Case #116

NAME Educational Activities Committee

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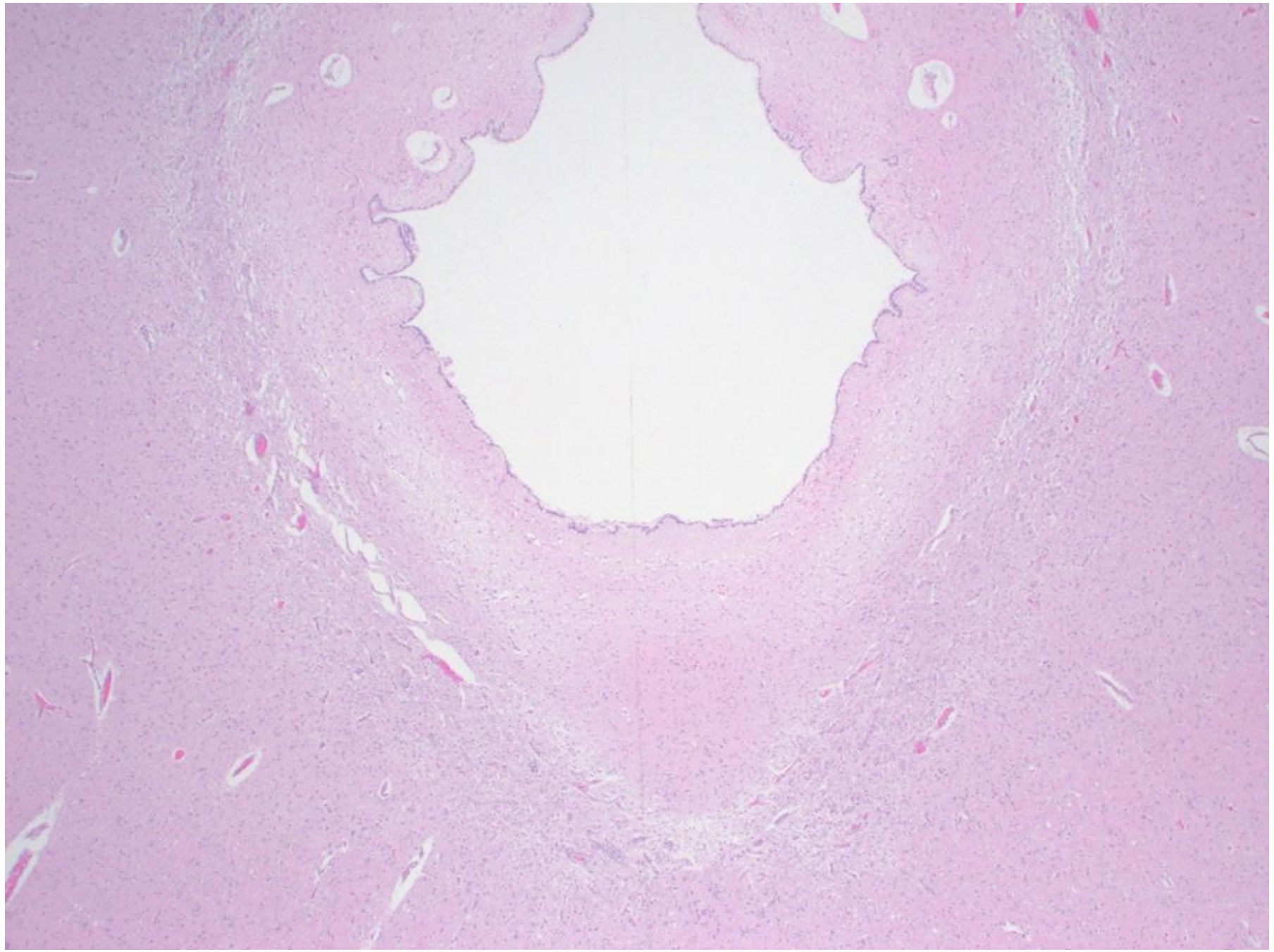

