Periventricular lesions of brain in adults - a pictorial review

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Learning objectives

• Provide a pictorial overview of periventricular lesions of brain in adults

• Depict the key clinical and imaging findings (including CT and MRI) which can suggest the accurate diagnosis

Background

Periventricular lesions of the brain are a common finding encountered in daily practice in CT or MRI of the brain. Many lesions have preference for periventricular location. A spectrum of causes and overlapping imaging findings always cause diagnostic dilemma.

Imaging findings OR Procedure details

The common periventricular lesions that we encountered include:

1. Age-related white matter changes
2. Lacunar infarcts
3. Virchow Robin spaces
4. Vascular lesions- Watershed infarction, Vasculitis and CADASIL (Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)
5. Demyelinating lesions -Multiple Sclerosis
6. Infectious lesions - Cytomegalovirus, Toxoplasmosis and cryptococcosis
7. Tumour - Primary CNS Lymphoma and gliomatosis cerebri
8. Tumour treatment related lesions - Radiation necrosis and chemotherapy related white matter changes
9. Miscellaneous - Migraine and Transependymal cerebrospinal fluid flow
10. Multifocal lesions - Brain abscess and metastasis

AGE RELATED WHITE MATTER CHANGES
They are differentiated into periventricular white matter lesions [PVWML] and deep white matter lesions [DWML] according to their locations [1, 2]. Both these lesions may be punctate, patchy or confluent.

The periventricular white matter lesions are further classified into smooth and irregular hyperintensities. Smooth and well defined PVWML like caps and halos are mostly non-ischaemic lesions while irregular PVWML and DWML are mostly due to microcystic ischaemic lesions [1] [Figures 1 and 2].

**LACUNAR INFARCTS**

Lacunar infarcts are defined as deep, cavitating small vessel infarcts usually less than 1.5 cm in size [3]. They are commonly asymptomatic [1].

Acute lacunes appear mostly as focal lesions with diffusion restriction in the deep white matter while chronic lacunes appear as multiple white matter hyperintensities on T2w images [3] [Figure 2].

FLAIR images of older lacunes appear as a central CSF density area surrounded by hyperintensity [1].

**VIRCHOW ROBIN SPACES**

Perivascular or Virchow Robin spaces are fluid filled structures present around the penetrating arteries and arterioles, usually bilateral and symmetrical.

Lenticulostriate arteries entering the basal ganglia and perforating medullary arteries that enter the cortical grey matter are the most common sites. They are also found in subinsular region, dentate nuclei and cerebellum.

On MRI the perivascular spaces often appear as clusters of round to oval fluid filled cysts with smooth margins, characteristically not exceeding 5 mm diameter. On all pulse sequences the perivascular spaces appear isointense to CSF [Figure 3] [1].

**WATERSHED INFARCTION**
Watershed infarctions typically occur at the point where the two major cerebral arteries distally meet. It is of two types - cortical and internal.

Watershed infarctions are usually caused by internal carotid stenosis or occlusion, systemic hypotension and emboli.

The cortical water shed infarctions characteristically show fan or wedge shaped T2w hyperintensities that are seen from lateral wall of lateral ventricles to the cortex.

In internal watershed infarcts the infarcts run parallel to the lateral ventricles that may be confluent or focal and also unilateral or bilateral [3, 4] [Figure 4].

CNS VASCULITIS

Vasculitides are a heterogeneous group of diseases that include inflammation and necrosis of blood vessel wall. Cerebral vasculitis usually occurs in middle aged women. It can be haemorrhagic or ischaemic occurring due to various primary and secondary causes involving the small vessels of the meninges and cerebral parenchyma [1, 5, 6]. Multiple lesions are common and solitary lesions are rare [5].

Digital subtraction angiography and MRI are sensitive modes of diagnosis. T2w and FLAIR imaging shows multiple, nonspecific, small hyperintensities in the deep and subcortical white matter and deep grey matter. The thick vessel walls showing oedema and enhancement may be demonstrated on MRI [Figure 5]. Presence of non-atherosclerotic arterial stenosis may be seen in MR/CT angiography [1].

Presence of multiple infarcts in young age or multiple tiny scattered haemorrhages should point towards cerebral vasculitis [1].

CADASIL

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy [CADASIL] is a hereditary disease that can manifest from childhood to middle age due to NOTCH 3 gene mutation. MRI findings include infarcts, lacunes and diffuse leukoencephalopathy.

