Episodic Central Nervous System Ischemia of Undetermined Cause: Relation to Occult Left Atrial Myxoma

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Abstract:
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Left atrial myxoma should be considered seriously in patients with unexplained cerebral dysfunction, particularly those in whom there are multiple recurrent cerebral vascular episodes, despite the absence of suggestive heart findings. Substantiating this observation are two such illustrative cases with embolic disease leading to neurological involvement who otherwise lacked cardiac symptomatology and did not exhibit auscultatory, roentgenological or electrocardiographical evidence of heart disease. The first patient died without antemortem recognition of the tumor and, in the second, the myxoma was removed after eventual identification by cardiac angiography and histological examination of embolic material. Thus, it is recommended that left atrial myxoma be definitely sought by heart catheterization with contrast study as a potentially curable cause of chronic nervous system disease with transient episodes of vascular insufficiency even in patients without cardiac manifestations.

ADDITIONAL KEY WORDS cerebrovascular disease heart catheterization cineangiography emboli tumor stroke

In the differential diagnosis of recurrent episodic cerebral disease, consideration of an embolic process is included as a diagnostic possibility. Cerebral embolism is nearly always associated with heart disease, and it is generally acknowledged that careful evaluation of cardiovascular history, auscultation, electrocardiogram and chest roentgenogram suffice in the evaluation of this etiology. The extent to which the search for a cardiac source of emboli should be carried out is the subject of interest in this report. Thus, reliance is placed upon detection of the murmurs of valvular dysfunction, arrhythmias, episodes of congestive failure, and related findings to incriminate the heart as a possible embolic source. However, it is the purpose of this report to emphasize that left atrial myxoma can be responsible for repeated emboli and “strokes” in the absence of any cardiac signs or symptoms. Two illustrative cases are presented with chronic central nervous system disorders and multiple episodic cerebral events in whom there were otherwise no suggestive cardiac findings. The underlying cause of neurological disease was left atrial myxoma which was either undetected during life or not appreciated for several months.

Case Reports
CASE 1
This 46-year-old female lawyer was admitted in August 1964 to the New York University Hospital with a right-sided seizure which became generalized. The history revealed that in February of 1963 she had been admitted to another hospital because of sudden left hemiplegia and left homonymous hemianopia; a short time later a right-sided motor deficit developed with a right lower quadrantic visual field defect. Also observed was a transient episode of swelling of her
Coronal section of cerebrum at the level of the caudate head demonstrating multiple areas of embolic infarction (arrows) (case 1).

Fingertips with some purplish discoloration and hyperesthesia. At that time, the electroencephalogram showed a right posterior quadrant abnormality which later cleared, the lumbar puncture was normal, and the right brachial angiogram showed normal right carotid and vertebral extracranial and intracranial vessels. There had been no cardiac symptoms and routine cardiac evaluation was negative. After discharge her motor deficits improved but she remained confused. She also complained of upper abdominal burning sensations and calf cramps. A syncopal episode precipitated a second outside hospital admission in May of 1963, during which an extensive evaluation was negative. There were two further admissions that year for syncope and right hemiplegia and aphasia. At a fifth admission in July 1964 her electroencephalogram showed a diffuse abnormality in the left temporal area; retrograde femoral cerebral angiography was normal, and diagnoses of a collagen disorder with vasculitis and a demyelinating disease were considered.

Physical examination revealed an aphasic middle-aged female, crying and agitated with spastic right hemiparesis. There were no murmurs, arrhythmias, or evidence of cardiovascular dysfunction, and the electrocardiogram was normal. After an extensive multiple-systems evaluation which was unrevealing, she was discharged with the suspected diagnosis of atypical disseminated lupus erythematosus. Subsequently, the patient was admitted to another hospital where she presented a management problem because of her marked aphasia, depression with hostility, and spastic quadripareis. She was treated with tranquilizers and, in July 1965, was transferred to the state hospital with the diagnosis of "chronic organic brain syndrome." The patient remained neurologically stable until she died in February 1966, a few days following an acute gastrointestinal hemorrhage and three years after her first cerebral episode.

