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REVIEW ARTICLE

Brain microbleeds: Epidemiology and clinical implications☆

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Abstract
Introduction: Brain microbleeds (BMB) are haemosiderin deposits contained within macrophages, which are displayed as hypointense images in some T2-weighted magnetic resonance imaging sequences. There are still many questions to be answered about the pathophysiology and clinical relevance of BMB.
Development: We conducted a literature review of the main epidemiological, clinical, and anatomical pathology studies of BMB performed in the general population, in patients at risk of or already suffering from a vascular disease, and in patients with cognitive impairment. We analysed the prevalence of BMB, risk factors, and potential pathophysiological mechanisms and clinical implications.
Conclusions: The prevalence of BMB is highly variable (3%-27% in the general population, 6%-80% in patients with vascular risk factors or vascular disease, and 16%-45% in patients with cognitive impairment). BMB are associated with ageing, Alzheimer disease (AD), and in particular haemorrhagic or ischaemic cerebrovascular disease. The pathological substrate of BMB is either lipohyalinosis (subcortical BMB) or cerebral amyloid angiopathy (lobar BMB). BMB exacerbate cognitive impairment, possibly through cortical—subcortical and intracortical disconnection, and increase the risk of death, mostly due to vascular causes. BMB also increase the risk of cerebral haemorrhage, particularly in patients with multiple lobar BMB (probable cerebral amyloid angiopathy). Therefore, anticoagulant treatment may be contraindicated in these patients. In patients with lower risk of bleeding, the new oral anticoagulants and the combination of clinical and magnetic resonance imaging follow-up could be helpful in the decision-making process.

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PALABRAS CLAVE
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Microhemorragias cerebrales: epidemiología e implicaciones clínicas

Resumen
Introducción: Las microhemorragias cerebrales (MHC) son depósitos de hemosiderina, fagocitados por macrófagos, que se visualizan como imágenes hipointensas en determinadas secuencias de adquisición T2 de resonancia magnética cerebral. Existen muchas incógnitas acerca de su fisiopatología y significado clínico.
Desarrollo: Revisión bibliográfica de los principales estudios epidemiológicos, clínicos y anatomopatológicos de MHC en la población general, en pacientes con enfermedad o riesgo vascular y en pacientes con deterioro cognitivo. Descripción de la prevalencia, factores de riesgo, mecanismos fisiopatológicos y posibles implicaciones clínicas de las MHC.
Conclusiones: La prevalencia de las MHC es muy variable (3-27% en la población general, 6-80% en pacientes con enfermedad o riesgo vascular, 16-45% en pacientes con deterioro cognitivo). Las MHC se asocian a la edad, a la enfermedad de Alzheimer y, en particular, a la enfermedad vascular (hemorrágica o isquémica) cerebral. El sustrato patológico es la lipohialinosis (MHC subcorticales) o la angiopatía amiloide cerebral (MHC lobulares). Las MHC contribuyen al deterioro cognitivo, posiblemente a través de una desconexión córtico-subcortical e intracortical, y se asocian a una mayor mortalidad, especialmente de causa vascular. Las MHC aumentan el riesgo de sufrir hemorragia cerebral, especialmente en pacientes con múltiples MHC lobulares (probable angiopatía amiloide cerebral), por lo que el tratamiento anticoagulante podría estar contraindicado en estos pacientes. En pacientes con menor riesgo de sangrado, los nuevos anticoagulantes orales y la realización de un seguimiento combinado—clínico y mediante resonancia magnética—podrían ser útiles en la toma de decisiones.

Introduction

Few neuroradiological phenomena have drawn so much attention as cerebral microbleeds (CMB), which were first described barely 2 decades ago. A frequent finding in brain magnetic resonance imaging (MRI) studies, CMBs cause alarm in patients and confusion in healthcare professionals. Are CMBs merely ''innocent bystanders'' in cerebrovascular disease (CVD), or do they play a role in symptom pathogenesis, prognosis, and treatment? On the basis of some common pathogenic mechanisms, CMBs are thought to constitute the pathophysiological connection or ''missing link'' between CVD and Alzheimer disease (AD) that may explain the frequent co-occurrence of these 2 entities.[1]

We conducted a literature review to gather data on the prevalence, localisation, and risk factors of CMBs, with a view to furthering our knowledge of the pathophysiology and the clinical and therapeutic implications of CMBs.

Definition and pathological substrate

CMBs are foci of haemosiderin-laden macrophages which appear on T2-weighted MRI sequences as black lesions, round or oval in shape, measuring less than 10 mm in diameter. The sequences used to detect CMBs, from most to least sensitive, are susceptibility weighted imaging (SWI), gradient-recalled echo-planar imaging (GRE-EPI), gradient-recalled echo (GRE), gradient echo (GE), and spin echo (SE). Sensitivity increases with accelerated high-spatial-resolution 3D imaging,[2] greater magnetic field strength, greater section thickness, and reduced distance between sections.[3] Diagnostic criteria for CMBs have changed over time; the criteria currently used were established by an expert group in 2009 (Table 1).[4] Precisely defining CMB size has no impact on detection, although microbleed size is standardised at 5-10 mm on T2-weighted GRE sequences.[5]

Table 1 Diagnostic criteria for cerebral microbleeds.

Black lesions, round or oval in shape
Visible on T2-weighted MRI sequences
Blooming effect
Do not appear hyperintense on T1- or T2-weighted sequences
At least half surrounded by brain parenchyma
Different characteristics from those of iron deposits, calcifications, bone, or blood vessels
Clinical history rules out traumatic diffuse axonal injury

Adapted from Greenberg et al.[4]
MRI: magnetic resonance imaging.

The first autopsy studies of CMBs were performed in patients who died due to intracerebral haemorrhage (ICH). According to these studies, vessels located near CMBs showed 2 distinct histopathological patterns: lipohyalinosis and cerebral amyloid angiopathy.[6]

Lipohyalinosis (also known as hypertensive microangiopathy or arteriolosclerosis) is a focal, segmental condition affecting vessel walls and associated with