Hypertensive Crisis and Left Ventricular Thrombi after an Upper Respiratory Infection during the Long-term Use of Oral Contraceptives

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Abstract

A 34-year-old woman who had been using oral contraceptives for 10 years developed hypertensive crisis with papilloedema after an upper respiratory infection. Laboratory data showed hyperreninemic hyperaldosteronism and elevated levels of fibrinogen, fibrin, and fibrinogen degradation products. Echocardiography demonstrated two masses (18 mm) in the left ventricle. On the fourth hospital day, cerebral infarction, renal infarction, and upper mesenteric artery occlusion suddenly occurred despite the blood pressure being well-controlled using anti-hypertensive drugs. Echocardiography revealed the disappearance of the left ventricular masses, which suggested left ventricular thrombi. Cessation of the contraceptives and administration of heparin, warfarin, and anti-platelets drugs improved her general condition.

Key words: hypertensive crisis, malignant hypertension, left ventricular thrombi, oral contraceptives, hypercoagulation, cardiac hypofunction

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Introduction

Malignant hypertension has been defined as a significant rapid increase in blood pressure over baseline and the presence of papilloedema with flame-shaped hemorrhages or soft exudates. Recently, the National International Blood Pressure Control guidelines recommended replacing the term “malignant hypertension” with “hypertensive crisis” (1, 2). Hypertensive crisis occurs in up to 1% of patients with essential hypertension. Several risk factors, such as smoking, black race, male gender (3), age greater than 40 years, and oral contraceptive use, have been identified (4).

We herein report the findings of a 34-year-old woman who had been using oral contraceptives for 10 years developed hypertensive crisis and left ventricular thrombi after an upper respiratory infection that induced systemic infarction. We additionally discuss the relationship among oral contraceptive use, upper respiratory infection, hypertensive crisis, and cardiac thrombi.

Case Report

A 34-year-old Japanese woman was admitted to Aichi Medical University Hospital because of dyspnea and systemic edema. She had had atopic dermatitis since 10 years of age. She was treated with second-generation oral contraceptives for 10 years before admission for uterine fibroids and menstrual complaints. Her father died from lung cancer with scleroderma. She had no history of smoking. She did not receive anti-hypertensive drugs because of no detection of hypertension. Three weeks prior to admission, she had a sore throat and a high fever, up to 38°C. Two weeks prior to admission, she visited a local doctor due to the persistence of these symptoms, and she was found to have proteinuria, but a normal blood pressure. Clarithromycin relieved her fever; however, she began to have a cough and hoarseness at night and in the early morning. One week before admission,
she experienced dyspnea and edema in both legs, and her complaints were not improved by the use of furosemide. Therefore, she was referred to our hospital because of extremely severe hypertension (200/140 mmHg).

On this admission, her mental status was normal, height was 153 cm, and weight was 60 kg, an increase of 10 kg over one week. Her body temperature was 36.4°C, pulse was 115 beats/min and regular, respiratory rate was 20 breaths/min, and blood pressure was 250/160 mmHg. A physical examination revealed redness in the left eye, coarse crackles in both lower lung fields, and bilateral lower extremity edema. A funduscopic examination demonstrated flame-shaped hemorrhages or soft exudates with papilloedema (Fig. 1). Laboratory studies indicated 4


Figure 1. Funduscopic examination findings. Swelling of the optic disc (papilledema), hemorrhage, and a macular star were observed on admission.

A plain chest X-ray demonstrated an enlarged cardiac silhouette, with a cardiothoracic ratio of 56% (Fig. 2A). Electrocardiography (ECG) showed inverted T waves in V1, V2, V3 (Fig. 2B). Echocardiography revealed two 18 mm masses in the left ventricle with a small amount of pericardial effusion with normal thickness of the ventricular wall (posterior wall thickness: 9.5 mm). The ejection fraction was 0.55 (Fig. 3A, B).

After making a diagnosis of hypertensive crisis, we administered 12.5 mg of captopril, which decreased her blood pressure from 250/160 mmHg to 154/97 mmHg three hours after administration. Thereafter, a long-acting angiotensin-converting enzyme inhibitor (ACE-I) and an angiotensin II receptor blocker (ARB) were prescribed to maintain the blood pressure. Human atrial natriuretic peptide (hANP) and furosemide were started to improve the cardiac function and systemic edema. Regarding the left ventricular masses, we initially suspected cardiac myxoma. On the fourth hospital day, the patient suddenly exhibited disorientation and memory disturbance. Enhanced abdominal CT demonstrated renal infarcts and occlusion of the mesenteric arteries (Fig. 4A). MRI revealed multiple cerebral small emboli (Fig. 4B, C). Echocardiography revealed the disappearance of the left ventricular masses (Fig. 3C, D), which suggested left ventricular thrombi. We initiated heparin, warfarin, and antiplatelet therapy. A hormonal examination demonstrated no abnormal findings with regards to the cortisol, ACTH, adrenalin, noradrenalin, and dopamine levels. The patient was discharged with complete recovery from systemic embolism on the 27th day after admission. A plain chest X-ray demonstrated a normal cardiac size with a cardiothoracic ratio of 48% (Fig. 2C). An ECG showed no abnormal findings (Fig. 2D). Echocardiography revealed no pericardial effusions and an ejection fraction of 0.72 without ventricular wall thickness. There were no significant increases in the levels of antibodies, such as enteric cytopathic human orpham (ECHO) virus and Coxsackievirus in paired serum samples taken one week apart. Urinary abnormality disappeared at discharge. The patient’s condition has been good
Figure 2. Chest X-ray and electrocardiogram findings on admission and at discharge. A cardiothoracic ratio (CTR) of 56% and mild pulmonary and pleural effusions were observed on admission (A). Electrocardiography showed inverted T waves in V5 (B). The CTR was 48% at the time of discharge, with no pulmonary or pleural effusions (C). T waves in V5 were normal at the time of discharge (D).

