PATHOLOGY FAQ

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TABLE OF CONTENTS

FOREWORD

The main objective of this book is to guide the readers on the important facts in pathology. These facts encompass the knowledge of general and systemic pathology. The book covers the overall human anatomy systems based on carefully selected cases encountered during our clinical practice. The aim is to present these salient points in a clear and concise manner that benefits students. High-quality pictures with coloured arrows have been used to highlight the vital pathological changes essential for diagnosis. This book will also guide readers on how to describe individual pathological features for each case.

Pathology FAQ contains case scenarios accompanied by relevant common questions, whether in preclinical tutorials or during clinical ward rounds. The answers to the question are complemented by explanatory insights.

The question and answer approach (Q&A) has been proven to facilitate the teaching and learning process in the medical curriculum. It presents a systematic method to help medical undergraduates to master knowledge in an easy manner and within a short time. Through these Q&As, we wish to provide a tool for student to assess themselves whether what has been learnt has been understood and applicable. At the same time, we are hopeful that this book will raise more questions to be answered and ultimately generate further interest in pathology.

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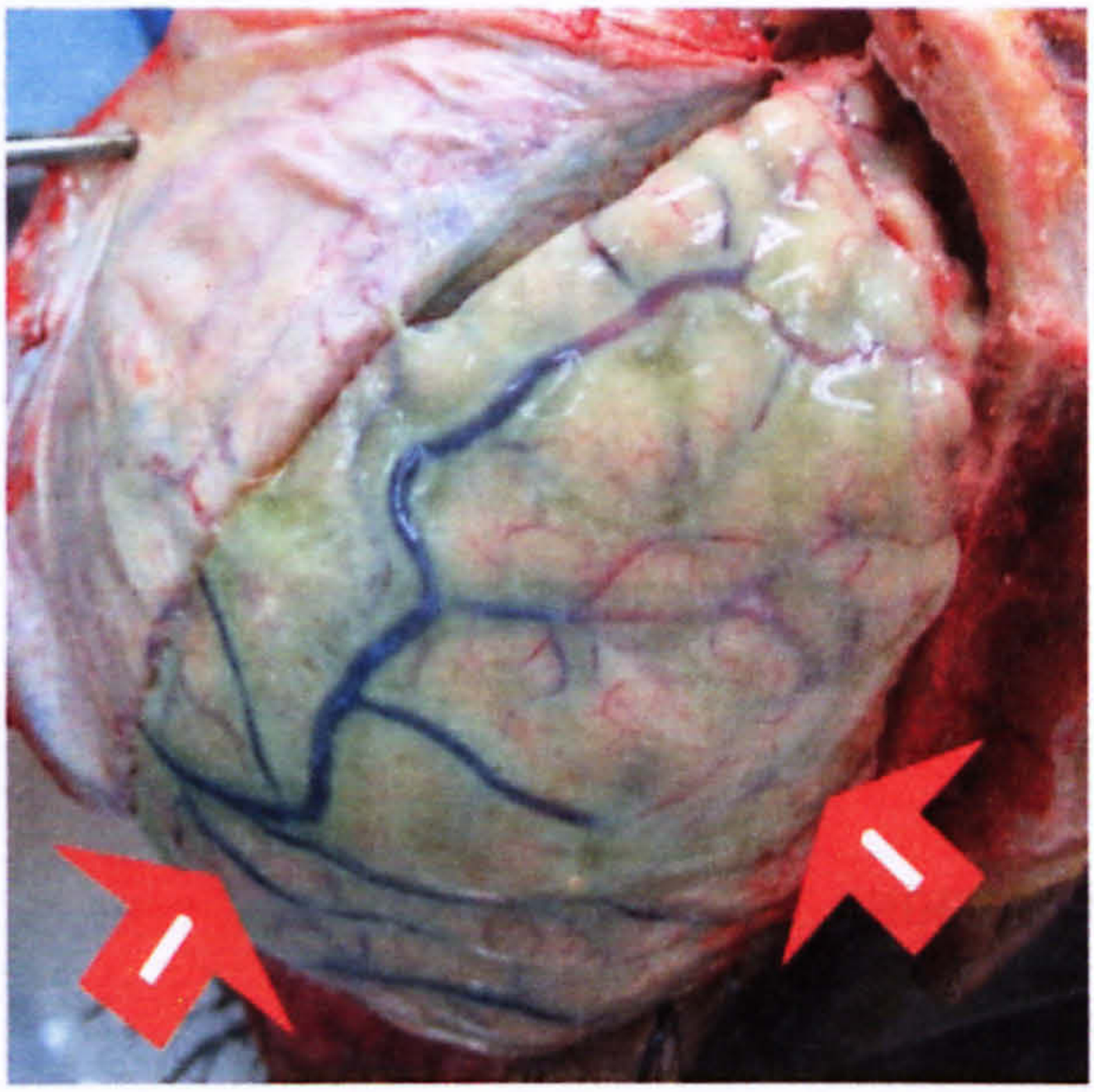
ZAINAL ABIDIN IBRAHIM