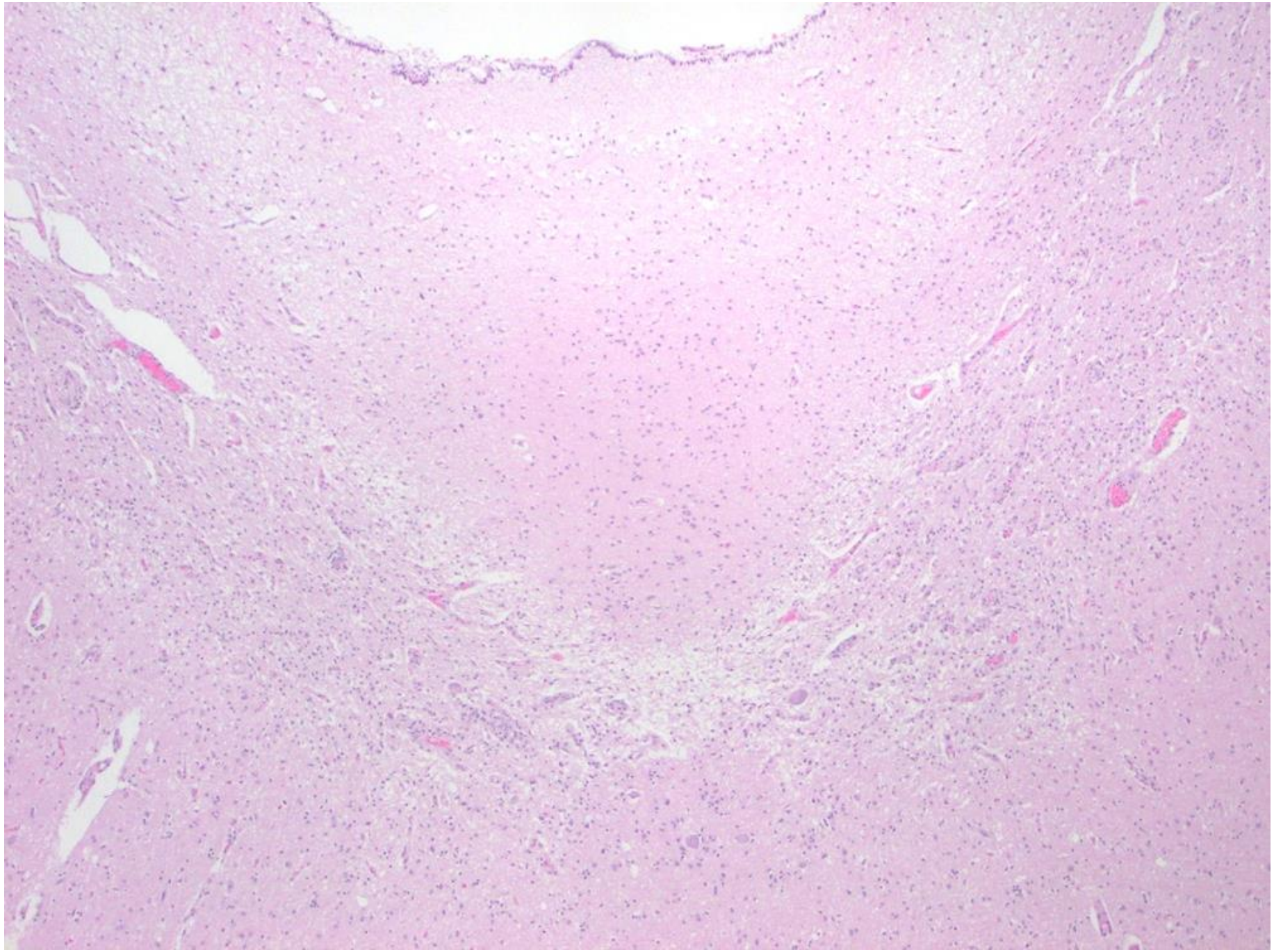

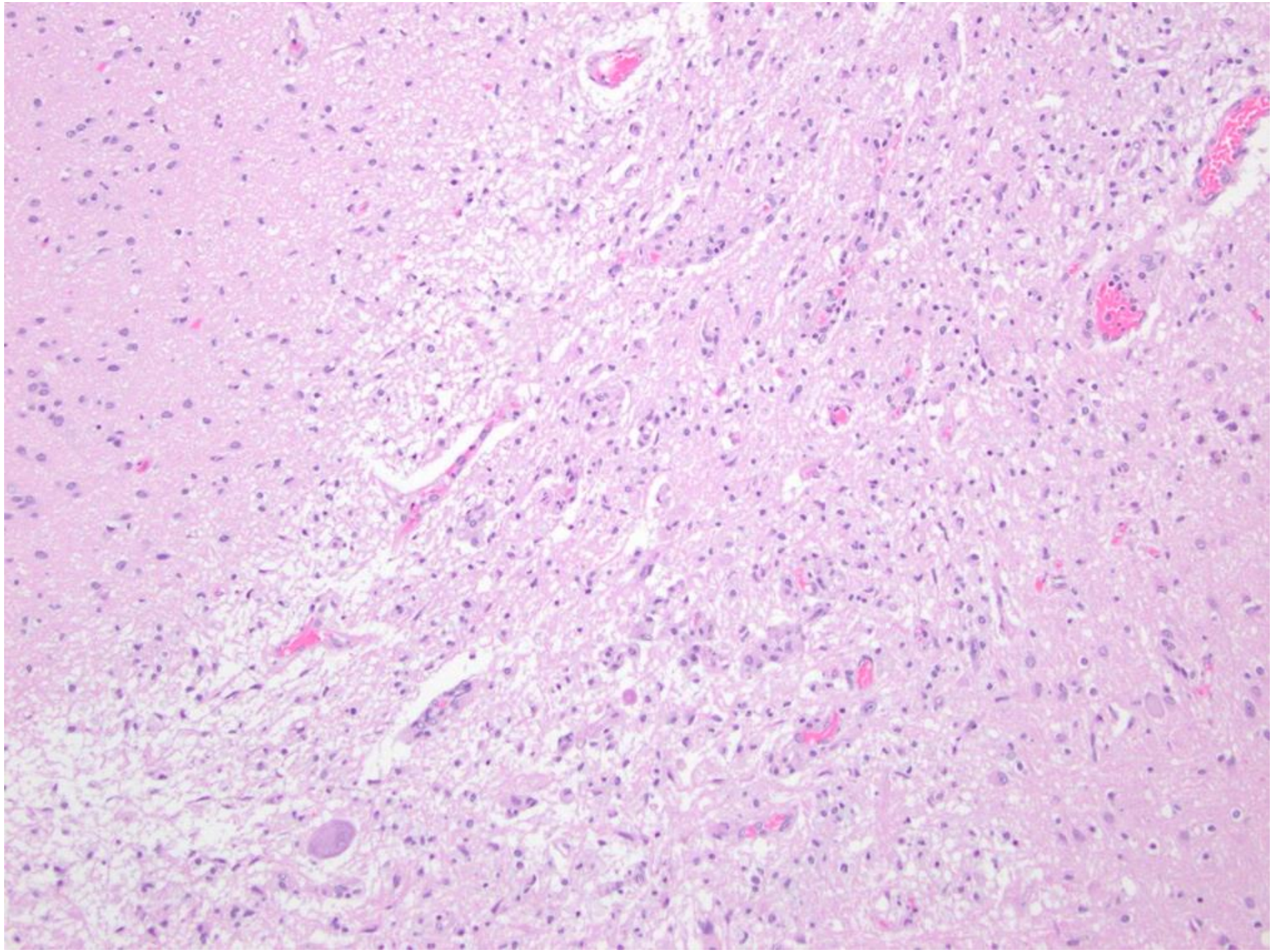

1. A 25-year-old male decedent is examined after a two-month history of poor health. The first month was marked by severe gastrointestinal illness. The second was notable for somnolence and a prolonged hospitalization complicated by recurrent deep vein thromboses and fatal saddle pulmonary embolism. Additional past medical history includes morbid obesity (BMI 50kg/m2).

What is the most likely source of the microscopic lesion depicted?

- ◯ Thromboembolic event
- ◯ Transient global ischemia
- ◯ Inborn error of metabolism
- ◯ Nutritional deficiency
- ◯ Infectious organism

Answer...

