



Case #112

NAME Educational Activities Committee

Case provided by:

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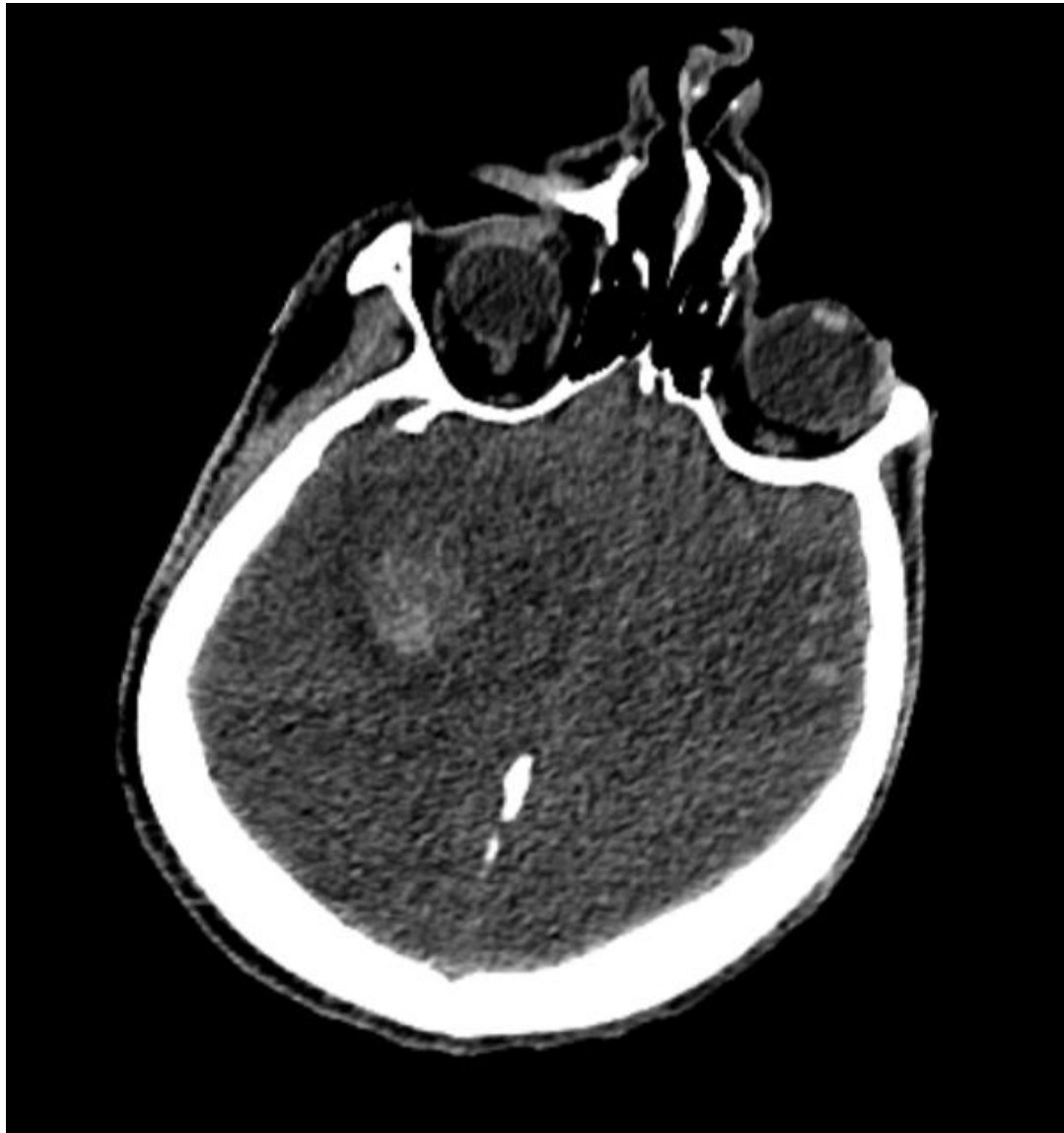
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Oklahoma Office of the Chief Medical Examiner

