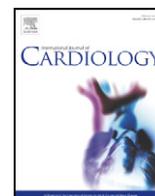




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Letter to the Editor

Coronary vessel floating sign and vasospastic angina in a patient with cardiac lymphoma

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A 59-year-old immunocompetent man was referred to our emergency room with syncope. The patient's Glasgow Coma Scale was E4V5M6, and neurological examination revealed no palsy. He reported no history of trauma or prescribed medication use, and his vital signs were as follows: body temperature, 37.3 °C; blood pressure, 104/74 mm Hg, pulse rate, 30 beats per minute (bpm) with irregular rhythm; and oxygen saturation in room air, 100%. Physical examination revealed distention of the jugular vein in the sitting position. On auscultation, his lung sounds were normal, and the pericardial friction rub was not clearly heard. Lower leg edema was not evident. Chest X-ray revealed cardiomegaly without pulmonary congestion. Electrocardiography (ECG; 12-lead) showed atrial fibrillation with bradycardia and ST elevation in the inferior leads. Soon after admission, atrial fibrillation spontaneously restored to sinus rhythm, and ST elevation also improved (Fig. 1A and B). Emergency coronary angiography revealed no significant stenosis (Fig. 2A and B; see Supplementary Videos 1 and 2). We suspected vasospastic angina (VSA) because of ST elevation without coronary artery stenosis. Laboratory findings were as follows: white blood cell count, 11,400 mm³; C-reactive protein, 3.9 mg/dL; procalcitonin, 0.06 ng/mL; creatine phosphokinase, 165 IU/L; troponin T, negative; and brain natriuretic peptide, 15.7 pg/mL. Thyroid function was normal and antinuclear

antibody was negative. The lactate dehydrogenase (LDH) level was slightly elevated (422 IU/L), the serum soluble interleukin-2 receptor (sIL2R) level was within normal limits (445 U/mL). Paradoxical pulse became overt in sinus rhythm. Transthoracic echocardiography revealed circumferential pericardial fluid retention (Fig. 3 and Supplementary Video 3). Pericardiocentesis yielded 1 L of bloody pericardial fluid containing an extremely high LDH (7752 IU/L) level. Cytological examination of pericardiocentesis fluid revealed numerous mid- to large-sized atypical lymphoid cells with prominent nucleoli. Subsequent ECG-gated, contrast-enhanced multidetector row computed tomography (MDCT) revealed a mass located around the atrioventricular (AV) groove and encasing the right coronary artery (RCA) without arterial invasion or compression (vessel floating sign; Fig. 4A–D). The tumor extended to the inferoposterior wall of the left ventricle (LV) along the RCA (Fig. 4E and F). Abnormal accumulation was observed at the same site on a gallium 67 scan. Immunohistochemical analysis of the cell block section of the effusion showed that the lymphoid cells were positive for CD20, with a high MIB-1 index, and negative for CD3. A final diagnosis of B-cell lymphoma was made (Fig. 5A and B). Complete remission of the tumor was achieved after 6 cycles of rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone (R-CHOP) therapy (Fig. 6A–F). An acetylcholine (Ach) provocation test by injection of Ach into the coronary artery after tumor remission due to R-CHOP therapy did not induce coronary spasm (Fig. 2C and Video 4).

Primary cardiac lymphoma (PCL) is a rare entity with variable clinical presentations. Although PCL is more common in immunocompromised patients, it is exceedingly rare in the immunocompetent population. The presenting symptoms are often nonspecific because they may vary according to the heart sites involved by PCL. The most frequent cardiac manifestations are pericardial effusion, heart failure, and AV block. PCL sometimes follows a fulminant course and is associated with a high mortality rate because of pulmonary embolism, arrhythmia, and heart failure [1]. Patients with malignant lymphoma occasionally experience ischemic heart disease (IHD) due to complications of lymphoma therapies. A causative link between radiation therapy to the mediastinum and coronary artery disease is well recognized in patients with Hodgkin lymphoma [2]. Also, Vinca alkaloids and granulocyte colony stimulation factor are suggested to be associated with IHD [3,4]. However IHD-related lymphoma itself is very rare. Lymphoma can reportedly cause IHD due to direct

