ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Paradoxical Cerebral and Coronary Embolism in a Young Patient Due to Right Atrial Appendage Aneurysm: A Case Report

Sağ Atriyal Apendiks Anevrizmasına Bağlı Genç Bir Hastada Paradoksal Serebral ve Koroner Emboli: Bir Olgu Sunumu

ABSTRACT

A 32-year-old male patient was admitted to the hospital with an ischemic stroke. Transesophageal echocardiography revealed an echogenic structure consistent with a thrombus within the aneurysm of the right atrium, along with a patent foramen ovale (PFO) in the interatrial septum. Cardiac magnetic resonance imaging (MRI) confirmed the presence of a right atrial appendage aneurysm (RAAA) with thrombus formation. Coronary angiography demonstrated occlusion of the circumflex artery. Concurrently, the patient was diagnosed with antiphospholipid syndrome. Given the presence of a PFO, paradoxical embolism was postulated as the etiology for both the coronary and cerebral artery occlusions. Antithrombotic and anticoagulant therapy was initiated, and surgical intervention for the RAAA and PFO was recommended. However, the patient declined surgical treatment, and medical management was continued. The patient has been regularly followed for approximately two years without any complications.

Keywords: Acute coronary syndrome, acute ischemic stroke, right atrial appendage aneurysm

ÖZET

32 yaşında erkek hasta iskemik inme nedeniyle hastaneye kaldırıldı. Transözofageal ekokardiyografi, sağ atriyum anevrizması içinde trombüsle uyumlu ekojenik bir yapının ve interatriyal septum içinde foramen ovale'nin (PFO) varlığını gösterdi. Kardiyak MRI, trombüslü sağ atriyal apendiks anevrizmasının (RAAA) varlığını ortaya koydu. Koroner anjiyografi, sirkumfleks arterin tıkalı olduğunu gösterdi. Eş zamanlı olarak, antifosfolipid sendromu tanımlandı. PFO'nun varlığı göz önüne alındığında, paradoksal emboli, hem koroner hem de serebral arter tıkanıklığının etiyolojisi olarak varsayıldı. Antitrombotik ve antikoagülan tıbbi tedavi başlatıldı ve RAAA ve PFO için cerrahi müdahale önerildi. Ancak, hasta cerrahi tedaviyi reddetti ve bu nedenle tıbbi tedavisine devam edildi. Hasta yaklaşık iki yıldır düzenli ziyaretlerine gelmektedir ve herhangi bir sorun olmadan takip edilmektedir.

Anahtar Kelimeler: Akut koroner sendrom, akut iskemik inme, sağ atrial apendiks anevrizması

CASE REPORT
OLGU SUNUMU

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Received: August 11, 2024
Accepted: December 03, 2024

Cite this article as: Usalp S, Dereli Bulut SS, Çelebi F, Altuntaş E. Paradoxical Cerebral and Coronary Embolism in a Young Patient Due to Right Atrial Appendage Aneurysm: A Case Report. *Turk Kardiyol Dern Ars.* 2025;53(0):000-000.

DOI: 10.5543/tkda.2024.36737

Ischemic stroke (IS) is a relatively rare condition in young adults, with an incidence ranging from 7 to over 100 per 100,000 person-years, depending on the population studied.[1] Among the most common causes of IS in individuals under 50 years of age are atrial myxoma, intracardiac thrombus, dilated cardiomyopathy, nonbacterial thrombotic endocarditis, atrial septal defects, patent foramen ovale (PFO), and hematologic disorders predisposing to thrombosis.[1]

Acute coronary syndromes are also rarely observed in young patients, with underlying causes including genetic abnormalities, hyperlipidemias, coagulation disorders, and coronary artery anomalies. It is exceedingly uncommon for an individual to present with both acute coronary artery syndrome and acute IS concurrently. Such a presentation should prompt consideration of a systemic coagulation disorder or an intracardiac thrombus/embolism.