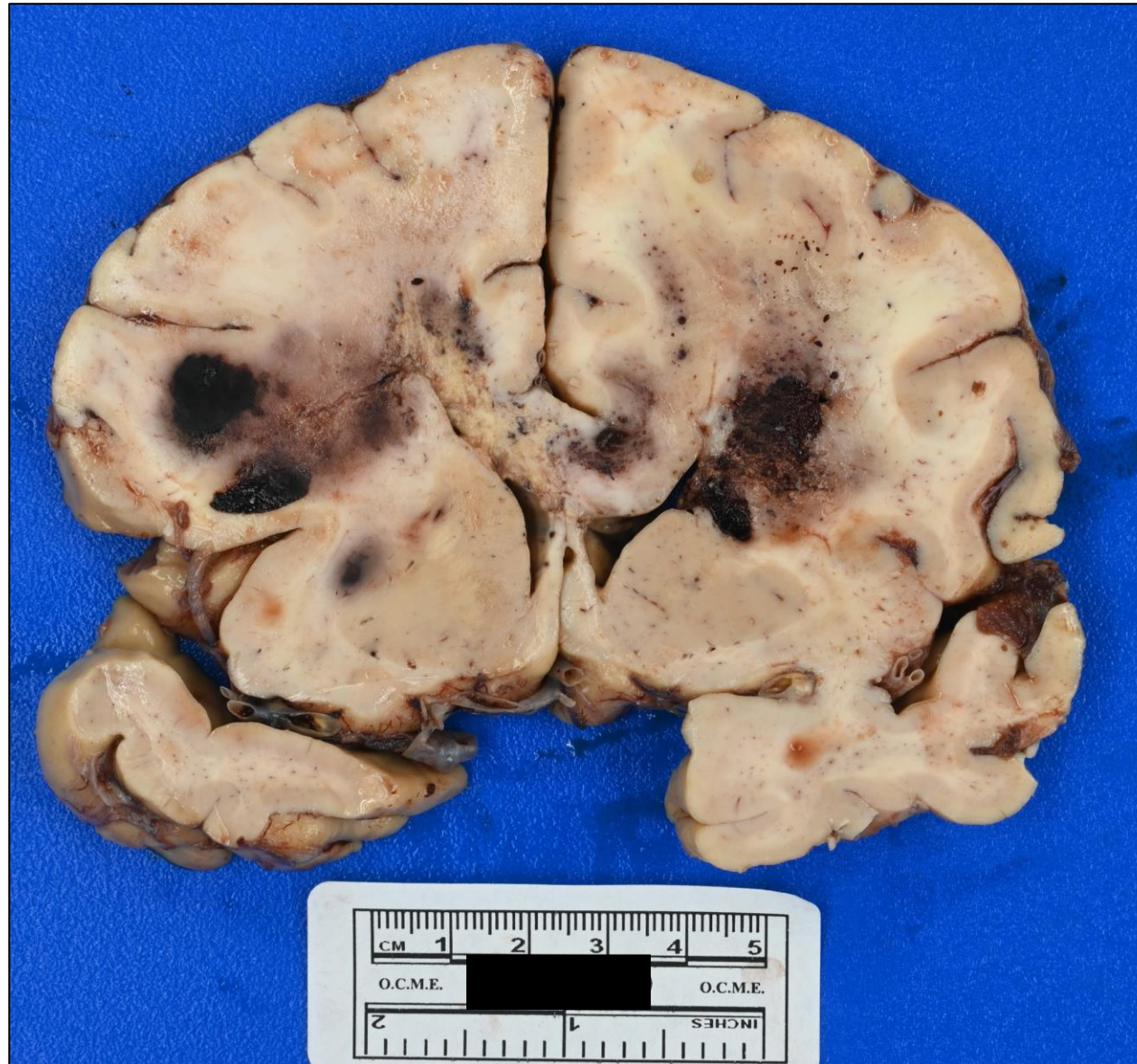
Oklahoma City, OK



Postmortem Head CT (Axial and Coronal)