D. Nutritional Deficiency (specifically Thiamine/Vitamin B1)

(CORRECT ANSWER, 18.27% of responses)

The microscopic lesion shows the periaqueductal gray matter of the midbrain with a horseshoe-shaped, near circumferential ring of endothelial hypertrophy, neuropil vacuolation, focal neuronal loss, and hemosiderin laden macrophages. Similar lesions were identified in in the medial thalamus, and bilateral mammillary bodies. The periaqueductal/periventricular lesions showed a rim of subependymal sparing. The findings were consistent with a neuropathologic diagnosis of Wernicke's Encephalopathy.

Wernicke's encephalopathy is one the neurologic manifestation of Thiamine/Vitamin B1 deficiency (the other being dry/wet beriberi). The classic association is chronic alcohol use disorder, but it can be associated with a variety of gastrointestinal disorders that reduce intake and/or intestinal absorption: hyperemesis gravidarum, gastric malignancy, AIDS, gastric bypass, or prolonged periods of emesis. Rare cases of total parenteral nutrition as the cause have also been described. The classic clinical triad is that of gait instability, oculomotor abnormalities, and altered mental status. It may co-occur with Korsakoff psychosis, with patients showing retrograde and anterograde amnesia, and confabulation.

Neuropathologically, the gross and microscopic pathology evolve over time. Gross lesions appear as brown in color, and may show petechial hemorrhage, particularly in tissues immediately adjacent to the third ventricle and cerebral aqueduct. Microscopically, the lesions evolve acutely from edematous lesions with loss of myelinated fibers and erythrocyte extravasation, to chronic lesions with gliosis, spongiosis, and loss of myelinated fibers. In the subacute phase, reactive capillary endothelial hyperplasia may be prominent, with variable perivascular inflammation composed of macrophages. Hemosiderin laden macrophages and reactive astrocytes may be seen in late subacute to chronic lesions. Variable neuronal loss may also be evident.

Wernicke’s pathology is classically described as involving the mammillary bodies, but lesions are also often seen in other regions of the medial hypothalamus, medial thalamic nuclei, tegmentum of the 3rd ventricle, and periaqueductal gray matter of the midbrain. The periventricular/periaqueductal lesions typically show a rim of spared subependymal parenchyma, as is seen in this case.

Other Answers...

A. Thromboembolic event (16.10% of responses)

Though subacute ischemic events may show a similar microscopic appearance to that seen in the provided image, the anatomic site provided does not have typically have a sole arterial supply, making a thromboembolic event (which would need to be bilateral and symmetric) less likely. A very rare anatomic variant dubbed the Artery of Percheron may be considered whereby a single trunk arising from the superior cerebral artery supplies the bilateral paramedian thalamus rather than each side receiving individual arteries from their ipsilateral superior cerebral arteries. Such variants may be present with bilateral paramedian thalamic infarcts with or without rostral midbrain involvement. Additionally, more diffuse neuronal loss would be expected in a thromboembolic event.

B. Transient global ischemia (15.17% of responses)

Transient global ischemic changes may be profound and diffusely identified throughout the neuraxis. In severe cases complete destruction of neuroglial tissue may be evident. Sites of selective vulnerability include the CA1 region of the hippocampus, reticular neurons of the thalamus, and the Purkinje cell layer of the cerebellum, none of which are shown in this case.

C. Inborn error of metabolism (5.88% of responses)

Leigh syndrome/subacute necrotizing encephalopathy is a progressive neurodegenerative disorder secondary to defects in oxidative metabolism in mitochondria that may be secondary to nuclear and mitochondrial DNA defects. This results in a widely variable inheritance pattern, including autosomal recessive, X-linked, and mitochondrial. Disease onset is typically in infancy or early childhood. Neuropathologically it shows microscopic lesions similar to those seen in Wernicke's Encephalopathy, with particular predilection for the basal ganglia, brainstem, and diencephalic structures with notable sparing of the mamillary bodies. These lesions are bilateral.

E. Infectious organism (44.58% of responses)

The provided image does not demonstrate the presence of an acute neutrophilic or lymphocytic infiltrate, vasculitis, abscess, viral cytopathic effect, or infectious organisms.

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