CHAPTER 1

CENTRAL NERVOUS SYSTEM

CASE 1: CNS INFECTION



Red arrow: The meninges

This picture is courtesy of Dr Siew Sheue Feng

CASE SCENARIO

A 20-year-old man presented with a 1-day history of increasing headache, photophobia and high fever. Physical examination showed presence of neck stiffness with clouding of consciousness. A lumbar puncture showed cloudy cerebrospinal fluid (CSF). His CSF result was as follows: leucocytes: 450 wbc/mm^3 (90% neutrophils), 5 red blood cells/mm3, protein 9g/L, glucose 0.5 mmol/L (blood glucose 6.0 mmol/L). Gram stain of his CSF showed intracellular Gram-negative diplococci. Study the picture of the meninges.

QUESTIONS

1. **Describe the macroscopic pathology seen.**

   The brain is extensively covered by meninges with yellowish

purulent exudates obscuring the sulci. There are visible signs of multiple engorged blood vessels.

2. Interpret his CSF investigation result.

The CSF showed leukocytosis consists predominantly of neutrophils. The increased protein and reduced glucose levels are features of bacterial meningitis. This is confirmed by the Gram stain study of the CSF which detected intracellular Gram-negative diplococci.

3. State the diagnosis.

Bacterial meningitis

4. State the most likely cause.

The aetiological agents of meningitis vary with age groups. In neonates: *E.coli* and group B streptococci. In infants and children: *S. pneumonia* and *H.influenzae* (which is now reduced with immunization). Adolescent and young adults: *N. meningitides.* Elderly: *S. pneumonia* and *L. monocytogenes.* CSF result and Gram stain showed that the most likely pathogen is *N.meningitidis. N.meningitidis* is Gram-negative intracellular diplococci.

5. Describe the possible routes on how microorganism can reach the nervous system.

a. Haematogenous route: This is the commonest route of entry. Microorganism usually enters arterial circulation from distant foci of infection. However, retrograde venous route can occur through anastomoses with veins of the face.

b. Direct implantation: Commonly through trauma or in association with congenital anomaly such as neural tube defects.

c. Local extension: From infected adjacent anatomical structures such as air sinuses or infected tooth.

d. Ascending infection via peripheral nervous system: Transport along peripheral nerves occurs with certain virus infection such as rabies and herpes zoster.