There is increased signal intensity in T2w and FLAIR images within the periventricular white matter, basal ganglia, thalamus, internal capsule and pons. [1].
CADASIL is characteristically diagnosed by T2w hyperintensity in the anterior part of temporal lobe, external capsule, insula and corpus callosum and without cortical infarcts [Figure 6]. Unlike multiple sclerosis the lesions are not juxtacortical or juxtaventricular [7].

MULTIPLE SCLEROSIS

Multiple sclerosis affects women in their thirties and forties more than men [1].

Diagnosis using MRI is based on Mc Donald criteria according to which, the presence of multiple T2w lesions in at least two regions among periventricular, juxtacortical, infratentorial and spinal cord, which demonstrates the dissemination in space and presence of a new T2w lesion with or without a gadolinium enhancing lesion on follow up irrespective of the time of baseline scan demonstrates the dissemination in time [7].

The characteristic periventricular lesions are ovoid, lying at right angles to the ventricles and are called Dawson fingers [Figures 7 and 8].

Lesion may show diffuse, nodular, ring or horse shoe like pattern of enhancement. [Figure 9] In T1w images, presence of hypo intense lesions called black holes correlate with the clinical symptoms and disabilities of the patient [1].

Other common locations of Multiple Sclerosis lesions are corpus callosum, subcortical region, brainstem, optic nerves, visual pathway and subcortical U fibres. Patients with multiple sclerosis commonly present with optic neuritis [1, 7].

CYTOMEGALOVIRUS

Cytomegalovirus commonly affects adults in the form of latent infection. However in immunocompromised patients it causes severe opportunistic infections.

In the central nervous system, Cytomegalovirus usually lodges in the ependymal and subependymal regions causing ventriculoencephalitis.

On MRI, ventriculitis is seen as linear enhancement in periventricular subependymal lining of lateral ventricles, septum pellucidum, corpus callosum and fornices. These changes are better seen on diffusion weighted images as diffusion restriction [Figure 10]. Diffuse or focal periventricular hyperintensities may also be seen [8].
TOXOPLASMOSIS

Cerebral toxoplasmosis occurs due to chronic infection in immunocompromised patients.

CT may show solitary lesion or multiple hypo to iso attenuating lesions in basal ganglia, corticomedullary junction, white matter and periventricular regions. Calcifications are seen after therapy [9].

MR - The lesions are hypointense with peripheral hyperintensity on T1w [differentiates it from lymphoma]. On T2w and FLAIR images the lesions appear with mixed intensities [10]. With contrast, the lesions appear with a thin, smooth, or poorly defined rim of enhancement [Figure 11].

The most common differential diagnosis of cerebral toxoplasmosis in immunocompromised individuals is lymphoma. Compared to toxoplasmosis, lymphomas are locally infiltrative, show diffusion restriction, occur more commonly in periventricular region and show butterfly pattern on imaging [9].

CRYPTOCOCCOSIS

Cryptococcus neoformans usually affects AIDS patients and presents as disseminated infection.

The characteristic pathologic changes are meningitis, dilated perivascular spaces and cryptococcomas of which the latter two have similar imaging appearances [11].

As the infection reaches the Virchow-Robin spaces, a mucoid gelatinous material from the capsule of the organism dilates the perivascular spaces forming multiple gelatinous pseudo cysts. These pseudo cysts are round or oval, appearing similar to cerebrospinal fluid and are present in the basal ganglia, thalami, midbrain, cerebellum and periventricular regions [12].

On MRI, the cysts are hypointense on T1w and hyperintense on T2w. Absence of enhancement in these lesions is attributed possibly due to the patient's immunocompromised state or the blood brain barrier is not breached since the lesions are in the perivascular spaces [11, 12] [Figure 12].

PRIMARY CNS LYMPHOMA
Primary CNS lymphoma [PCNSL] constitutes 16% of all CNS tumours and most of them are of non-Hodgkin's B-cell type [13].

PCNSL in immunocompetent individuals presents commonly in men after their fifth decade and occur as solitary lesions commonly located in periventricular [14] and supratentorial white matter in frontal and parietal regions. Classically presents in a butterfly pattern across the corpus callosum [Figure 13].