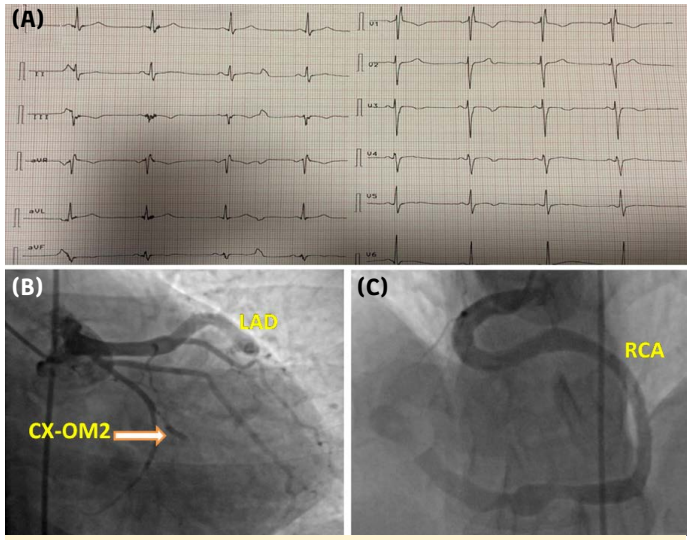

Figure 1. (A) Electrocardiogram obtained at the patient's initial hospital admission. (B) Coronary angiography image showing total occlusion of the left circumflex artery starting from its distal segment. (C) Coronary angiography image showing a severely ectatic right coronary artery.

In this article, we present an intriguing case of a 32-year-old male patient with positive antiphospholipid antibodies, diagnosed with both IS and acute coronary syndrome, along with a rare right atrial appendage aneurysm (RAAA) containing a thrombus.

Case Report

A 32-year-old male patient was admitted to the hospital with complaints of sudden-onset speech difficulty, confused speech, and amnesia, which began approximately 30 minutes prior to presentation. He had no known medical history, was a non-smoker, and had no history of drug or substance use. Upon admission, the patient was conscious, and his vital signs were within normal limits. There was no evidence of speech or motor aphasia/paraphasia. The absence of pathological findings during the initial neurological examination in the emergency department suggested that the occluded cerebral artery might have spontaneously recanalized.

Laboratory investigations revealed the following results: Troponin I: 0.056 µG/L (reference range: 0-0.014), Anti-beta-2 glycoprotein 1 immunoglobulin M (IgM): 36.06, (normal <20 U/mL), Anti-beta-2 glycoprotein 1 IgG: <2 U/mL (within normal range). Other laboratory findings were within normal limits.

Electrocardiography revealed sinus rhythm with an incomplete right bundle branch block and a heart rate of 51 beats per minute. T-wave inversions were observed in leads V3-V6 (Figure 1). A 24-hour Holter rhythm monitor showed no abnormalities.

Cranial diffusion magnetic resonance imaging demonstrated hyperintense signal changes on diffusion-weighted images and hypointensities on apparent diffusion coefficient (ADC) maps in the subcortical area at the level of the ventricle corpus, left cerebral hemisphere, and left posterior frontal lobe. These findings were consistent with acute cerebral infarction. Brain computed tomography (CT) and carotid-vertebral artery CT angiography findings were normal.

ABBREVIATIONS

ADC	Apparent diffusion coefficient
APS	Antiphospholipid syndrome
CT	Computed tomography
EULAR	European League Against Rheumatism
IS	Ischemic stroke
MRI	Magnetic resonance imaging
PFO	Patent foramen ovale
RAAA	Right atrial appendage aneurysm
TEE	Transesophageal echocardiography
TTE	Transthoracic echocardiography