6. List the complications that can occur in this patient.

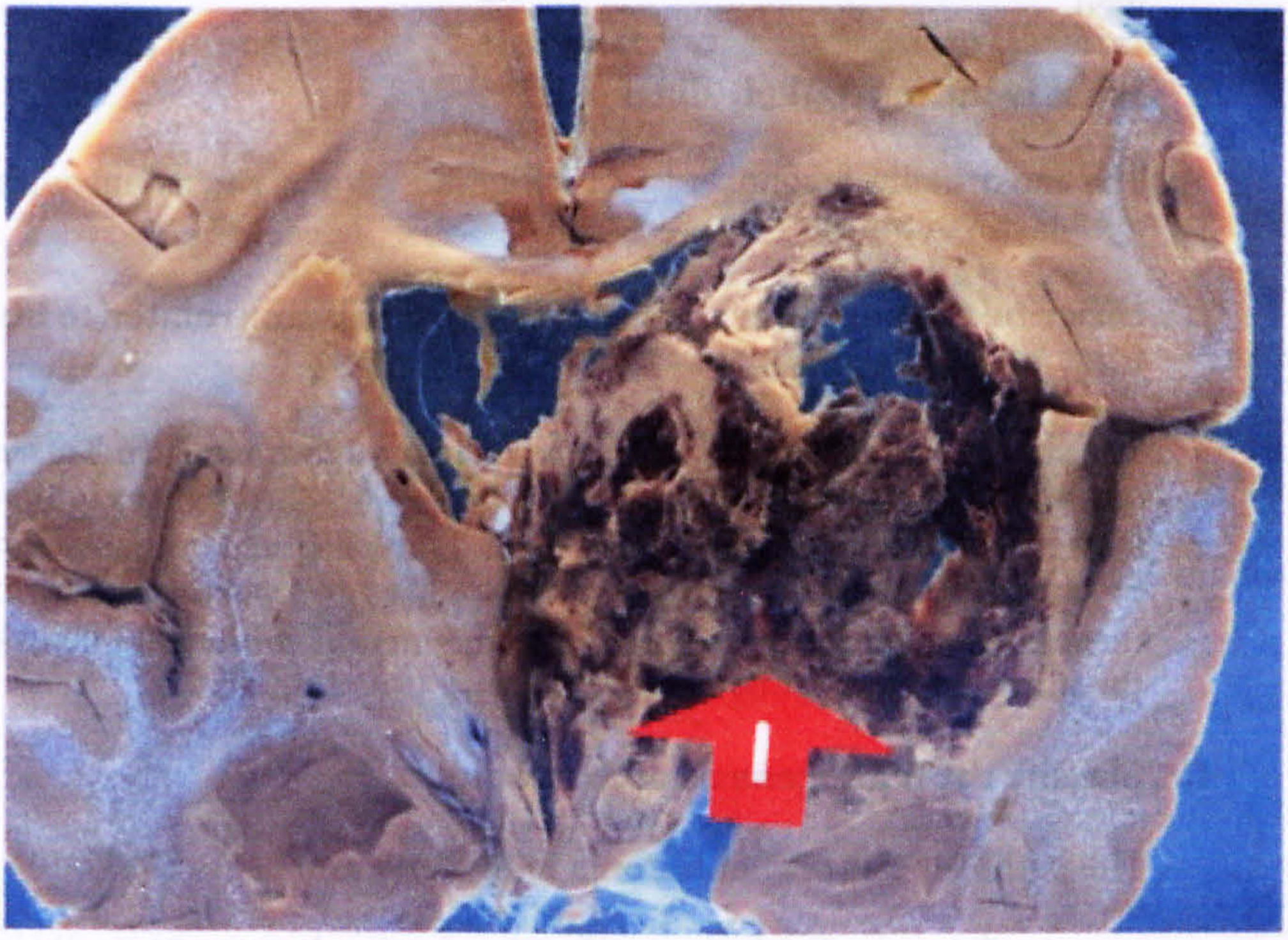
a. Seizures or focal neurological deficit.

b. Cranial nerve palsies

c. Sensorineural hearing loss.

d. Hydrocephalus: Communicating and non-communicating.

CASE 2: AN AGGRESSIVE BRAIN NEOPLASM



Red arrow: The brain tumour

CASE SCENARIO

A 55-year-old man presented with seizures and increasingly severe headaches over the past three months. He claimed to have episodes of uncontrollable shaking of his left arm and leg. This was associated with progressive left lower limb weakness. On physical examination, he was found to have mild papilloedema. He had no known significant past medical illness. A CT scan of the brain revealed a large tumour with irregular edge involving the right and left cerebral cortex. Biopsy of this tumour showed pleomorphic tumour cells with area of necrosis. Presence of vascular proliferation was noted.

QUESTIONS

1. **Describe the macroscopic pathology seen.**

   Sections of the brain show a large and an irregular, haemorrhagic, grayish-tan infiltrating tumour mass. The tumour mass is pre-

dominantly on the right side and extends into the contralateral hemisphere. Area of necrosis and cystic degeneration are noted as well.

2. **What is the most likely diagnosis?**

   The most likely diagnosis is a high-grade glioma consistent with glioblastoma multiforme.

3. **Describe the pathophysiology of essential tremor related to his uncontrollable shaking of his left arm and leg.**

   The shaking of his left arm and leg is a primary motor seizure. This is caused by excessive neuronal firing in the right motor cortex which is triggered by the adjacent right frontal lobe lesion. Manifestation of signs is seen on the contralateral site because most axons from these cortical motor neurons cross in the medulla oblongata before the fibres descend along the spinal cord.