CT shows iso to hypodense lesion while in MRI the lesion is well delineated appearing iso to hypo intense on T1w and hypointense on T2w images. Both CT and MRI show homogenous contrast enhancement. The characteristic finding of diffusion restriction of lymphoma due to high cellularity is helpful in differentiating it from other similar lesions like glioma and metastases [Figure 14] [14].

GLIOBLASTOMA MULTIFORME

Glioblastoma multiforme is the commonest primary brain tumour prevailing among the age group of 45 to 70. It commonly originates from the white matter. Distant spread is also possible via white matter tracts and perivascular spaces. They are characteristically solitary, large and irregular with intratumoral arteriovenous shunting caused due to associated necrosis and neovascularity [15]. It frequently crosses the midline via the corpus callosum [Figure 15] [16].

On MRI, the lesions are hypointense in T1w whereas they are hyperintense in T2w. The lesion shows nodular and irregular rim enhancement on contrast with central necrosis [15, 16]. Characteristic appearance is the presence of ill-defined margins and oedema around the lesion [Figure 16] [15, 17].

RADIATION NECROSIS

Radiation necrosis occurs within two years after radiation therapy.

Characteristic appearance of radiation induced necrosis is the presence of periventricular foci of enhancement that is seen within the port of radiation. In addition periventricular white matter is common site for post irradiation vasculopathy as it has poor collateral vessels and poor blood supply [18].
In spite of all advanced techniques it is however difficult to differentiate radiation necrosis from other conditions like glioma and recurrent tumours [18, 19].

The findings favouring glioma include diffusion restriction, increased cerebral blood volume [18], involvement of corpus callosum with multiple enhancing lesions with or without subependymal spread [19]. On MR spectroscopy, increased choline / creatine ratio and choline / N-acetyl aspartate ratio signifies recurrent tumour. A rise in lipid lactate peak and drop in other metabolite levels signifies radiation necrosis [18] [Figure 17].

CHEMOTHERAPY RELATED CHANGES

Chemotherapy related white matter changes can be observed as early as 2 months, initially appearing as patchy periventricular white matter hyperintensities on T2w/ FLAIR which later progresses to confluent changes which are usually symmetrical [20,21].

Initially there is relative sparing of the deep white matter and subcortical U fibres, which are involved in the late stages [1].

Acute neurotoxicity may be seen in patients receiving intrathecal methotrexate, particularly when accompanied with chemotherapy. Initially they manifest as cytotoxic oedema manifesting as diffusion restriction and later as diffuse confluent periventricular white matter hyperintensities on T2w/FLAIR [22][Figure 18].

"Disseminated necrotizing leukoencephalopathy" refers to delayed encephalopathy which occurs due to combined effects of radiation and chemotherapy [23].

MIGRAINE

Females among the age group of 10-45 are commonly affected and are usually associated with deep white matter lesions. Migraine patients with an aura are usually positive for white matter hyperintensities. Brain infarction is also more common in migraine [1, 24].

The white matter hyperintensity on T2w and FLAIR images are mostly present in the deep white matter, periventricular and juxacortical region. Callosal and subcallosal region are rarely affected [Figure 19]. The lesions are usually located within the frontal lobe and are multiple in most cases [1].
TRANSEPENDYMAL CSF (Cerebrospinal fluid) FLOW

Transependymal CSF flow across the ventricles is commonly encountered in obstructive hydrocephalus where the cerebrospinal fluid passes across the ependymal barrier into the extracellular space in the periventricular regions because of the increased intracranial pressure. It is better appreciated on MRI as thin rim of T2w/FLAIR hyperintensity outlining the dilated ventricles [25] [Figure 20].

MULTIFOCAL LESIONS

The other lesions which can be widely distributed anywhere in the brain can also be located in the periventricular regions and cause diagnostic confusion.

Brain abscess which are commonly located in the grey-white matter junction show ring enhancement on contrast and diffusion restriction on DWI and ADC maps [Figure 21].

Metastatic lesions are also commonly multiple and located in the subcortical regions. When solitary lesions are encountered it usually causes diagnostic dilemma with other primary brain tumours [16] [Figure 22].

Images for this section:
**Fig. 1:** Axial FLAIR images (a and b) of a 75 year old female showing the typical age related changes. There is diffuse confluent irregular FLAIR white matter hyperintensities in the periventricular regions. In addition, there are also multiple scattered FLAIR subcortical and deep white matter hyperintensities (arrows in a and b).