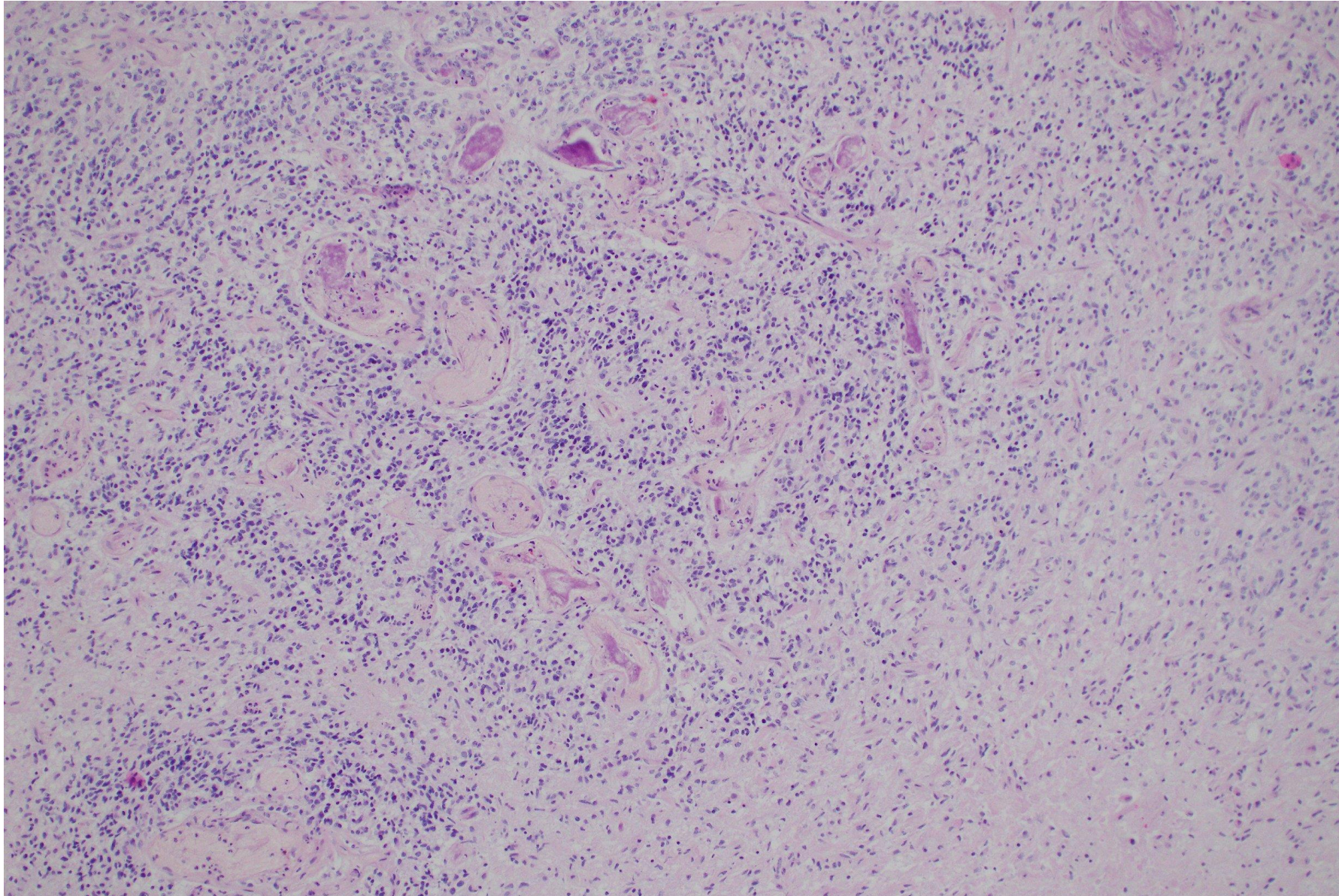
Neuropathologic Exam Findings:



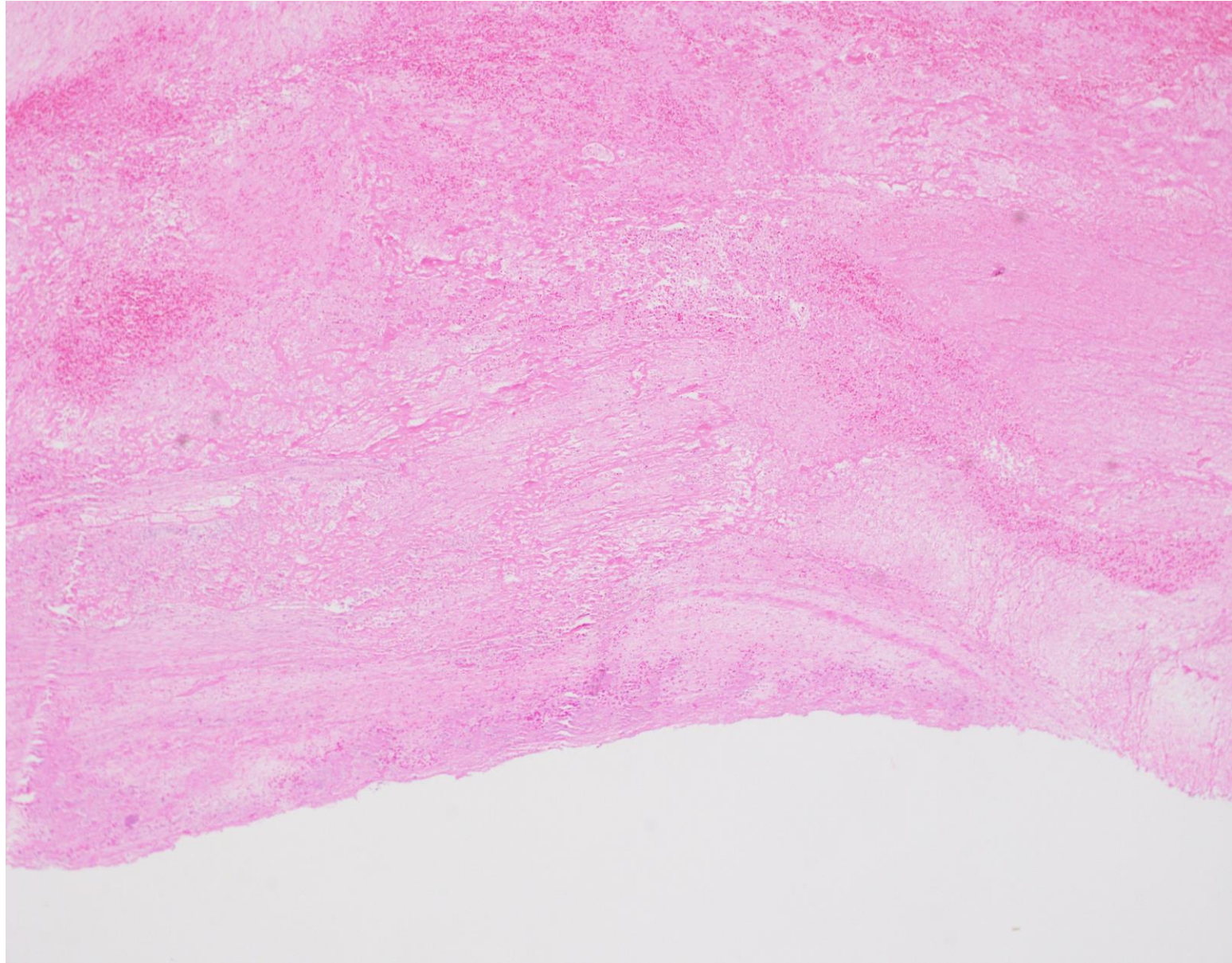
Autopsy Findings:



Microscopic Findings (Brain):



Microscopic Findings (Heart):



1. A 70-year-old male was found deceased at his residence with no recent medical intervention or documented medical history due to his religious beliefs. He was bed-ridden and underweight. A postmortem computed tomography (CT) scan revealed multifocal intraparenchymal hemorrhages within the bilateral cerebral hemispheres. Subsequent autopsy revealed atherosclerotic and hypertensive cardiovascular disease, and a large, organizing, mural thrombus occupying the left ventricle of the heart.