4. **Classify the pathogenesis of this tumour.**

   The pathogenesis of glioblastoma multiforme can be divided into:

   a. Primary glioblastoma: Neoplasm arise de novo, typically in older individuals.

   b. Secondary glioblastoma: Malignant progression of low-grade astrocytoma to glioblastoma, usually in younger patients.

5. **State the spectrum of astrocytic neoplasms that occur in the brain.**

   a. Pilocytic astrocytoma WHO Grade I.

   b. Diffuse astrocytoma WHO Grade II.

   c. Anaplastic astrocytoma WHO Grade III.

   d. Glioblastoma multiforme WHO Grade IV.

6. **State the histological features that lead to the diagnosis of glioblastoma multiforme.**

The presence of all of these features supports the diagnosis:

a. Astrocytic differentiation hence it is a glioma.

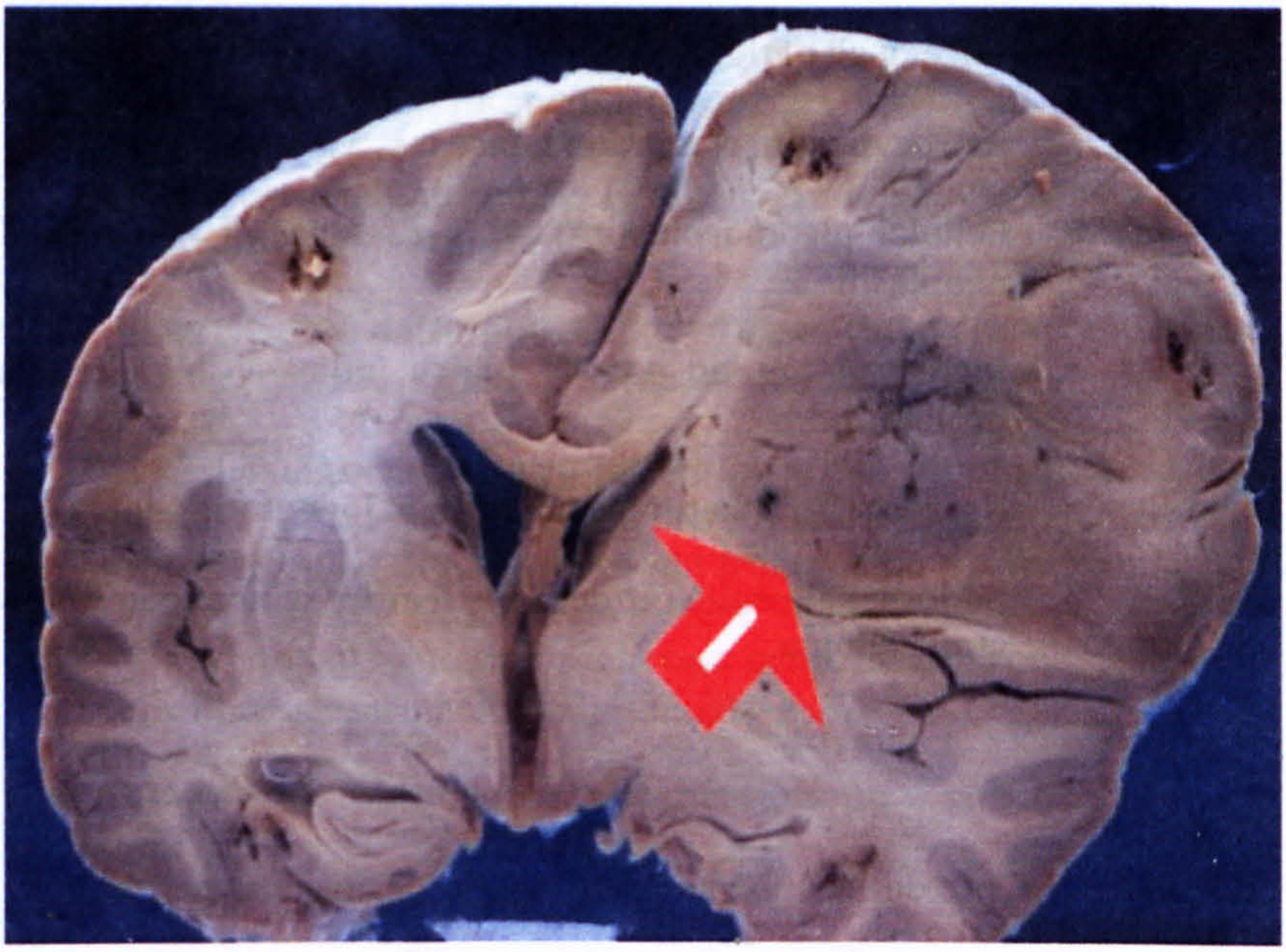
b. Cellular pleomorphism. This is a feature of a high-grade neoplasm.

c. Increased mitotic activity which indicates high cellular proliferation.

d. Necrosis. This feature is not seen in low-grade glioma.

e. Endothelial proliferation. This feature is not seen in low-grade glioma.