![Fig. 1: Axial FLAIR images (a and b) of a 75 year old female showing the typical age related changes.](image)

**Fig. 2:** Axial T2w (a) and FLAIR (b) images of a 67 year old man showing the typical age related changes and chronic lacunar infarcts. There are multiple chronic lacunar infarcts which are hyperintense on T2w and hypointense on FLAIR (arrows in a and b). Background diffuse extensive T2w/FLAIR hyperintensities in the periventricular white matter due to age related changes are noted.

![Fig. 2: Axial T2w (a) and FLAIR (b) images of a 67 year old man showing the typical age related changes and chronic lacunar infarcts.](image)
Fig. 3: Axial T2w (a) and FLAIR (b) images of a 53 year old man shows prominent perivascular space (Virchow Robin space) which is noted at the characteristic location along the anterior commissures on either side (arrows in a and b). They typically follow CSF signal on all sequences appearing hyperintense on T2w and hypointense on FLAIR.

Fig. 4: 55 year old male who presented with right side weakness. Axial DWI (a) and ADC map (b) demonstrate characteristic wedge shaped acute infarct in the left MCA-
PCA cortical watershed region showing diffusion restriction (long white arrows). Chronic infarct is noted in the right MCA-PCA cortical watershed region (long black arrows). There are also multiple linear foci of acute infarcts parallel to left ventricle suggestive of partial internal watershed infarcts (small arrows).

Fig. 5: Vasculitis in a young adult with stroke. Axial DW images (a and b) demonstrate multiple scattered foci of acute infarcts in bilateral frontal lobes and in corona radiata. Axial TOF image (c) demonstrates diffuse thickening of the walls of both internal carotid arteries (small arrows). MIP image of intracranial circulation (d) demonstrates diffuse irregularities in the intracranial circulation, predominantly involving bilateral internal carotid (small arrows) and middle cerebral arteries.
Fig. 6: CADASIL in a 50 year old male patient who presented with bilateral spastic gait for few years. Patient also had family history of young stroke. Axial FLAIR images (a,b) show abnormal diffuse confluent high signal and multiple chronic lacunar infarcts in periventricular white matter. There are also confluent regions of high signal in the anterior part of the temporal lobes (small black arrows) and the images also demonstrate involvement of external capsules (small white arrows) and corpus callosum (long black arrows).
**Fig. 7:** Classical findings in multiple sclerosis in a 38 year old male. Sagittal (a) and axial (b) FLAIR images of brain demonstrate multiple linear hyperintense signal in periventricular location, which are located perpendicular to the ventricles (small arrows). Sagittal T2w image of the cervical spine (c) demonstrates associated cord changes appearing as hyperintensity at C2/C3 level (long arrow).
**Fig. 8:** 36 year old male with multiple sclerosis. Axial FLAIR image demonstrates focal well circumscribed hyperintense lesion located adjacent to the left lateral ventricle (arrow) in addition to the multiple linear hyperintensities perpendicular to the ventricles.
**Fig. 9:** Enhancement in multiple sclerosis. Axial FLAIR (a) demonstrates a large area of hyperintensity in the left posterior parietal lobe. Multiple scattered foci of white matter hyperintensities are also seen. Post contrast T1w image (b) demonstrates irregular ring like enhancement. Axial FLAIR (c) and post contrast T1w images (d) of the same patient obtained after 6 months are shown. There is interval progression of the white matter hyperintensity on FLAIR but the contrast enhancement is no longer seen.
**Fig. 10:** A case of cytomegalovirus ventriculitis in a 32 year old female who is a known case of HIV. Axial FLAIR (a) and DW images (b) demonstrate a thin linear hyperintensity along the walls of lateral ventricles which are better appreciated on the DWI (white arrows). Post contrast axial T1w (c) shows linear enhancement along the ventricular walls (black arrows).