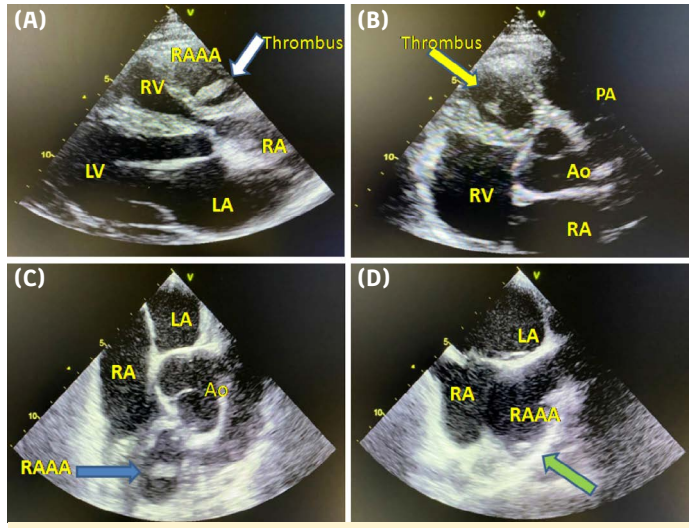

Figure 2. (A) Transthoracic echocardiography, longitudinal axis view: an aneurysmal structure with suspected thrombus is observed in the upper vicinity of the right ventricle (white arrow). (B) Transthoracic echocardiography, short axis view: an aneurysmal structure with suspected thrombus is observed between the right ventricle and right atrium (yellow arrow). (C) Transesophageal echocardiography mid-esophageal view: a mobile echogenic structure is observed within the aneurysmal formation, adjacent to the aorta and right ventricle (blue arrow). (D) Transesophageal echocardiography, bicaval view: a right atrial aneurysm is visualized with a suspicious thrombus (green arrow).

Transthoracic echocardiography (TTE) showed an ejection fraction of 60%, and a cystic structure with a mobile echogenic component was observed exerting pressure on the lateral wall of the right ventricle (Figure 2A-B, Video 1). Transesophageal echocardiography (TEE) revealed an aneurysmal formation adjacent to the right atrium, with an echogenic structure consistent with a thrombus and a PFO tunnel (Figure 2C-D, Videos 2–4). However, the right atrial appendage aneurysm could not be clearly visualized on TEE. Cardiac MRI was subsequently performed both to better evaluate the right atrial appendage and to rule out extracardiac masses. Treatment with acetylsalicylic acid (100 mg), and subcutaneous enoxaparin was initiated. A fourfold increase in troponin levels compared to baseline was noted. Coronary angiography demonstrated occlusion of the obtuse marginal branch of the circumflex artery and an ectatic

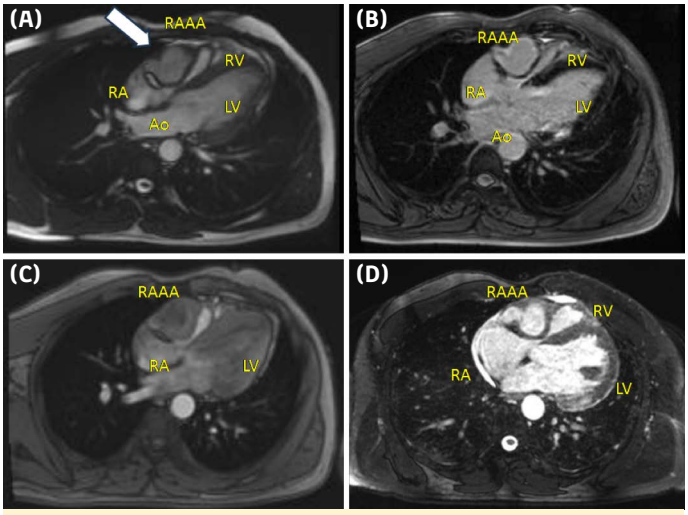

Figure 3. (A–D) Cardiac magnetic resonance imaging of the right atrial appendage aneurysm from various sequences (white arrow). The thrombus within the aneurysm is clearly visible.

