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Lacunair Syndromes: An Updated Review

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Abstract

Cortical small vessel disease (CSVD) is the main cause of vascular dementia. However occlusion of a single perforating branch can lead to a lacunar syndrome (LS). Miller Fisher described 5 types of LSs: a pure motor stroke, a pure sensory stroke, a sensorimotor stroke and, the ataxic hemiparesis, and the dysarthria-clumsy hand types. Only the pure motor stroke had a favourable outcome. LSs are frequently progressive due to the extension of the occlusion to nearby branches. LSs can also be due to territorial infarcts in a minority of cases. Treatment modalities are not successful. Only prevention of the cardiovascular risk factors can slow down the occurrence of LSs. Mainly early treatment of arterial hypertension is important. Only acute Intravenous alteplase treatment seems to reduce the severity of the LS.

Keywords: Lacunar syndromes; Lacunar infarcts; Pure motor stroke; Pure sensory stroke; Sensorimotor stroke; Ataxic hemiparesis; Dysarthria-clumsy hand; Prevention; Treatment

Introduction

Lacunar syndromes (LSs) are due to small deep cerebral infarcts within the territory of a single perforating artery with a maximum diameter of less than 25 millimetres on neuro-imaging [1]. Cerebral small vessel disease (CSVD) causes 25% of the overall number of strokes [2]. The occurrence rate of vascular dementia due to lacunar strokes is 37% [3]. With an incidence of 15%, it is the second most important cause of dementia after Alzheimer's disease [4]. Asymptomatic lacunar infarcts (LIs) are 5 times more common than symptomatic ones. However, they must be considered as preceding risk factors for a stroke and cognitive impairment leading to dementia [5].

In the 1960s, C Miller Fisher performed autopsy studies showing that vessels supplying LIs display segmental arteriolar disorganization, characterized by vessel enlargement, haemorrhage and fibrinoid deposition, that he called "lipohyalinosis" [6]. However, still a minority of LIs is suspected to be due to a cardiac embolic source or to a symptomatic carotid stenosis [7-9].

CSVD is not only responsible for LIs but also for ischemic white matter changes [10,11]. Magnetic resonance imaging (MRI) shows very well the hyperintensive white matter changes, but probably underestimate the number of LIs [12]. Cerebral micro-infarcts are overall considered as the invisible lesions on MRI [13]. The present review will only discuss the LSs due to involvement of a single deep perforating branch as vascular dementia due to CSVD has been already extensively been discussed previously [14,15].

Vascular supply of lacunar infarcts

On post-mortem examination LIs, due to CSVD, are most observed in the lentiform nucleus (100%), followed by the thalamus (70%) and the internal capsule (55%). In the periventriclar white matter the incidence is 51% and in the caudate nucleus 41%. The lowest frequency is observed in the brainstem (19%) [16]. The lenticulo-striatal arteries, issued from the middle cerebral artery, supply the superolateral part of the caudate nucleus, the superior part of the internal capsule, most of the putamen and partly the globus pallidus. The perforating branches from the anterior cerebral artery perfuse the medial segment of the globus pallidus and the inferior part of the internal capsule [17]. The periventricular white matter is supplied in the

fronto-central part of the brain by ventriculofugal end-branches of the lateral lenticulo-striatal arteries, while in the parieto-occipital regions it is supplied by ventriculofugal branches issued from the choroidal arteries [18]. The thalamus is mainly supplied by performing branches, issued from the basilar artery, and from the posterior communicating and posterior cerebral arteries [19]. On post-mortem angiograms the deep perforating arteries are poorly filled and show several narrowing's and post-stenotic dilatations in brains with LIs. A responsible occlusion is observed in 80% of the lesions [20].

Risk Factors

CSVD is predominantly observed in aged patients with a strong previous history of early occurring adulthood vascular risks [21]. Arterial hypertension is the most established vascular risk factor for the occurrence of CSVD [22]. The incidence of white matter lesions is less severe in hypertensive adults with well-treated arterial hypertension compared to those in which the treatment was less severe and less well followed up [22]. Increased body mass index, cardiovascular disease, lack of physical activity, heavy alcohol consumption, smoking, hypercholesterolemia and diabetes are considered as additional risk factors when already occurring in young adulthood [23]. Atrial fibrillation and carotid stenosis are associated more with non-lacunar than with lacunar infarction [24]. Hyperhomocysteinemia has also been considered as an increased risk of LIs in the basal ganglia [25].