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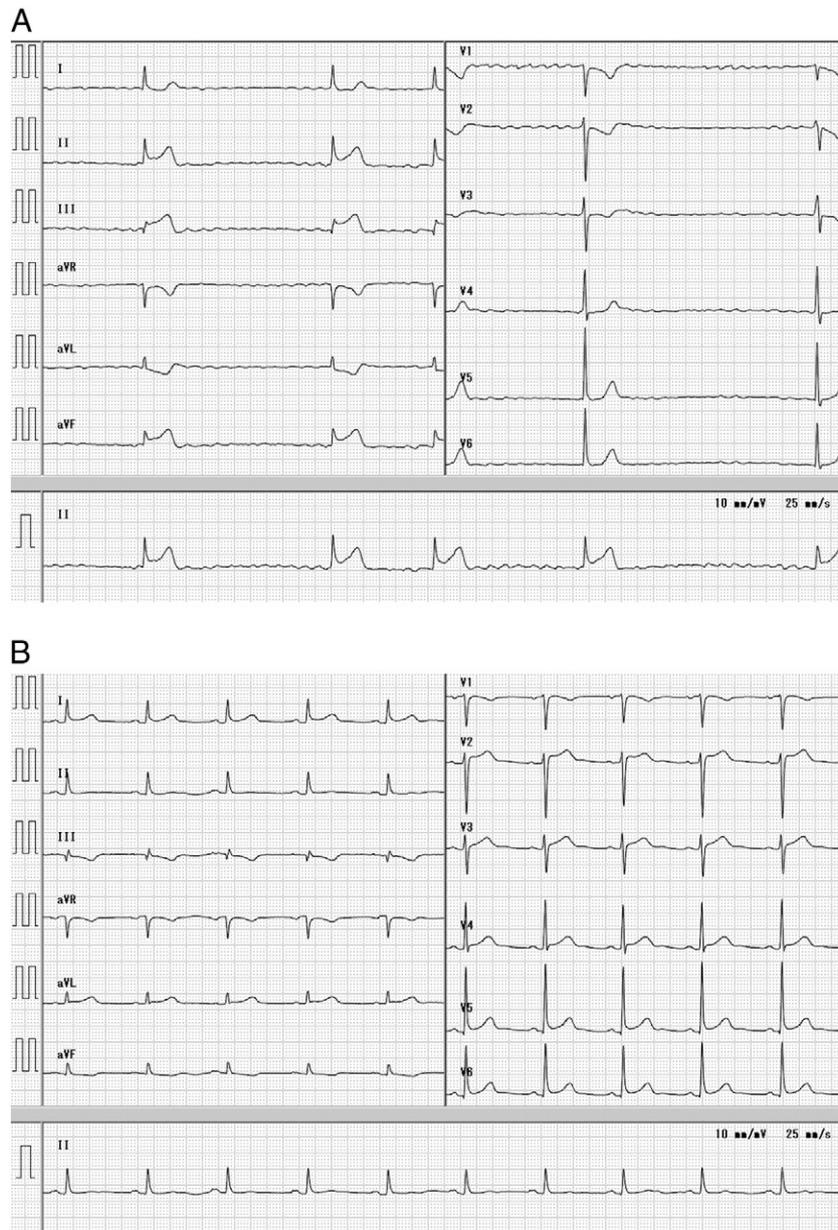


Fig. 1. Twelve-lead electrocardiography reveals atrial fibrillation with bradycardia; ST elevation in inferior leads II, III, and aVF; and reciprocal ST depression in leads V1–3 (A). Atrial fibrillation spontaneously restored to sinus rhythm, and ST elevation also improved (B).