What is the most likely explanation for the observed cardiac and cerebral findings in this case?

- Septic emboli secondary to endocarditis
- Cardiac myxoma with embolization to the brain
- Intracranial aneurysm with hemorrhage and thrombus formation
- Cerebral amyloid angiopathy with associated hemorrhage
- Hypercoagulability due to malignancy-related thromboembolism

Answer.....

C. Hypercoagulability due to malignancy-related thromboembolism

(CORRECT ANSWER, 28.76% of responses)

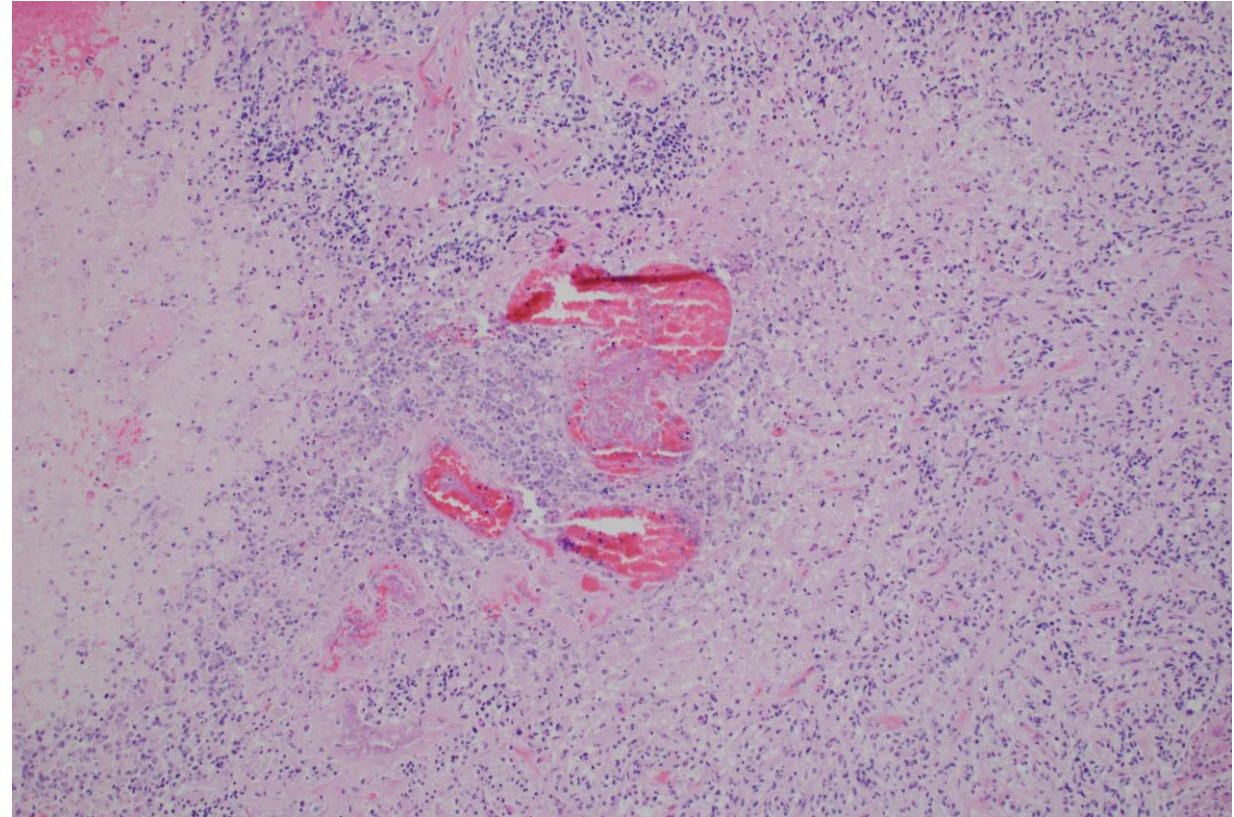
