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Cases of Brainstem Infarcts after Cessation of Heparin Treatment: Is It a Rebound Effect?

Heparin Tedavisinin Kesilmesinden Sonra Gelişen Beyin Sapı İnfarkt Olguları: Bir Rebaund Etki Olabilir mi?

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Abstract

The presented cases represent patients with acute coronary syndrome treated with heparin infusion who developed brainstem infarction after discontinuation of heparin treatment. The patients did not present genetic coagulopathy. Others risk factors were analyzed, and the discontinuation of heparin infusion was also considered to have a predominant role in the development of infarction.

Key Words: Cerebrovascular diseases, Heparin, Rebound effect

Özet

Akut koroner sendrom tanısı ile heparin tedavisi almakta olan ve heparin tedavisi kesildikten sonra beyin sapı infarktı gelişen iki olgu sunuldu. Hastalarda genetik koagülopati saptanmadı. Diğer risk faktörleri analiz edildi ve heparin infüzyonunun kesilmesinin de infarkt gelişiminde öncül bir rolü olabileceği düşünüldü.

Anahtar Kelimeler: Beyin damar hastalıkları, Heparin, Rebaund etkisi

Atherosclerosis is a systemic condition that may simultaneously involve different arterial distributions. Patients with established vascular disease represent high-risk cohorts if they have coronary artery diseases or cerebrovascular diseases, and secondary vascular disease prevention is likely to be particularly effective and cost effective [1]. Small-artery diseases and microembolisms, which affect penetrating arteries, may cause brainstem infarctions. The predisposing factors include blood stasis, endothelial lesions and coagulation disorders [2]. Herein, we present a case of acute pontine infarction after interruption of heparin therapy.

Case 1

A 58-year-old woman with hypertension and diabetes mellitus presented with sudden onset of binocular diplopia when looking to the left side and right facial weakness in the coronary intensive care unit. In her clinical history, she had chest pain, abnormal electrocardiographic findings and increased cardiac enzymes, suggesting acute coronary syndrome. However, she had a normal coronary arteriogram. The patient was excluded from heparin therapy because of acute coronary syndrome on the day when these neurological symptoms were occurred. On neurological examination, cognition was intact and there were no signs of limb weakness. The pupils were equal in size and normally reactive to light and a near stimulus. Ocular motor examination revealed combination of right gaze paresis and right internuclear ophthalmoplegia, suggesting horizontal one-and-a-half syndrome. Nystagmus was observed on left-horizontal gazing of the abducting eye. Vertical ocular movements from the primary position were normal. She also had palsy of the right peripheral seventh nerve, which led to the diagnosis of a brainstem lesion.

Cranial magnetic resonance imaging showed a right paramedian tegmental pontine lesion (Figure 1). Brain computed angiography showed vascular irregularities on the large vessels and a mild stenosis on the basilar artery. A transthoracic echocardiogram was normal. Our patient exhibited no risk factors, such as a history of oral contraceptive use or protein C, protein S, or antithrombin III deficiency; no other risk factors for stroke were found except hypertension and diabetes mellitus.

Case 2

In the coronary intensive care unit, heparin therapy was given to a 61-year-old male diabetic patient for acute coronary

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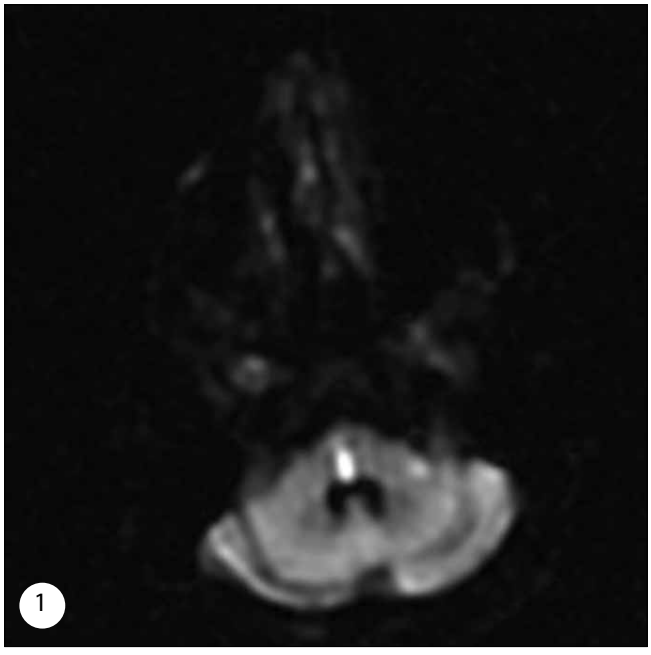