Clinical Syndromes

Miller Fisher described five types of classical clinical syndromes: pure motor stroke, pure sensory stroke, sensorimotor stroke, ataxic hemiparesis, and dysarthria-clumsy hand [26]. On MRI with diffusion-weighted imaging performed within 5 days after the appearance of the LS, only pure motor stroke correlated with the presence of the LI in the controlateral posterior limb of the internal capsule. In the other syndromes no clinico-neuroimaging correlation was observed [27]. Pure motor hemiparesis is observed in 57% of the LSs. Sensorimotor syndrome in 20%, ataxic hemiparesis in 10%, pure sensory syndrome in 7% and dysarthria-clumsy hand syndrome in 6% are the incidences in the remaining types [28]. The pure motor stroke involves to the same degree the face, the arm and the leg. Although the main location is the internal capsule, a minority is due to a pontine lacuna. The long-term prognosis is excellent with in the majority of cases a complete recovery within six months [29].

The pure sensory stroke syndrome is difficult to delineate because the symptoms are mainly subjective, linked to the thalamus [30]. Also cases of pure sensory stroke due to a pontine lacunes have been described [31,32]. Sensorimotor stroke is the most difficult defined LS as additional cortical signs cannot always been excluded clinically. Both equal sensory and motor involvement of the face, the arm and the leg with exclusion of cortical participation have to be confirmed mainly by neuroimaging techniques [33]. The atactic hemiparesis syndrome presents with cerebellar ataxia and with pyramidal signs involving the limbs at the same side [34]. The LI is limited to the basis pontis, opposed to the clinical symptoms [35]. Dysarthria-clumsy hand syndrome has similarities with the atactic hemiparese syndrome: moderate weakness of the face, and upper and lower limbs, moderate dysarthria and dysmetria, Babinski sign and, slight dragging and imbalance of the leg on the right side. Fisher found a 5 mm lesion in the pons on the side opposed the clinical deficit [36]. Also other sides have been observed [37,38]. Pseudo-lacunar syndromes have as well been described. However the extreme variety of the symptoms makes their inclusion as LSs highly improbable [39].

Outcome

When comparing visible symptomatic LIs on CT scans the average size of the lesions is smaller in the independent patients compared to in those with a remaining handicap. The LI decreases in average size from day 3 to 10 in the former group but remains unchanged in the group of still disabled patients [40]. LSs are a major cause of progressive motor deficits, probably because of stepwise occlusion of the branches of small perforating arteries [41]. LIs are more frequently progressive than large artery disease and cardio-embolism. Their pattern varies according to the location of the LI [42]. However, the main risk in patients with LIs is the progressive cognitive impairment, eventually leading to vascular dementia [43]. From the onset on LIs are associated with a moderately increased overall mortality compared to the normal general population. Post-stroke mortality risks from LIs associated to atherothrombotic and cardio-embolic strokes are significantly higher [44]. The mortality rate after a mean follow-up of 3.6 years is 1.78% [45].

Prevention and Treatment

The most widely accepted approach to prevention and treatment is to intensively control of the well-established vascular risk factors, of which arterial hypertension is the most important [2]. Antithrombotic treatment with aspirin has not been effective in the long-term lacunar stroke prevention and treatment [46]. Addition of clopidogrel did not reduce the risk of recurrent LS [47]. However, it significantly increases the risk of bleeding and death [48]. Aspirin plus extended–release dipyridamole also is not found to be very effective [49]. On the other end, an effective treatment with intravenous alteplase in patients with imaging-defined acute LAs is observed, similar to those experienced in

other subtypes [50]. Oral anticoagulants and left atrial appendage closure do not prevent recurrence of single LIs [51].

Discussion

Lis not due to CSVD represent between 16 and 20% of patients with a LS history. They are mainly the result of embolism due to atrial fibrillation [52,53]. Seizures are not observed in patients with pure LSs [54, 55]. When occurring they only reflect the existence of an underlying neurodegenerative process that is responsible for mental deterioration [56]. Another disease with LIs and severe white matter changes is the cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) due to Notch3 mutation [57]. However, in this disease only mild gait disturbances are associated to the vascular cognitive deterioration [58].

Positron emission tomography (PET) can already demonstrate a global decrease of cerebral blood flow in patients with silent LIs [59]. No PET studies are available in patients presenting a solitaty LS. However, cerebral blood flow is lower in the cerebral cortex and the white matter of subjects with intensive white matter hyper-intensities on MRI [60]. In our study LSs due to LIs only represent 11% of the whole stroke population [27] instead of the 25% observed in a more recent study [27].

Disclosure

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