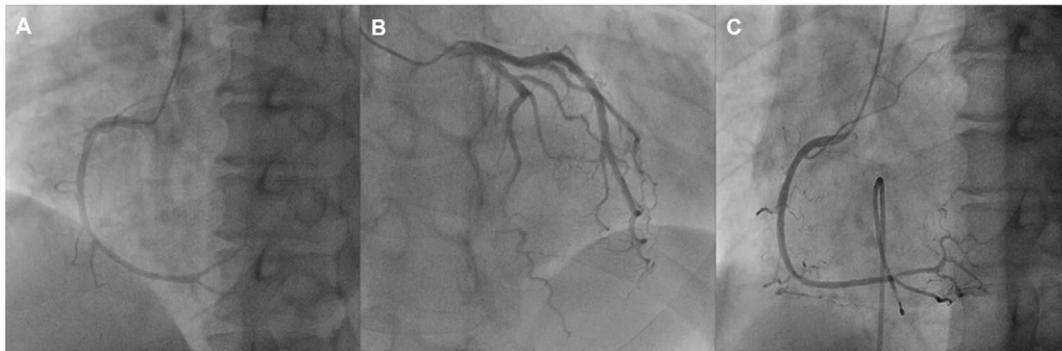


Fig. 2. Emergency coronary angiography shows no significant stenosis in the right coronary artery (RCA) in the right anterior oblique view (A and Supplementary Video 1) and left coronary artery in the left anterior oblique view with cranial angulation (B and Supplementary Video 2). Injection of 50 µg of acetylcholine into the RCA in an acetylcholine provocation test performed after tumor remission does not induce coronary artery spasm (C and Supplementary Video 4).

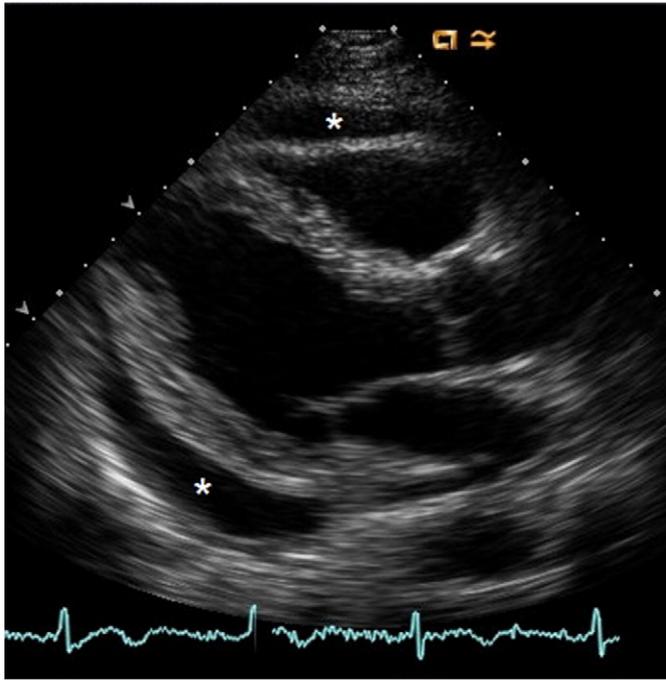


Fig. 3. In the parasternal long axis view, transthoracic echocardiography shows circumferential pericardial fluid retention (white asterisks).

compression myocardial injury by a bulky mass [5]. However, vasospastic angina due to PCL has not been previously reported.

The mechanisms proposed to underlie the substrate for susceptibility to coronary artery spasm (CAS) include endothelial dysfunction, hyper-reactivity of vascular smooth muscle cells, and other factors including autonomic imbalance [6]. Passive mechanical collapse was suggested to play a significant role in the pathogenesis of CAS. Adventitial abnormalities may also play some role in the pathogenesis of CAS. The adventitia is the site of sympathetic and vagal efferent nerve terminations and can also be the site of inflammatory infiltrations. Accordingly, excessive adventitial release of vasoconstrictor substances may cause CAS [7]. In our patient, lymphoma was present around the AV groove of the tricuspid valve and extended to the inferoposterior LV wall along the RCA. Reportedly, cardiac mechanoreceptors and chemoreceptors with vagal afferents are distributed in the inferoposterior LV wall [8]. Abnormalities in wall motion and ischemia in the inferoposterior LV wall can stimulate vagal tone [9]. In the present case, the lymphoma located around the RCA reached the inferoposterior LV wall, which may have precipitated adventitial inflammation of the RCA and induced autonomic imbalance. Negative results for the Ach provocation test performed after tumor remission suggested that coronary spastic angina (CSA) did not induce endothelial dysfunction.

