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**MRI Study of Brain and Incidental Finding of White Matter Hypertensities and Microbleeds**

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**Introduction**

As with any diagnostic test that screens for diseases, the risks of imaging need to be outweighed by the benefits of identifying a treatable disease with acceptable sensitivity and specificity. Plain skull X-ray with its inherent ionising radiation is therefore not recommended for routine assessments of the central nervous system except in the detection of skull lesions. CT used to be the modality of choice for non-invasive assessment of all brain diseases. However with the advent of MR, CT is now mainly employed in the setting of emergency or trauma in which CT serves as the quickest imaging modality for the detection of acute intracranial bleeding (traumatic or non-traumatic) and skull fractures.

MR studies of the brain is considered the better imaging technique than CT for two reasons. Firstly, MR has a much higher contrast resolution when compared with CT for exquisite depiction of normal anatomical structures and pathologies of the brain. Unlike CT angiography, intravenous contrast injection is not required for MR angiography. This is advantageous in patients with impaired renal function, contrast allergy or no intravenous venous access. Secondly, MRI does not involve radiation exposure. CT brain scans which use X-ray to produce images may expose patients to about 2 mSv of radiation which is twenty times that of chest X-rays. In simple terms, the radiation exposure from one non-contrast CT brain study is equivalent to the amount of background radiation one experiences in about 8 months, considering that the average person in Hong Kong receives an effective dose of about 3.2 mSv per year from naturally occurring radioactive materials and cosmic radiation. MR imaging has thus replaced CT in the imaging of the brain white matter hyperintensities (WMHs) and brain microbleeds.

While MRI study of the brain is increasingly utilised in clinical practice and health screening owing to its increased availability and recognition among clinicians, incidental findings showing abnormalities of potential clinical relevance that are unrelated to the purpose of the study are unexpectedly discovered on these MR brain studies. Reports and studies on the prevalence of these incidental abnormalities are growing in number. However, the clinical course of some of these incidental findings is still uncertain, and their management is not standardised. It is the purpose of this review article to categorise the major groups of incidental findings and to discuss their clinical relevance.

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**Prevalence of Incidental MR Brain Findings**

No large scale study of incidental MR brain findings is available in Hong Kong but the significance of this issue is well reflected in studies conducted abroad. In a recent systemic review with meta-analysis on incidental findings in brain magnetic resonance imaging by Morris et al, it was found that neoplastic incidental brain findings had a prevalence of 0.7% (135 of 19559 people out of 16 studies) with increased prevalence with age. The non-neoplastic incidental findings were even more prevalent at 2.0% (375 of 15595 in 15 studies). The overall prevalence of incidental brain findings on MRI was 2.7%, equivalent to one for every 37 subjects scanned.

Another remarkable observation is that the prevalence was further increased from 1.7% to 4.3% when the sensitivity was enhanced by more state-of-the-art MR scanners and higher resolution MRI sequences, including MR angiography. Nowadays, advanced sequences such as three-dimensional TI spoiled or fluid attenuated inversion recovery (FLAIR) or MR angiography are commonly included in routine clinical scans, leading to discoveries of more incidental findings. This overall prevalence of 2.7% pointed out by the Morris group was in fact ‘conservative’ as their study had already excluded the most common incidental findings, namely the white matter hyperintensities (WMHs), silent brain infarcts and brain microbleeds (BMB). In a study of MRI brain scans on patients of the general population, it was found that the prevalence of asymptomatic infarcts was 7.2% (145 of 2000).

Incidental findings on brain MRI studies can be broadly divided into three groups; vascular, neoplastic and non-neoplastic cystic lesions. This article mainly focuses on brain white matter hyperintensities and microbleeds. Detailed discussion on other vascular lesions (vascular malformations and aneurysms), incidental neoplasms or non-neoplastic cysts will be covered by other authors.

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**White Matter Hyperintensities (WMH) & 'Silent' Infarcts**

The most common incidental vascular lesion is white matter hyperintensities (WMHs). These lesions are sometimes referred to as leukoaraiosis or age-related white matter change (ARWMC). MRI is highly sensitive for the detection of white matter pathologies with
conventional PD or T2 weighted spin echo or fast-spin echo sequences but are even more conspicuous on fluid-attenuated inversion recovery (FLAIR) images. FLAIR sequences have the advantage of making cerebrospinal fluid (CSF) looks dark while the white matter lesion still appears bright. This improves the lesion conspicuity, especially in areas close to the CSF spaces such as periventricular areas (Figure 1c).

Pathologically, WMH or ARWMC is an area of myelin pallor, tissue rarefaction associated with loss of myelin and axons, and mild gliosis. These lesions are most commonly located in the deep white matter and often associated with disease of small vessels (intraparenchymal cerebral arteries and arterioles), which probably induce the WMH lesions through chronic or transient but repeated hypoperfusion of the white matter. The hypoperfusion results in an incomplete form of infarction with disruption of the blood-brain barrier, leading to chronic leakage of plasma into the white matter and activation of astrocytes. Activated and swollen astrocytes, typically seen in areas of WMHs may contribute to the alterations commonly detected by MRI.