Discussion

The present case demonstrates two unique points: 1) the presence of hypertensive crisis (malignant hypertension) after an upper respiratory infection during the long-term use of contraceptives, and 2) left ventricular thrombi with mild cardiac hypofunction, which induced systemic dissemination of thromboemboli and systemic infarction.

Malignant hypertension, defined as a condition characterized by a very high blood pressure with bilateral retinal hemorrhages or exudates with or without papilloedema, was recently replaced by the term hypertensive crisis (1). There are two types of hypertensive crises: hypertensive urgency and hypertensive emergency. The former is defined as no sign of organ failure even during the hypertensive state. The latter shows organ involvement and requires the use of intravenous anti-hypertensive drugs to improve the patient’s clinical condition. The natural history of malignant hypertension was associated with a one-year mortality rate in excess of 79% and median survival of 10.5 months in untreated patients (5). Recently, the survival rate of malignant hypertension has increased to ≥70% after the use of ACE-I. The superior efficacy of captopril compared to nifedipine was demonstrated by a randomized controlled trial with an evidence level of 1b (2, 6). The present patient fulfilled the diagnostic criteria for malignant hypertension because of severe hypertension with papilloedema; however, her condition corresponds to hypertensive urgency because there were no definite signs of other organ failure despite proteinuria and hematuria at admission; she additionally had a good response to an oral ACE-I (6).

Regarding the relationship between hypertensive crisis and oral contraceptive use, an association has been reported since the 1960s (7-10). The incidence of hypertensive crisis in women between the ages of 15 and 44 years is 0.5 per 100,000 persons. Approximately 30% of these patients have renal disease; the remaining 70% use oral contraceptives (4). However, Lip et al. claimed that malignant hypertension in young women is related to previous hypertension in pregnancy, not oral contraceptive use (11). The risk of develop-
ing oral contraceptive-induced hypertension increases significantly with age, cigarette smoking, duration of oral contraceptives use, and obesity. Current Guidelines suggest that contraceptive prescriptions be limited to 6 months to ensure
regular BP monitoring throughout contraceptive therapy. Although the exact mechanism of hypertensive crisis in the present case remains unclear, the patient was not noted as having hypertension before the present episode, even following the long-term use of oral contraceptives. After an upper respiratory infection, severe hypertension was recognized. We speculate that the upper respiratory infection led to cardiac hypofunction and cardiac thrombi (according to the vascular endothelial damages) and the hypercoagulable state (according to the use of oral contraceptives), which stimulated the renin-angiotensin aldosterone system. ACE-I treatment blocked this vicious cycle.

Abnormalities of coagulation and fibrinolysis occur with oral contraceptive use. Oral contraceptives are known to increase the plasma levels of factor VIII (11, 12) and decrease the levels of protein S and ATIII (13), consistent with a hypercoagulable state. Third-generation contraceptives in particular are associated with activated protein C and fibrinogen. The present patient’s laboratory data on admission showed a hypercoagulable state, with elevated levels of fibrinogen (545 mg/dL), factor VIII activity (264%), as well as a fibrinolytic state, with increased levels of FDP-DD (20.78 μg/mL). Factor VIII is produced by reticuloendothelial cells, and is increased during an acute inflammatory response (14). Elevated levels of coagulation factors and oral contraceptive use have a synergistic effect on thrombosis (13, 15).

There have been several reports on cardiac thrombi involved in cardiac hypofunction states such as myocardial infarction (16), cardiomyopathy (17, 18), myocarditis (19), Takotsubo cardiomyopathy (20), and arrhythmias (21). Cardiac thrombi are divided into two types: right-sided and left-sided. The former is related to deep vein thrombosis and pulmonary thromboembolism. The latter is the cause of systemic thromboembolism, such as cerebral infarction, renal infarction, and mesenteric artery occlusion (22, 23). The present patient showed the typical clinical course of left-sided cardiac thrombi. Regarding the combination of hypertensive crisis and cardiac thrombi, it has been speculated that both the hypercoagulable state due to contraceptive use and mild cardiac hypofunction (EF 0.55) after an upper respiratory infection produces left ventricular thrombi, which may induce a hypertensive crisis with microthrombi in the renal arteries. To the best our knowledge, this is the first case report to show left ventricular thrombi accompanied by hypertensive crisis. Cessation of oral contraceptives and administration of warfarin and anti-platelet drugs successfully relived the effects of the systemic emboli.

The authors state that they have no Conflict of Interest (COI).

References


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