These findings indicate that CSA was induced by impaired adventitia-dependent vascular function and an imbalance in the autonomic nervous system precipitated by PCL.

Diagnosis of PCL may be delayed because of various clinical presentations and sometimes requires invasive procedures. Diagnostic delay contributes to a poor prognosis, and in some cases, a diagnosis is not made until autopsy. Several diagnostic techniques can be used for PCL diagnosis; however, noninvasive techniques specific to PCL are limited. Reportedly, an increase in serum sIL2R levels can be an important signal of PCL [10]. However, this parameter was within normal limits in our patient. Although gallium scintigraphy and (18)F-fluorodeoxyglucose positron emission tomography are useful for diagnosis of PCL [11], these imaging techniques are expensive and institutions equipped with such systems are limited. In our patient, the lymphoma was located around the AV groove and encased the RCA without invasion, as observed on ECG-gated, contrast-enhanced MDCT. This phenomenon has been reported as the vessel floating sign, which is a specific characteristic of cardiac dominant diffuse large B-cell lymphoma [12]. These facts indicate that the coronary vessel floating sign on ECG-gated contrast-enhanced MDCT can be a noninvasive and specific finding for the diagnosis of cardiac lymphoma.

In conclusion, this case highlights that cardiac lymphoma can trigger syncope or sudden cardiac death due to VSA. The coronary vessel floating sign is useful for the early diagnosis of cardiac lymphoma.

Conflict of Interest

The authors report no relationships that could be construed as a conflict of interest.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.ijcard.2014.06.081>.

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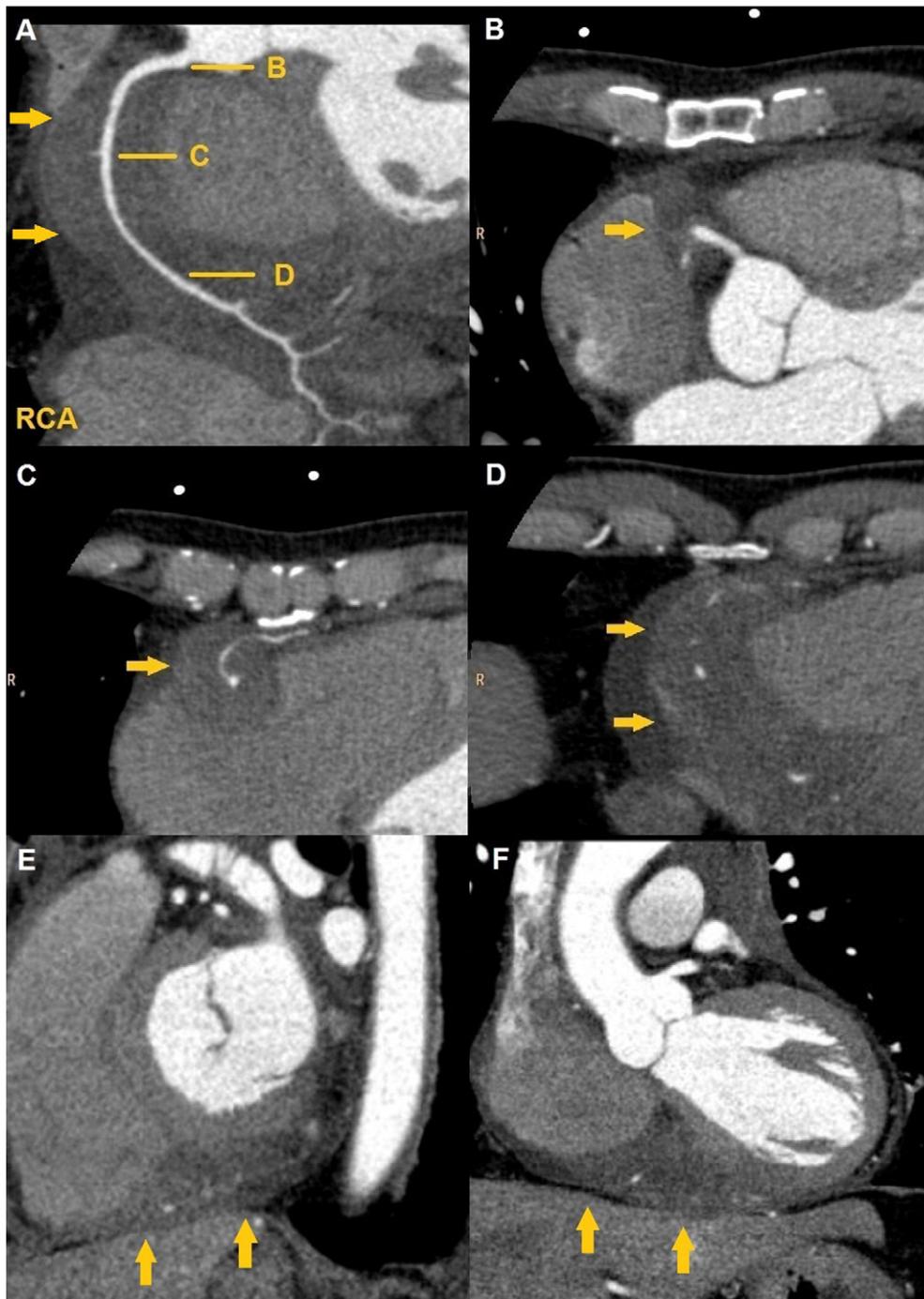