As the name ARWMC implies, the WMHs are dependent on the age of patients (Figure 1a and 1b). In the general population, their prevalence shows obvious positive correlation with age, ranging from only 4% in the age group of 45-59 to 6.8% in age group of 60-74. An even higher prevalence of 18.3% was found in the age group of 75-97.

WMHs are indeed more common and extensive in patients with symptomatic cerebrovascular diseases or cardiovascular risk factors which include hypertension, hypercholesterolaemia, hyperlipidaemia and diabetes mellitus among other less common causes. Numerous researches have been done on this subject with various systems to scale the WMH load either using visual assessment (Figure 2) or quantitative analysis. Mild lesions are usually punctate lesions less than 5 mm in diameter. The more severe lesions are comprised of patchy confluent lesions in the periventricular and deep white matter.

A meta-analysis study by Debette et al included 22 studies which evaluated the association of white matter hyperintensities with risks of stroke, cognitive decline, dementia or death. It was concluded WMHs were associated with an increased risk of stroke, dementia and death. An association with a faster decline in global cognitive performance, executive function, and processing speed was also suggested. WMHs therefore predict an increased risk of cerebrovascular events. The discovery of significant WM load on MR scan should prompt detailed screening for risk factors of stroke and dementia, especially in relatively young patients.

**Brain Microbleed (BMB)**

Brain microbleeds (BMBs) are typically seen as tiny homogeneous foci of low signal intensity with a ‘blooming’ appearance on magnetic resonance imaging gradient echo (GRE) T2* sequences. The recently introduced susceptibility-weighted imaging (SW) can even detect these microhaemorrhages better than a gradient-recalled echo sequence due to its high sensitivity to blood degradation products as in Figure 3.

Pathologically, BMBs are found in areas fed by deep perforating arteries showing lipohyalinosis and occasional amyloid deposits or ruptured arteriosclerotic microvessels. BMB can therefore be considered a biomarker of bleeding-prone small-vessel diseases, in particular hypertensive small-vessel arteriopathy and cerebral amyloid angiopathy (CAA).

Cordonnier et al systematically reviewed and critically appraised 54 studies of 53 case series involving 9073 participants, 4432 of whom were people with cerebrovascular diseases. The prevalence of BMBs was 5% in healthy adults, 34% in people with ischaemic stroke, and 60% in people with non-traumatic intracerebral haemorrhage (ICH). BMBs were more prevalent among recurrent strokes than first-ever strokes; recurrent intracerebral haemorrhage (ICH) than first-ever ICH.

BMBs are usually related to hypertensive illness, especially in the setting of uncontrolled or untreated patients. In elderly patients, old microbleeds can also be related to amyloid angiopathy which occurs mainly in older patients. In CAA, accumulation of amyloid β-protein renders vessel walls less elastic and more fragile, resulting in microhaemorrhages.

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**Figure 1** – Axial T2 weighted images of the same octogenarian taken 5 years apart showed obvious progression of the white matter hyperintensities (WMHs) in both the deep and periventricular white matter. The confluent periventricular WMHs are also more obvious in the parietal lobes (open arrow). These WMHs are well depicted on the coronal FLAIR images (figure 1c). Please note that the age-related prominent perivascular spaces (arrows on figure 1b) are confirmed to be CSF-filled linear structures on the FLAIR study (arrow on figure 1c) with no hyperintense signals.

**Figure 2** – Axial FLAIR images demonstrate different grades of white matter hyperintensities (WMHs) in the brain. Figure 2a in a 55-year-old lady shows mild degree of WMHs with only a few punctate hyperintense lesions in the subcortical and deep white matters (bold arrow). The normal age-related periventricular hyperintense smooth thin rims as well as triangular-shaped “caps” around the frontal horns (short arrow) are also depicted. Figures 2b and 2c in two different elderly gentlemen in their seventies show moderate and severe degrees of WMH with patchy confluent WMHs in the deep and periventricular white matters, most obvious in the parietal lobes.
Although a definite relationship of BMB and use of antiplatelet treatment cannot be established, it may be prudent in taking extra caution in administrating this kind of drug to patients who have a significant degree of BMB on MR brain. There was one study\(^\text{11}\) considering BMB a biomarker for bleeding-prone small-vessel diseases and might be associated with antiplatelet-related ICH. The risks of ICH could outweigh the benefits of antiplatelet therapy in patients with significant lobar microbleeds. In another local study of BMB as a risk factor for aspirin-associated ICH\(^\text{12}\), it was found that BMBs are more frequent and more extensive in the intracerebral haemorrhage group than in the control group.

Figure 3 – Axial GRE T2* weighted and susceptibility-weighted images of a 65 years old patient with poorly controlled hypertension. Multiple old microbleeds are demonstrated at the thalami and basal ganglia (arrow). The subcortical microbleeds are only vaguely seen on GRE T2* weighted sequence (figure 3a) but appear more conspicuous and numerous on the SWI.

References