CASE 3: A GLIAL CELL NEOPLASM



Red arrow: The tumour mass

CASE SCENARIO

A 50-year-old woman presented with severe headache which had become more frequent over the past two months. Her past medical history was unremarkable.

QUESTIONS

1. **Describe the macroscopic pathology seen.**

   A section of the brain shows an irregular and ill-defined tumour mass at the parietal lobe of the right cerebral hemisphere. The mass is rounded and greyish in colour with a mild midline shift.

CASE SCENARIO CONTINUED

Tissue biopsy showed a tumour composed of diffuse fibrillary cells lacking nuclear atypia with low mitosis.

2. **What is your final diagnosis?**

   Diffuse astrocytoma.

3. **Classify your diagnosis according to the WHO grading system and describe the natural history of this tumour.**

   This tumour is classified as WHO Grade II. The natural history of diffuse astrocytoma may progress along two distinct pathways:

   a. It can remain well-differentiated and continue to grow slowly with prolong survival for many years.

   b. It can undergo transformation to an anaplastic astrocytoma or glioblastoma multiforme with shorter survival time.

4. **Describe the pathophysiology of headache in this woman.**

   The brain is enclosed in a rigid cranium. Therefore, the space for expansion is very minimal. The presence of brain tumour increases the mass of intracranial content. This increases the intracranial pressure resulting in headache. In such cases, a change in the pattern of headache is a significant finding. One should look for the presence of papilloedema to confirm an increased in the intracranial pressure.

5. **State other space occupying lesions that can lead to an increased in intracranial pressure.**

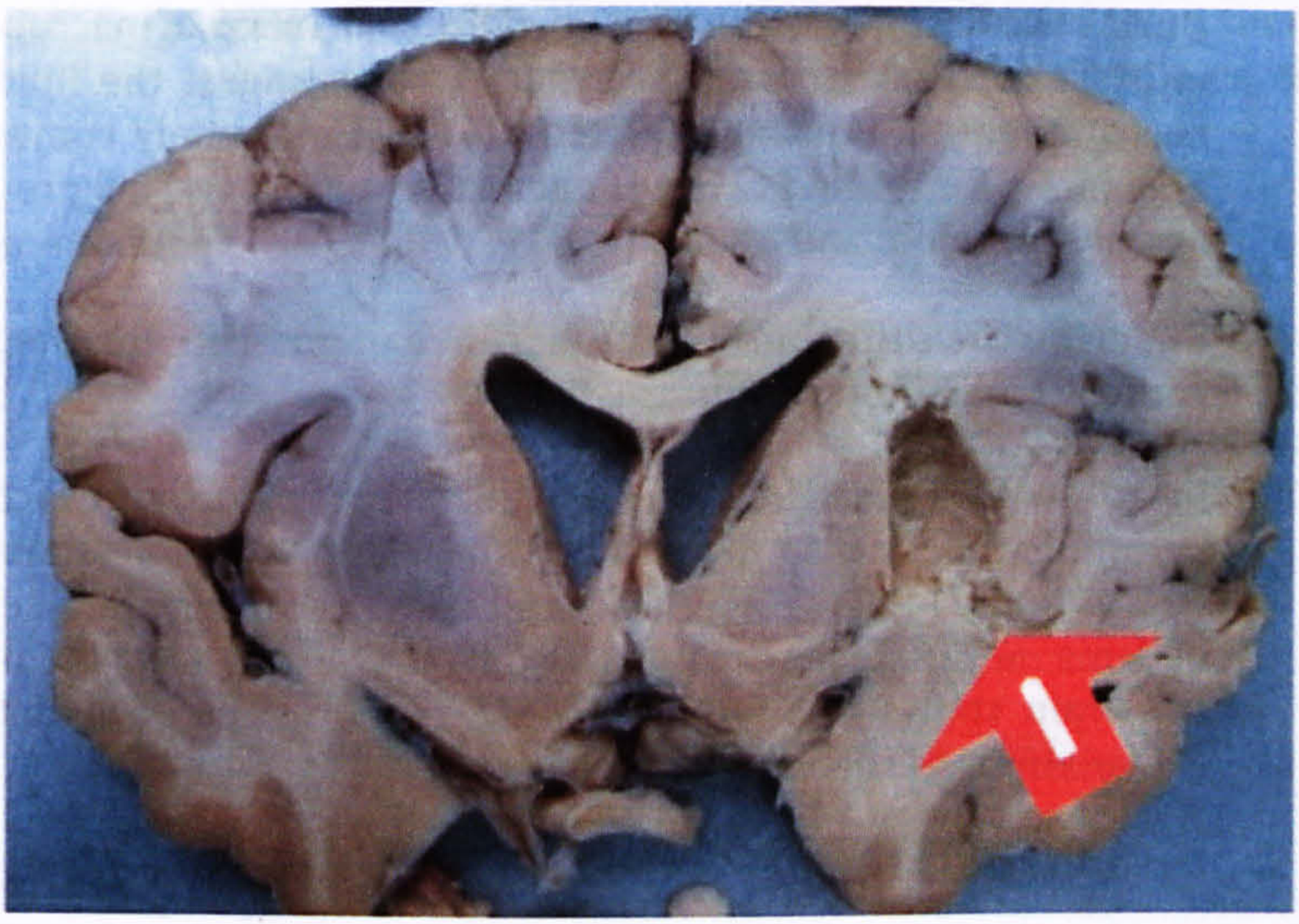
   Besides brain tumour, abscess and haemorrhage can also occur as space occupying lesions.