Fig. 4. A curved multiplanar reformatted image along the course of the right coronary artery (RCA) (A) and transaxial images (B–D) show a lymphoma located around the atrioventricular groove and encasing the RCA without arterial invasion or compression (coronary vessel floating sign). Oblique coronal images reveal a mass extending to the inferoposterior wall of the left ventricle along the RCA (E and F) (arrows).

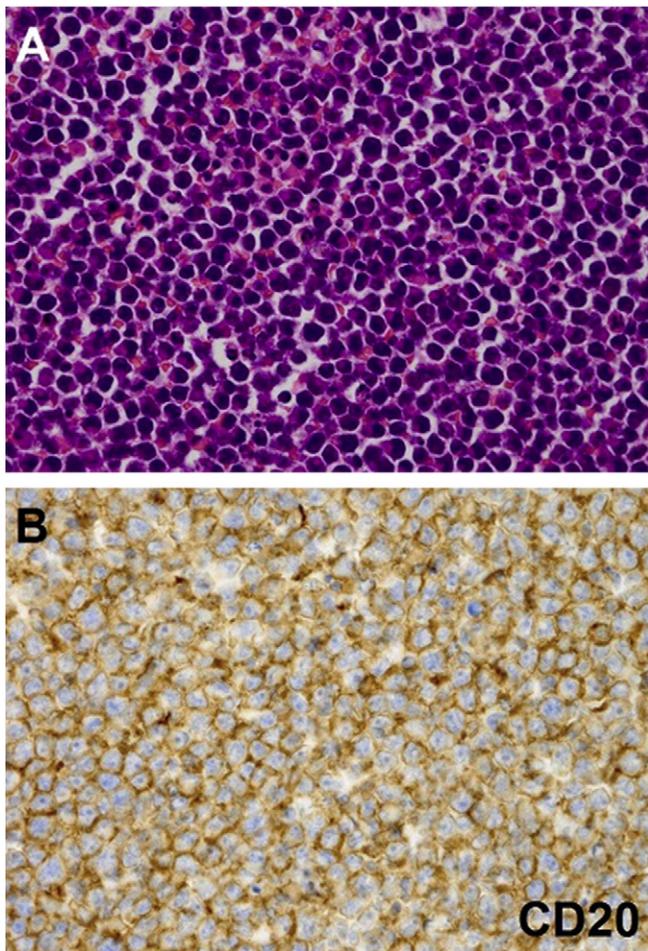


Fig. 5. Histopathology of the cell block section obtained from pericardial effusion. Large atypical lymphoma cells show prominent nucleoli (hematoxylin–eosin staining; original magnification, $\times 400$; A). Positive immunostaining for CD20 is evident on the cytoplasmic membranes of the tumor cells (original magnification, $\times 400$; B).