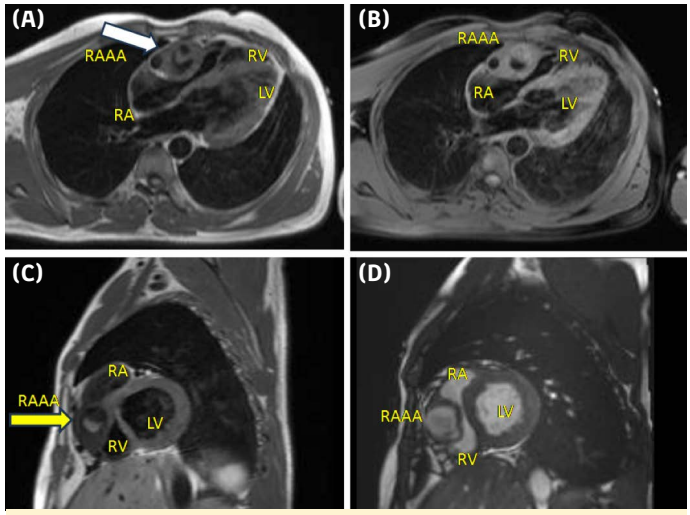

Figure 4. (A–D) Cardiac magnetic resonance images obtained from different segments show a thrombus embedded in the tissue of the right atrial appendage (white and yellow arrows).

right coronary artery (Figure 1B-C). As the obtuse marginal branch was non-dominant, had a small vessel diameter, and supplied a relatively limited territory, a decision was made to manage the patient with medical therapy.

Cardiac MRI confirmed the presence of a thrombus within a large RAAA (Figures 3, 4).

Discussion

To the best of our knowledge, this is the first and only reported case in the literature of a young male patient presenting with a RAAA containing thrombus, acute coronary syndrome, antiphospholipid syndrome (APS), and acute IS concurrently.

It is hypothesized that the thrombus formed in the RAAA embolized to the left atrium, and subsequently to the coronary and cerebral vessels, through the PFO. Additionally, the presence of anti-beta-2 glycoprotein 1 IgM antibodies likely contributed to an increased tendency toward arterial thrombosis.

The occurrence of IS and acute coronary syndrome in young patients is exceedingly rare.[2] TTE is typically the first imaging modality used to investigate cardiac etiologies. However, RAAA, usually located on the free wall of the right atrium, can be easily misidentified or overlooked on TTE. TEE is the preferred modality for evaluating RAAA, typically visualized in the mid-esophageal bicaval view by rotating the probe between 90° and 130°. Nevertheless, even with TEE, RAAA can be missed in up to 16% of cases.[3] Indeed, in our case, the RAAA could not be clearly visualized on TEE. Therefore, cardiac MRI was performed to better evaluate the RAAA. Studies conducted using TEE have found that RAAAs are approximately 12 times less common than left atrial aneurysms.[4] Compared to the left, RAAA often exhibit low-flow velocity spontaneous contrast echoes, and this slow flow predisposes to thrombus formation. Surgical resection is recommended for patients with thromboembolic events or large aneurysms, while regular follow-up is advised for asymptomatic patients.[5]

Beta-2 glycoprotein 1 plays a role in the etiopathogenesis of various conditions characterized by both arterial and venous thrombosis.[5] The presence of anti-beta-2 glycoprotein antibodies is one of the diagnostic criteria for APS.[5] These antibodies can induce platelet activation *in vivo*, thereby increasing the risk of thrombosis.[6] One study suggested that more than 20% of strokes occurring in individuals under the age of 45 are associated with APS.[6] Warfarin therapy is generally recommended for patients diagnosed with APS.[6]

B2 glycoprotein 1 is a molecule composed of amino acids synthesized by hepatocytes, endothelial cells, and trophoblast cells. By binding electrostatically to negatively charged phospholipids on the plasma membrane, it becomes a target for antiphospholipid antibodies.[5] *In vitro*, phospholipid antibodies that cause prolongation of coagulation tests involving phospholipids are referred to as "lupus anticoagulants."[5] Although these antibodies are called "anticoagulants" because they prolong coagulometric test results *in vitro*, they induce platelet activation *in vivo* and therefore increase the risk of thrombosis. For the diagnosis of APS, at least one of the beta-2 glycoprotein 1 antibodies or lupus anticoagulant antibodies must be positive in laboratory analyses, accompanied by clinical features such as thrombosis, recurrent fetal loss, or signs of low platelet count.[5,6] In our patient, anti-beta 2 glycoprotein IgM was positive, and he presented with arterial thrombosis.