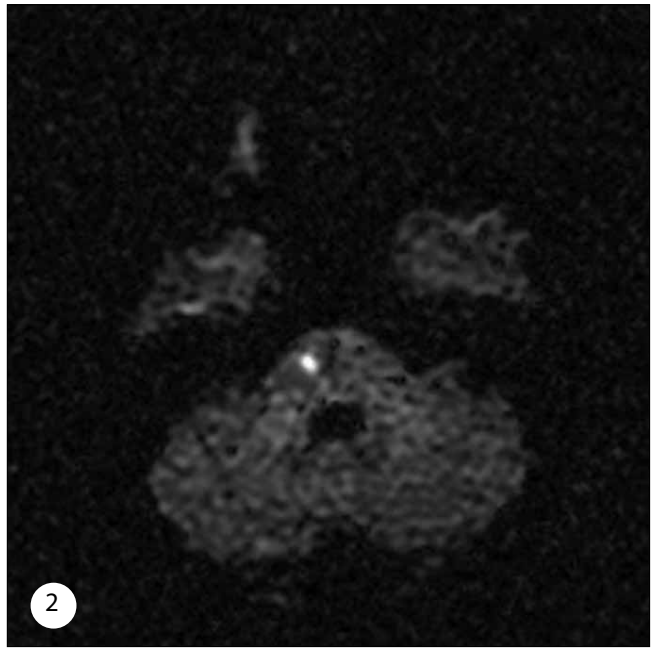

Figure 1 and Figure 2. *Diffusion weighted images (DWI) showed high signal intensity lesion (corresponding to the anatomical correlate) in the brainstem.*

syndrome. After he had been excluded from heparin therapy, he attended by a neurologist because of numbness of the left hemifacial region and right hemiparesis. Cranial MRI revealed an infarct at the left inferior dorsolateral pontine region (isohypointense at T1 weighted, hyperintense at T2 weighted images and FLAIR sequence). There was no contrast enhancement (Figure 2). CT angiographies of the carotid and vertebral arteries showed no abnormality. A mild increase in the cholesterol level was detected through routine blood analyses.

Discussion

The clinical features of our patients, in association with brainstem lesions as a result of cerebrovascular disease, include the presence of diabetes mellitus and hypertension. The patients also had acute coronary syndrome. Heparin therapy is considered to be an important and widely used therapy in the treatment of acute coronary syndromes.

A reactivation of unstable angina after the discontinuation of intravenous heparin therapy has been described in patients with acute coronary syndromes [3]. Another study suggests the presence of a rebound in ischemic events after the discontinuation of heparin therapy in patients with acute coronary syndromes [4]. The same study offers further evidence that an increase in death or myocardial infarction within 12 hours of heparin discontinuation occurs in patients with acute coronary syndromes. In this study, if probable stroke is considered to be one of the causes of death, a new activation or a reactivation of cerebrovascular disease may occur [4]. A possible mechanism underlying the interaction between heparin rebound and antiplatelet therapy is presented in a study showing that platelet activation and aggregation increases during treatment with heparin. This platelet-activating effect of heparin may outlive its therapeutic anticoagulant effect [5]. These findings suggest that the accumulation of prothrombotic factors during antithrombin therapy leads to a relative hypercoagulable state after drug withdrawal. A slow taper of anticoagulation therapy with heparin appears to reduce the risk of cerebrovascular events and may improve outcomes in patients with cerebrovascular diseases. We have not found a consensus regarding the duration of anticoagulation treatment in the course of discontinuation, and the optimal duration of anticoagulation therapy has not yet been determined in the patients who have coronary artery disease concurrently with cerebrovascular disease. Further studies are necessary to delineate whether tapering of heparin may suppress the rebound effect in coronary and cerebral circulation.

Conflict of interest statement: The authors declare that they have no conflict of interest to the publication of this article.

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