6. **Describe the possible effects of space occupying lesion.**

   A space occupying lesion can increase the volume of the brain beyond its limit. The cranial vault is divided by rigid dural folds (the falx and tentorium). Therefore, a space occupying lesion such as a tumour can cause it to be displaced in relation to these partitions. If the expansion is sufficiently severe, a *herniation syndrome* may occur. The following herniations can occur within these conditions:

Subfalcine herniation	Occurs when unilateral expansion of a cerebral hemisphere displaces the cingulate gyrus under the falx cerebri.	The anterior cerebral artery branches can be compressed.
Transtentorial herniation	Occurs when the medial aspect of the temporal lobe is compressed against the free margin of the tentorium.	The third cranial nerve is compromised, resulting in pupillary dilation and impairment of ocular movements on the side of the lesion. The posterior cerebral artery may also be compressed, resulting in ischaemic injury to the territory supplied by that vessel. In extensive herniation, the contralateral cerebral peduncle can be compressed, resulting in hemiparesis ipsilateral to the side of the herniation Progression of transtentorial herniation is often associated with haemorrhage in the midbrain and pons, known as *secondary brainstem* or *Duret haemorrhage.*
Tonsillar herniation	Occurs when there is displacement of the cerebellar tonsils through the foramen magnum	This pattern of herniation is life-threatening because it causes brainstem compression and compromises vital respiratory and cardiac centers in the medulla oblongata.

CASE 4: STROKE



Red arrow: The brain lesion

This picture is courtesy of Dr Siew Sheue Feng

CASE SCENARIO

A 75-year-old woman presented with a few months history of slurred speech. According to her son, prior to the presentation, his mother suddenly fell from her seat. Soon after, her speech became incomprehensible and this was associated with imprecise movement of her hands and feet. She has been known to have hypertension and diabetes mellitus for the past 30 years. Study the brain specimen.

QUESTIONS

1. **State the most likely clinical diagnosis.**

   The most likely diagnosis is cerebrovascular accident (CVA).

2. **Describe the macroscopic pathology seen.**

   Cut section of the brain shows a cavitating lesion at the area of globus pallidus. The lesion shows irregular outer margin. No solid lesion is seen.

3. **How does an infarct become cystic?**

During the first week of infarction, there is an influx of macrophages into the area of necrosis. The macrophages ingest the lipid-rich, necrotic material of the infarcted area and ultimately convert the area into a fluid-filled cavity (liquefactive necrosis). This process is usually complete and turns into a cystic defect in about 6 months.

