

mobilization might be reasonable. However we acknowledge that the reduced prophylactic dose of LMWH might have been a contributing factor in this particular case.

Patent foramen ovale is present in 10 to 35 % of general population (4) and in one study it was diagnosed in 35 % of patients with pulmonary embolism, accounting for a high risk of death and thromboembolic complications such as stroke and peripheral arterial embolism (8). However, patent foramen ovale accounts only for 2 % of arterial emboli of the extremities (9). In our case, the left subclavian artery, left common femoral artery and superior mesenteric artery were involved. Paradoxical embolism into superior mesenteric artery is extremely rare (10, 11).

As the vascular surgeon decided against surgical embolectomy, local pulse spray thrombolysis was considered and interventional radiologist was consulted. Taking into account the presence of emboli at 3 different sites as well as the extent of each one of them, the radiologist decided not to perform pharmacomechanical thrombolysis. Local pulse spray thrombolysis was not applied in any of the few cases of multiple-site paradoxical embolism with concomitant pulmonary embolism we found in the literature, most authors report a combination of surgical embolectomy and systemic thrombolysis (12, 13).

Systemic thrombolysis with alteplase following the protocol for pulmonary embolism was attempted in this case, leading within 48 hours to the resolution of the emboli in the left subclavian artery, the common femoral artery and the superior mesenteric artery. Fan et al. described a similar case of systemic thrombolysis for pulmonary embolism and

concomitant multiple-site paradoxical embolism with involvement of the left subclavian artery and the origin of the celiac artery (12). Ruiz-Bailen et al reported a case of successful administration of alteplase in a venous thromboembolism crossing through a patent foramen ovale to the left atrium and suggest that thrombolysis could be a therapeutic option in the presence of a paradoxical embolism in the context of a serious VTE when surgery is not feasible (14). According to current ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, therapeutic options for acute limb ischemia include thrombus extraction, thrombo-aspiration, surgical thrombectomy and catheter-directed thrombolytic therapy. Systemic thrombolysis has no role in the treatment of patients with acute limb ischemia (15). There are no guidelines addressing the treatment of multiple-site emboli in presence of PFO. Our case report supports the option of systemic thrombolysis for the treatment of multiple-site paradoxical embolism in context of pulmonary embolism when other therapeutic option (surgery, pharmacomechanical thrombolysis) is not possible.

## Conclusions

Prolonged antithrombotic prophylaxis might be reasonable in patients after orthopedic/traumatologic surgery until full mobilization.

Systemic thrombolysis may be attempted in case of multiple-site paradoxical embolism through patent foramen ovale, especially in cases where other treatment options (surgery, pharmacomechanical thrombolysis) are not possible.

## LIST OF REFERENCES

- White RH, Romano PS, Zhou H, et al. Incidence and time course of thromboembolic outcomes following total hip or knee arthroplasty. *Arch Intern Med* 1998; 158: 1525–1531.
- Kearon C. Natural history of venous thromboembolism. *Circulation* 2003; 107: (23 Suppl 1): 122–130.
- Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012; 141: (2 Suppl): e419S–e496S.
- Fisher DC, Fisher EA, Budd JH, et al. The incidence of patent foramen ovale in 1,000 consecutive patients. A contrast transesophageal echocardiography study. *Chest* 1995; 107: 1504–1509.
- Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014; 35: 3033–3069, 3069a–3069k.
- Douketis JD, Eikelboom JW, Quinlan DJ, et al. Short-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of prospective studies investigating symptomatic outcomes. *Arch Intern Med* 2002; 162: 1465–1471.
- Comp PC, Spiro TE, Friedman RJ, et al. Prolonged enoxaparin therapy to prevent venous thromboembolism after primary hip or knee replacement. *Enoxaparin Clinical Trial Group. J Bone Joint Surg Am* 2001; 83: 336–345.
- Konstantinides S, Geibel A, Kasper W, et al. Patent foramen ovale is an important predictor of adverse outcome in patients with major pulmonary embolism. *Circulation* 1998; 97: 1946–1951.
- AbuRahma AF, Downham L. The role of paradoxical arterial emboli of the extremities. *Am J Surg* 1996; 172: 214–217.
- Acosta S, Björck M. Acute thrombo-embolic occlusion of the superior mesenteric artery: a prospective study in a well defined population. *Eur J Vasc Endovasc Surg* 2003; 26: 179–183.
- Pirkl M, Myjavec A, Danek T, et al. A case of pulmonary thromboembolism with synchronous and metachronous paradoxical embolism through the patent foramen ovale. *Cor et Vasa* 2012; 54: E314–E322.
- Fan Z, Roedersheimer R, Lohr J. Systemic thrombolysis using tissue plasminogen activator for a patient with paradoxical embolism: a case report. *Vasc Endovascular Surg* 2007; 41: 136–139.
- Agarwal SK, Binbrek AS, Thompson JA, et al. Massive pulmonary embolism and acute limb ischaemia in a patient of hereditary spherocytosis and patent foramen ovale. *Heart Lung Circ* 2010; 19: 742–744.
- Ruiz-Bailen M, Ramos-Cuadra JA, Machado-Casas J, et al. Successful administration of alteplase in a venous thromboembolism crossing through a patent foramen ovale. *Interact Cardiovasc Thorac Surg* 2009; 9: 712–713.
- Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur Heart J* 2018; 39: 763–816.