Postmortem examination revealed a myxoma of the left atrium arising from the interatrial septal endocardium inferior to the obliterated foramen ovale; multiple cerebral infarctions (fig.
CENTRAL NERVOUS SYSTEM ISCHEMIA

FIGURE 3
Frame of pulmonary artery cineangiogram revealing filling defect in the posterior aspect of the left atrium and mitral ring during ventricular diastole (case 2).

1); old, multiple infarcts of the liver, spleen and kidneys; and terminal erosive gastritis with hemorrhage. The polypoid myxoma was 3.5 cm long by 3 cm wide, attached by a 2.5x2 cm base (fig. 2). In summary, this patient had eight hospital admissions to five different hospitals. Although the possibility of multiple emboli was considered, this diagnosis was dismissed since a source for emboli could not be ascertained on clinical examination or routine laboratory studies.

CASE 2 (SMC 376226)
This 53-year-old white right-handed male truck driver was referred to the Sacramento Medical Center in March 1969 for evaluation of episodic neurological dysfunction. There was a history of lightheadedness for the preceding three years, usually occurring while driving at high altitudes or during strenuous exertion. Two years prior to the current hospitalization, the patient experienced onset of pain, tingling and numbness of the left hand following prolonged use of an air compressor drill. He was admitted to another hospital where examination revealed an absent left radial pulse and a cool, pale hyperesthetic left hand. Cardiac evaluation, including electrocardiogram and chest x-ray, was normal. A polypoid mass measuring 2 by 1 by 0.9 cm was removed from the bifurcation of the left brachial artery. Postoperatively the pulse returned and he made a good functional recovery. The tissue removed from the artery was sent to another city for pathological examination but the results did not become available at that time.

In the intervening 20 months, the patient was in good health. One month before admission, while working in his yard, he had sudden onset of headache, lightheadedness, blurring of vision for distant objects and a numbness of the left side of his face and left extremities. All the symptoms subsided within one hour except for the residual left forearm numbness and a sensation of coldness in his left hand. At that time, an aortic arch angiogram revealed a 50% irregular stenosis of the right carotid bifurcation. A cervical sympathetic nerve block was performed and anticoagulation instituted. One week before admission, the patient had an attack of true vertigo with rotatory nystagmus and weakness of the lower limbs, followed shortly by four-limb distal paresthesias and left-sided hyperreflexia. He was given antihistamines and nicotinic acid. Although the vertigo disappeared, left upper extremity incoordination persisted, and he was transferred for the present admission for neurological evaluation.

At this time, examination revealed an absent left radial pulse and a normal nervous system. There was a grade one over six systolic murmur at the cardiac apex. Skull roentgenogram, radioactive brain scan, lumbar puncture, electroencephalogram and blood chemistries were normal. There
Excised left atrial myxoma consisting of a gelatinous mass (case 2).

was no fever or evidence of systemic illness. There were no abnormalities on electrocardiogram and cardiac roentgenograms. Although at this point cardiac examination did not reveal specific findings of an embolus from the heart, it was decided to carry out cardiac catheterization at the time of arch aortography to assess the possibility of a cardiac cause. While awaiting these studies, a search for the histological examination of the material removed from the brachial artery in 1968 was found to have revealed myxoma.

Right and left heart catheterization was then performed and cineangiography with injection into the main pulmonary artery showed an irregular filling defect on the posterior inferior aspect of the left atrium which prolapsed into the left ventricle during diastole (fig. 3). A selective retrograde left ventricular cineangiogram revealed minimal mitral regurgitation and a filling defect in the area of the atrioventricular annulus during early diastole. In addition, there was a variable transmural pressure gradient which averaged 3 mm Hg at end-diastole. The aortic arch angiogram showed only the previously described lesion at the right common carotid bifurcation. On March 18, 1970, a 3x2.5x2.5 cm friable myxoma was excised from the septum of the left atrium during cardiopulmonary bypass (fig. 4). The patient recovered without complications and has returned to a fully active and normal life.