**Fig. 11:** Toxoplasmosis in a 40 year old HIV positive female. Axial FLAIR image (a) demonstrates multiple focal hyperintensities in the periventricular white matter which shows ring enhancement (white arrows) on post contrast T1w images (b). Multiple foci of nodular enhancing foci (black arrows) are also noted. Another T1w post contrast image(c) at a higher level demonstrates a larger ring enhancing lesion with a central necrotic centre.
Fig. 12: 54 year old immunocompromised HIV-positive male with cryptococcosis. Axial T2w image (a) demonstrates a focal hyperintense lesion in the left basal ganglia. Post contrast axial T1w image (b) shows a non-enhancing hypointense lesion.
Fig. 13: A case of primary CNS lymphoma in 43 yr old immunocompetent female. Axial T2w image (a) demonstrate a homogeneous mildly hyperintense lesion located in the left centrum semiovale in periventricular location which extends along the genu of corpus callosum to the right side. Axial DWI (b) and ADC map (c) demonstrates diffusion restriction of the lesion, a characteristic finding seen in lymphoma. Post contrast T1w image (d) demonstrate homogeneous enhancement.
Fig. 14: Another case of primary CNS lymphoma involving the splenium of corpus callosum and extending on either side of midline. Axial DWI shows diffusion restriction of the lesion and also a hemorrhagic component is noted on the right side (arrow).
**Fig. 15:** 53 year old male with glioblastoma multiforme. Axial FLAIR image (a) demonstrates a large hyperintense mass in the right periventricular region associated with severe perilesional edema, mass effect and compression of the ventricles. The mass extends to the left of midline involving the genu of corpus callosum (arrows). T1w post contrast study (b) demonstrates irregular rim enhancement with necrotic center.
**Fig. 16:** 55 year old male with glioblastoma multiforme. Axial T2w image (a) demonstrate a large hyperintense mass with severe perilesional edema in the left parietal-occipital lobes which extends along the splenium of corpus callosum (small arrows) to the right side. T1w post contrast study (b) demonstrates irregular rim enhancement with necrotic center. Post-operative defect is also noted in the skull vault (large arrows) on left side from prior evacuation of hematoma.

![Fig. 16: MRI images of glioblastoma multiforme](image)

**Fig. 17:** A case of radiation necrosis in a patient who had prior surgical excision of glioblastoma multiforme in right frontal lobe followed by whole brain radiotherapy. Axial T1w post contrast image (a) shows an irregular enhancing necrotic lesion located closely abutting the frontal horn of right lateral ventricle (arrow). Semi-quantitative spectroscopy (b) showed minimal choline elevation with corresponding minimal depression of NAA possibly due to gliosis. The lesion also had reduced perfusion with increased fractional extracellular vascular volume (not shown) suggesting radiation necrosis. Chronic subdural collection is also noted in right frontal convexity (black arrow in a).

![Fig. 17: MRI images of radiation necrosis](image)
Fig. 18: Chemotherapy related white matter changes in a 20 year old female who received intrathecal methotrexate and high dose chemotherapy for ALL (Acute Lymphoblastic Leukemia). Axial FLAIR image (a) demonstrates diffuse confluent periventricular hyperintensity. Axial FLAIR image (b) obtained 2 months earlier demonstrates the periventricular regions to be normal.
**Fig. 19:** 53 year old female with migraine. Axial FLAIR images(a,b) show scattered hyperintensities in the subcortical and periventricular white matter (arrows) which are considered non-specific, however are noted commonly in patients with migraine.

![Fig. 19](image)

**Fig. 20:** Axial FLAIR image (a) demonstrates obstructive hydrocephalus with rim of periventricular hyperintensity due to transependymal seepage of CSF. The long arrow refers to the partially demonstrated sella mass. Sagittal post contrast T1w image (b) demonstrates the large sella mass causing obstructive hydrocephalus, proven to be a pituitary macroadenoma (arrows).
Fig. 21: 56 year old male with Klebsiella bacteremia and multiple brain abscesses. Axial post contrast T1w image (a) demonstrates multiple ring enhancing lesions in left parieto-occipital lobe (white arrows) closely related to the occipital horn of left lateral ventricle with moderate perilesional edema. Axial DWI (b) demonstrates diffusion restriction of these lesions (black arrows).
Fig. 22: A solitary metastasis from lung carcinoma in a 63 year old male. Axial post contrast T1w image demonstrates a large heterogeneously enhancing necrotic lesion in the right parieto-occipital lobe closely abutting the right lateral ventricle with moderate perilesional edema and mass effect.
Conclusion

Although there is overlap of imaging findings among these entities, the knowledge of key concepts and identification of important signs can be helpful in making a specific diagnosis.

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References