The European League Against Rheumatism (EULAR) recommends targeting an international normalized ratio (INR) of 3 to 4 is APS patients with ischemic stroke.[6] In contrast, the American College of Chest Physicians recommends an INR target range of 2 to 3. Additionally, the initiation of antiplatelet therapy in combination with warfarin is advised for patients with antiphospholipid syndrome who experience arterial thrombosis for the first time.[7]

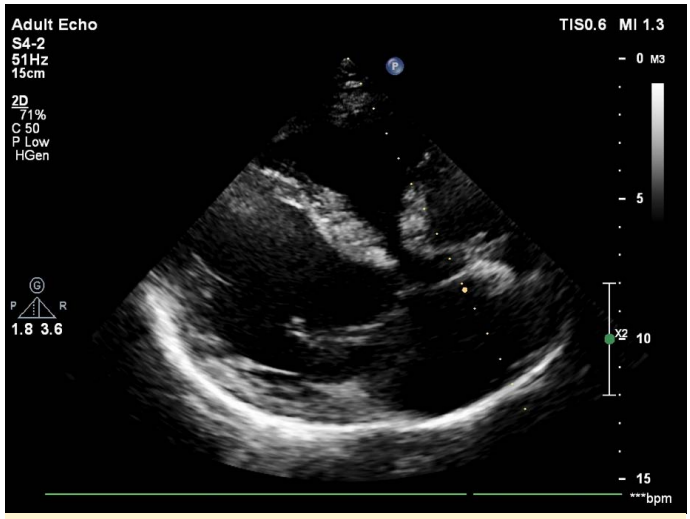

Figure 5. Transthoracic echocardiography performed four months after initiation of treatment shows no evidence of thrombus formation within the right atrial appendage aneurysm.

In our case, systemic embolism occurred due to a thrombus originating from the RAAA and passing through the PFO. There is a high incidence of coexisting prothrombotic conditions in young adults who experience stroke secondary to PFO. Recent studies have shown that newly developed devices, in combination with antiplatelet therapy, are superior to anticoagulant or antiplatelet therapy alone in preventing IS in patients with PFO.[6]

According to current knowledge, only a small number of RAAA cases have been reported in adults.[8,9] Most case reports in the literature involve pediatric patients. However, since most adult patients with RAAA are asymptomatic, they are typically managed conservatively. One case in the literature reported a patient presenting with simultaneous ischemic stroke, acute coronary syndrome, and pulmonary embolism, but without the presence of RAAA.[10] To date, there are no documented cases in the literature of RAAA causing both cerebrovascular accident and acute coronary syndrome, with associated thrombus formation and concurrent APS, as observed in our patient.

Our patient is currently being managed with a combination of acetylsalicylic acid and warfarin, as he declined invasive treatment. On the most recent transthoracic echocardiography performed four months after initiating treatment, no thrombus was detected within the RAAA (Figure 5). The patient has been attending regular follow-ups for approximately two years to monitor INR levels and has remained stable without any complications.

Conclusion

Ischemic stroke in young patients requires a thorough and comprehensive diagnostic evaluation. When conventional diagnostic methods are inconclusive, advanced diagnostic techniques should be employed.

Ethics Committee Approval: This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

Informed Consent: Written consent was obtained from the patient for the publication of this case report and associated personal information.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: Artificial intelligence assisted technologies were not used in the writing of this article.

Author Contributions: Concept – S.U.; Design – S.S.D.B.; Supervision – S.U.; Resource – F.Ç.; Materials – E.A.; Data Collection and/or Processing – F.Ç.; Analysis and/or Interpretation – S.S.D.B.; Literature Review – S.U.; Writing – S.U.; Critical Review – E.A.

Peer-review: Externally peer-reviewed.

Video 1. Transthoracic echocardiography showing a mobile thrombus within the right atrial appendage aneurysm.

Video 2–5. Transesophageal echocardiography recordings of the patient.

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