In summary, this patient experienced multiple emboli from a small left atrial myxoma which did not induce symptoms relative to abnormal cardiac hemodynamic performance or specific findings on physical examination. Eventually, the presence of myxoma was recognized by tissue examination of embolic material and the site localized to the left atrium by cardiac catheterization; the tumor was successfully removed.

Discussion

In evaluating multiple episodes of cerebral dysfunction, the possibility of embolic phenomena is given careful consideration. Indeed, cerebral embolism is becoming increasingly recognized as the cause of cerebral infarction. The heart is the most common source of such emboli, particularly in the presence of mitral stenosis, atrial fibrillation, myocardial infarction with mural thrombus, infectious or marantic endocarditis, advanced cardiomyopathy, valvular aortic stenosis, prostatic heart valves, and cardiac tumor. Pulmonary disease with emboli via pulmonary veins, extracerebral vascular disease of the aortic arch including ulcerated and atherosclerotic lesions, and paradoxical embolism from the deep systemic venous system via an intracardiac or great vessel communication are extracardiac and less common sites.

In a necropsy series, Vost, Wolochow and Howell found that 54% of 340 patients with heart disease had cerebral infarctions compared to 12% of 100 patients without known heart disease, although infarction is not necessarily equated with embolism in this study. Except for the 90% incidence in bacterial endocarditis, in their series the incidence of infarction was essentially the same in the various types of heart disease which give rise to emboli. Viewing the problem from the central nervous system vantage point, two sets of authors were impressed by the high incidence of etiological cardiac disease in reviewing ischemic accidents in the internal carotid artery distribution. Thus, in an antemortem study of 122 patients with the arterial lesion thought responsible for cerebral infarction in either the internal carotid artery or the middle cerebral artery, L'Hermitte et al. found 20 cases with cardiac embolic origin.

Heart myxomas are reported in 0.025% of unselected autopsy material, mainly in middle-aged adults; 75% occur in the left atrium. The natural history of this tumor is quite variable. Thus, it may masquerade as primary mitral valve disease, traditionally as mitral stenosis, and lead to episodic symptoms.
of pulmonary venous hypertension with pulmonary congestion, cause syncope or sudden death, appear to be a diffuse systemic disease, simulate bacterial endocarditis, or be entirely free of symptoms.9-18 Central nervous system manifestations secondary to emboli are often the major and only clinical feature of the myxoma.14, 15 The embolic phenomena are due to either portions of this friable tumor breaking free or blood clot or fibrin material dislodging from the tumor surface.16 Thus, the fundamental cause of the embolus is recognized pathologically only when the removed embolus is true tumor material. Also, aside from causing infarction, on occasion myxoma tumor emboli have been reported to produce mycotic-like cerebral aneurysms.17 Unless the embolus is surgically accessible and subjected to histological evaluation,18, 19 these patients usually continue to have puzzling neurological and systemic symptoms.10, 14, 20, 21

The patients described in the present report were admitted to the hospital on numerous occasions and, despite repeated examinations by many physicians, the basic nature of this curable illness was not appreciated. Thus, from these observations and review of the literature it is pointed out that left atrial myxomas often are not associated with cardiac symptoms and definitive physical findings, even in the presence of multiple embolic events. In addition, as in our patients, chest roentgenograms and electrocardiography may not be helpful. It would appear that in such cases the myxoma is either too small or is so situated that it does not cause sufficient alterations of cardiac dynamics.

In conclusion, it is recommended that when faced with the problem of repetitive episodic cerebral disease, where emboli are considered a serious possibility, cardiac catheterization be carried out with left atrial visualization from pulmonary artery injection despite negative history, and physical and routine laboratory examination for cardiac disease. The risks inherent in right heart catheterization are minimal22 and appear justified in the search for this possible “silent” cardiac embolic source. It is emphasized, however, that transseptal left atrial catheterization should not be performed because of the risk of dislodging a left atrial mass or of wedging the mass into the mitral valve.28 Only with further information obtained by cardiac catheterization and cineangiography will a more accurate knowledge be achieved of the true incidence of left atrial myxoma causing embolic cerebral infarction without other suggestive cardiac findings.

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References
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