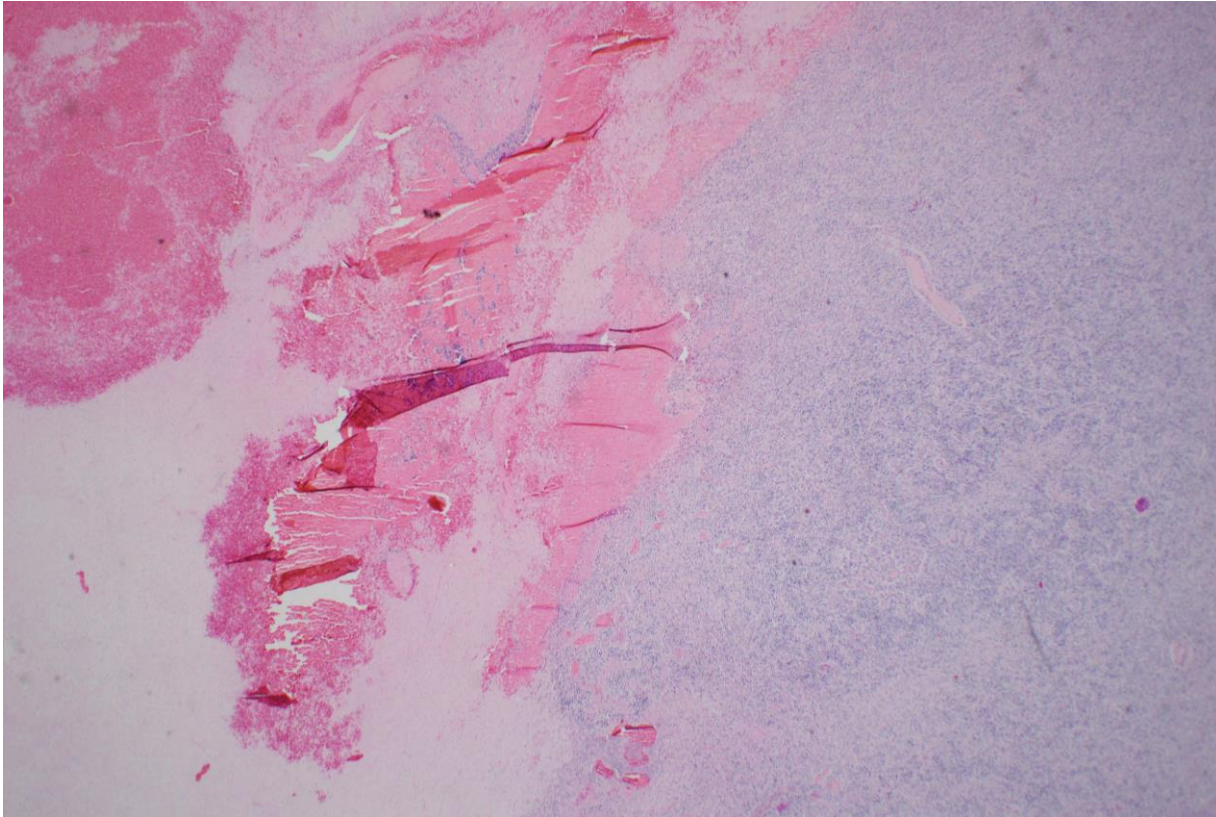
The case presented involves a complex interplay of systemic findings, which, upon detailed examination, reveal an underlying malignancy. The multifocal intraparenchymal hemorrhages observed on postmortem CT scan and the large organizing mural thrombus noted at autopsy raised suspicions of a prothrombotic state. Further microscopic examination of the brain revealed the presence of multifocal high-grade glioma involving the cerebrum and brainstem.