4. **Describe the difference in appearance of an acute infarct and a remote (old) infarct in of the brain.**

In an acute infarct the brain is swollen. This is due to the accumulation of fluid within the necrotic cells (cytotoxic oedema) as well as in the interstitium (vasogenic oedema). In severe cases, this oedema may increase the intracranial pressure. In a remote infarct, the brain shows cavitating defect as found in the accompanying explanations for question number 3.

5. **Describe the histology of the neurons in an acute infarct.**

Brain with acute infarct displays shrunken neurons with eosinophilic cytoplasm and pyknotic nuclei ("red" neurons). This is a classic feature of acute necrosis in the CNS and occurs 24 hours after an irreversible hypoxic/ischaemic insult. The red staining of the neurons is due to a combination of protein denaturation and loss of RNA within the cytoplasm of the affected neuron.

6. **Describe the two groups of infarct that can be seen in the brain.**

Brain infarct can be subdivided into two groups based on the presence or absence of haemorrhage:

a. Haemorrhagic (red) infarction is characterised by multiple, petechial haemorrhage and is typically associated with embolic events. The haemorrhage is presumed to be secondary to reperfusion damage of the non-viable tissue. Reperfusion may occur when the blood enters the necrotic area from the vessels in the adjacent vascular territories or when the initial occlusion is reversed. The latter mechanism is significantly commoner in an embolic event in the brain.

b. Non-haemorhagic infarct (pale or white) is usually

associated with thrombosis. A majority of these thombotic occlusions are due to atherosclerosis. The most common sites of primary thrombosis causing cerebral infarction are the carotid bifurcation, the origin of the middle cerebral artery and either end of basilar artery.

7. Describe the term selective vulnerability.

In some cases of hypoxic-ischaemic encephalopathy, usually after brief insults, neuronal death may occur without damage of the glial cells. This is called selective vulnerability where there is increased sensitivity to injury in localized area of the brain following a global insult. There are a few known vulnerable areas:

a. The hippocampal pyramidal cells of CA1,

b. The pyramidal neocortical neurons (layers 3, 5, and 6),

c. The Purkinje cell layer of the cerebellum.

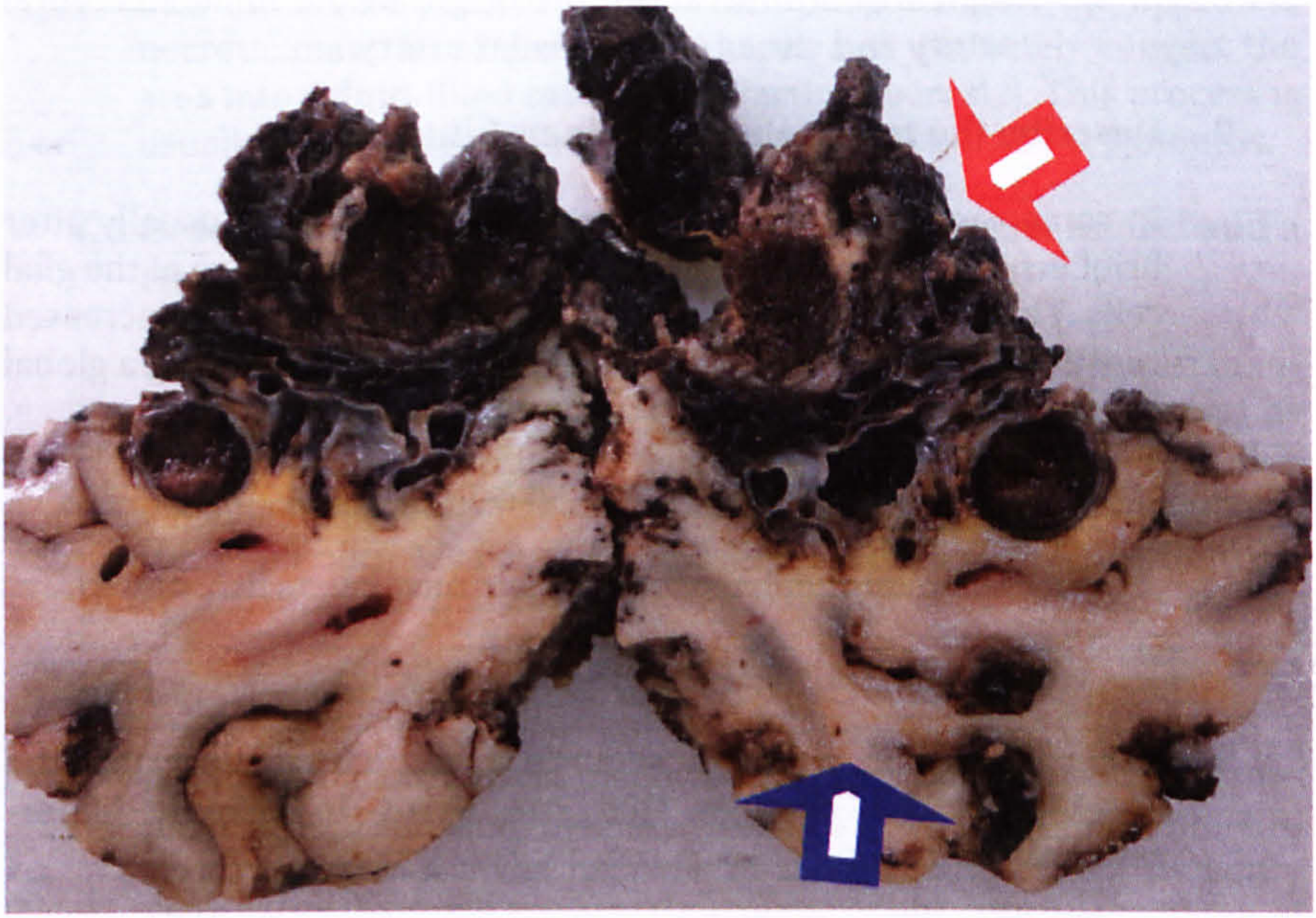
8. Other than the changes seen in the picture, describe the cerebrovascular changes that can occur in chronic hypertension.