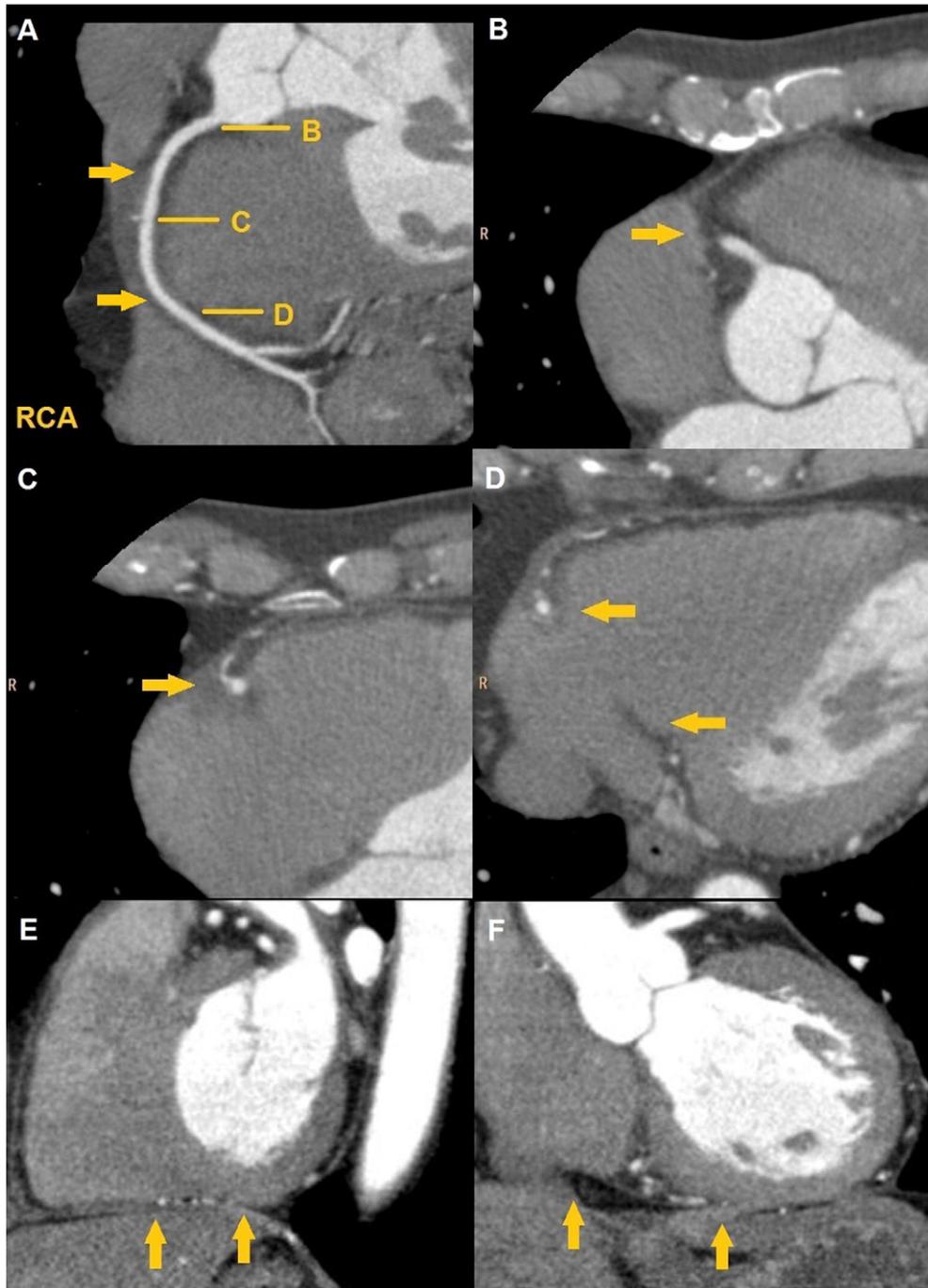


Fig. 6. Sixty four-slice coronary computed tomography angiography performed after 6 cycles of rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin, and prednisone therapy shows complete disappearance of the tumor (arrows).