High-grade gliomas are known to increase the risk of thromboembolic events due to the prothrombotic state they induce. This hypercoagulable state results from the release of procoagulant substances by the tumor cells, increased tissue factor expression, and the production of inflammatory cytokines. The etiology of thrombosis is multifactorial and includes a hypercoagulable state and immobility due to neurologic deficits. The large thrombus in the left ventricle is likely a direct consequence of this hypercoagulable state, exacerbated by the underlying heart disease.

Additionally, the multifocal hemorrhagic lesions in the brain align with the aggressive nature of gliomas, which often hemorrhage due to their abnormal and fragile vasculature.

This case emphasizes the importance of considering malignancy as a significant risk factor for thromboembolism and sudden death. Understanding the mechanisms behind neoplasia-induced hypercoagulability is crucial for forensic pathologists when evaluating unexpected deaths with complex presentations.

Additional Histology of Brain Lesions



Other responses:

A. Septic emboli secondary to endocarditis (25.44% of responses)

Septic emboli, in the setting of endocarditis, typically originate on one of the four heart valves due to an underlying bacterial infection. The pathophysiologic process involves the septic embolus breaking off the heart valve, traveling via the circulatory system to the brain, and occluding blood vessels leading to ischemic and hemorrhagic damage. While septic emboli may cause multifocal intraparenchymal hemorrhages, the ultimate cause for intraparenchymal hemorrhages in this case involved a high-grade glioma.

Additionally, the most common cause of infective endocarditis is *Staphylococcus aureus* due to intravenous drug abuse. This decedent did not have a past medical history involving illicit intravenous substance abuse.

B. Intracranial aneurysm with hemorrhage and thrombus formation (6.86% of responses)

Intracranial aneurysms are luminal dilatations that occur along weak points of the arterial vasculature within the brain. A majority of cerebral aneurysms are acquired lesions that are associated with hypertension, smoking, alcohol abuse, and atherosclerosis. There is also a genetic component associated with an increased rate of frequency involving certain conditions, such as: autosomal dominant polycystic kidney disease (ADPKD), fibromuscular dysplasia, Ehlers-Danlos syndrome, and tuberous sclerosis.

While an intracranial aneurysm is associated with intraparenchymal hemorrhages, the associated thrombus formation would most likely occur downstream to where the aneurysmal event transpired. The thromboemboli would not be able to travel backwards to the left ventricle after forming in the brain. The thrombus would instead progress downstream through the arterial system and obstruct smaller blood vessels.

D. Cardiac myxoma with embolization to the brain

(19.91% of responses)

Cardiac myxomas are the most common primary cardiac tumors in adults occurring most often in the left atrium. They are also classically associated with Carney Complex. Systemic embolization occurs in approximately 50% of patients with cardiac myxomas, frequently to the cerebral and renal vasculature. Cardiac myxoma embolization to the brain can result in ischemic and hemorrhagic infarcts.

However, there was no myxomatous tumor identified at autopsy for this decedent. A large, mural, thrombus was found occupying the entire left ventricular space. There was no tan-white, gelatinous tumor found in the left atrium, mitral valve, or left ventricle.

E. Cerebral amyloid angiopathy with associated hemorrhage

(19.03% of responses)

Cerebral amyloid angiopathy (CAA) is a vascular disorder characterized by the deposition of beta-amyloid within the walls of small to medium blood vessels inside the brain. The accumulation of beta-amyloid proteins in the vessel walls results in overall structural fragility leading to lobar intracerebral hemorrhages. CAA is classically characterized by pink, amorphous material that can be examined microscopically with a Congo red special stain or beta-amyloid immunostaining.

CAA most often causes lobar hemorrhages associated with the peripheral cortical ribbon. The intraparenchymal hemorrhages found in this case were widely distributed throughout the superficial and deep aspects of the bilateral cerebral hemispheres, which is not consistent with CAA.

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