a. Hypertension is the most common cause of spontaneous brain parenchymal haemorrhage. This is due to the rupture of tiny aneurysms, known as *Charcot-Bouchard microaneurysm.* These lesions are usually located in small arterial channels in the area of the basal ganglia or thalamus.

b. Lacunar infarcts are small (0.2 to 15 mm in diameter) non-cortical infarcts caused by occlusion of a single penetrating branch of a large cerebral artery.

c. Hypertension also gives rise to rupture of the small-calibre penetrating vessels and the development of small haemorrhages. In time these haemorrhages will be resorbed, leaving behind a slit-like cavity (slit haemorrhage).

CASE 5: VASCULAR MALFORMATION



Red arrow: The lesion

Blue arrow: The adjacent brain tissue

CASE SCENARIO

A 30-year-old man presented to casualty with sudden onset of severe headache followed by seizure. CT scan of the brain showed intracerebral haemorrhage. Angiographic study showed arteriovenous malformation at the temporal lobe of the brain. He had no history of hypertension and he was a non-smoker. Study the brain tissue.

QUESTIONS

1. **Describe the brain lesion.**

   There is a tangled network of vascular channels with features of rupture and surrounding areas of haemorrhage. There are

intervening brain tissues within the lesion. These are the typical features of arteriovenous malformation.

2. What does the brain lesion represent?

The arteriovenous malformation represents a tangle of deformed arterial afferents and draining veins without an interposed capillary bed. The complex vascular channels are associated with arteriovenous shunting of blood circulation (passage of blood from the arterioles to the draining veins bypassing the capillary bed).

3. Describe briefly the pathogenesis of the vascular rupture.

The shunting of blood from high pressure arterial system to the draining veins creates a turbulent blood flow. The turbulence is further aggrevated by the deformed structure of the blood vessels. This predisposes the blood vessels to endothelial injury, atherosclerosis and thrombosis. A prolonged exposure to the turbulence may cause damage to the blood vessels' wall. The wall may eventually weaken. The vessels may then form an aneurysm or succumb to rupture. The turbulence may sometimes be audible as cranial or orbital bruit.

4. Is this lesion a vascular neoplasm?

Arteriovenous malformation is a non-neoplastic lesion caused by focal anomalies in the development of cerebrospinal vasculature. It does not involve clonal proliferation of cells such as seen in neoplasm.

5. State another possible complication of the lesion.

Arteriovenous malformation can cause cardiac failure in infants and children. This can be seen in those harbouring extensive lesions in which the arterial afferents are drained by aneurysmally dilated galenic veins. This shunting will cause significant reduction in total peripheral resistance and lead to cardiac failure.

CHAPTER 2

CARDIOVASCULAR SYSTEM