite all our precautions, our patient developed a pelvic haematoma. Several factors, such as patient-related problems, the disease process of dengue, and the effects of anti-coagulants interacting with each other, would have given those outcomes. Therefore, it is difficult to judge the bleeding and thromboembolic risks.

There is no clear guideline for anticoagulant management in dengue patients. Therefore, successful management of these patients depends on clinical judgment and close monitoring with clinical assessments and serial monitoring of clotting profiles. Another dilemma was restarting anticoagulation in a patient with mechanical valve replacement and dengue fever. We restarted warfarin and bridging therapy with fractionated heparin when the platelet count rose above 100000µl. There are currently no clear guidelines about restarting anticoagulants following dengue haemorrhagic fever. We feel it is safe to restart anticoagulation when there is no evidence of fresh bleeding or exacerbation of hematoma and the platelet count rises above 100000 /µl.

REFERENCES

1. Chuansumrit A, Chaiyaratana W. Hemostatic derangement in dengue hemorrhagic fever. *Thrombosis Research* 2014; 133(1): 10-16. https://doi.org/10.1016/j.thromres.2013.09.028
2. Baumgartner H, Falk V, Bax J, De Bonis M, Hamm C, Holm P. et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *European Heart Journal* 2017; 38(36): 2739-91. https://doi.org/10.1093/eurheartj/ehx391
3. Puskas J, Gerdisch M, Nichols D, Quinn R, Anderson C, Rhenman B. et al. Reduced anticoagulation after mechanical aortic valve replacement: Interim results from the Prospective Randomized On-X Valve Anticoagulation Clinical Trial randomized Food and Drug Administration investigational device exemption trial. *The Journal of Thoracic and Cardiovascular Surgery* 2014; 147(4): 1202-11. e2. https://doi.org/10.1016/j.jtcvs.2014.01.004
4. Gamakaranage C, Rodrigo C, Samarawickrama S, Wijayaratne D, Jayawardane M, Karunanayake P. et al. Dengue hemorrhagic fever and severe thrombocytopenia in a patient on mandatory anticoagulation; balancing two life threatening conditions; a case report. *BMC Infectious Diseases* 2012; 12(1). https://doi.org/10.1186/1471-2334-12-272
5. Lum L, Chan M, Leo Y. Strategy in managing anticoagulation therapy following prosthetic heart valve replacement in a patient with dengue fever. 2022.http://dx.doi.org/10.1016/j.ijcard.2015.07.098