Multi-infarct dementia and Alzheimer disease, contribution of cerebral circulation ultrasonography to pathogenesis and differential diagnosis. Value of microembolisation

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Abstract

OBJECTIVES: Dementias are one of the most serious health and socioeconomic issues. Multi-infarct dementia (MID) and Alzheimer’s type dementia (AD) exhibit differences in cerebrovascular blood flow velocity profiles and in presence of microemboli, detected by transcranial Doppler sonography.

MATERIAL AND METHODS: A group of 77 persons was divided into 4 subgroups: 1. subgroup of patients with MID (n=19; 10 male and 9 female, mean age was 74.32±8.30 years); 2. subgroup of patients with AD (n=19; 11 male and 8 female, mean age was 70.37±8.75 years); 3. subgroup of patients with hypertension (n=19; 11 male and 8 female, age adjusted) and 4. sex and age adjusted control group (CG) of 20 persons without hypertension or other serious risk factors. The duplex ultrasonographic examination of extracranial and intracranial circulation was preceded by neurologic, neuropsychological and psychiatric examination. The presence of microemboli was determined using Multi Dop X2 device (maker DWL), 60 minutes monitoring. All patients underwent brain computer tomography (CT) or magnetic resonance imaging (MRI).

RESULTS: We found significantly higher incidence (68.4%, \( p=0.5267 \)) of asymptomatic microemboli in ACM in the group of patients with MID compared to the AD group, the group of patients with hypertension and CG.

CONCLUSION: The occurrence of “asymptomatic” emboli in the middle cerebral artery in patients with multi-infarct dementia is higher in the current study. Although these microemboli do not cause immediate symptoms, the evidence suggests, that they may be a risk factor for cognitive impairment, especially for multi-infarct dementia.
INTRODUCTION

Dementia is an acquired disorder of memory and other cognitive functions severe enough to impair activities of everyday life of the affected individual. Overall prevalence of dementia in general population is at least 1%, in persons over 65 years of age up to 10%, and with further increase in age dementia affects more than 30% of people over 80 years of age. The majority of dementias are caused by neurodegenerative diseases, mostly AD, which comprises 60–70% of all dementias; Lewy body disease, rarer are frontotemporal dementia and dementia in Parkinson’s disease and other neurodegenerative diseases (Križová et al. 2013). Vascular, or MID is the basis of up to 30% of all dementias and prevails among secondary dementias. One of the main risk factors of degenerative diseases of nervous system is age (Růžička 2010).

An early diagnosis of dementia, it’s distinguishing from other mental disorders, and detection of the underlying cause is important, because of the benefits of early symptomatic treatment, which can thus reduce social consequences of dementia. The diagnosis is based on patient history – most often from people in close contact with the patient, clinical and psychological examination of the patient, supplemented by biochemical and genetic examinations. In nerve system imaging the most commonly used methods are CT and MRI, which can detect possible cause of secondary dementia or other specific abnormalities, which can point to specific disease accompanied by dementia. Function imaging such as PET – positrone emission tomography SPECT – single photon emission tomography, function MRI or protone MRI spectroscopy can depict areas of reduced brain metabolism, even before atrophic changes, detectable by structural imaging methods, take place (Kollár et al. 2012). Examination of cerebrospinal fluid (CSF) and electroencephalogram (EEG) complete the range of examinations (Brežný et al. 2002). Brain biopsies are carried out only rarely in cases of otherwise unverifiable suspicion, which presents a possibility of treatable cause of dementia. In other cases it is possible to obtain the definite diagnosis through histopathological examination post mortem (Růžička 2010).

Ultrasonographic examination of brain circulation maps structural and functional parameters of cerebral extra- and intracranial circulation in a non-invasive way. Embolidetection (using transcranial Doppler -TCD monitoring) detects possible microembolization into brain circulatory system (HITS – high intensity transient signal). The source of these are most commonly atherosclerotic plaques in magistral arteries or a source in central circulation – thrombus in heart compartments. Embolidetection demands suitable scanning conditions (good echogenicity in transtemporal access – temporal bone area in front of and over ear lobe). The monitoring itself is carried out on patients in supine position with fixed TCD probe, during half up to one hour. The mean diameter of middle cerebral artery (arteria cerebri media – ACM) in the region of transtemporal access is 2.7 mm (range 1.5 to 3.5 mm). The diameter of anterior cerebral artery (ACA) is in the range 0.7–3.75 mm (mean 2.1 mm). The mean values of diameter of posterior cerebral artery (arteria cerebri posterior ACP) are 2.1 mm (0.7–3.0 mm) before connecting with a. communicans and 2.3 mm (1.2–3.0 mm) after the juncture (Šklovidík et al. 2003). Most of the microemboli (HITS) do not reach these sizes, and they remain clinically silent. Neuropsychiatric disorder and even cerebral ischemia can arise after repeated embolization.

Distal intcranial microangiopathy manifests in TCD as a rise in peripheral resistance in all arteries (PI index >1.0), and as a lowered function reactivity to changes in pCO$_2$ (Provinciali et al. 1990) in correlation to patient’s age. There are documented reports (Grossman et al. 1996) of markedly worse functional reactivity together with elevated indexes of peripheral resistance in vascular disorders and also in Alzheimer’s disease.

The aim of this work was to asses the ultrasonographic characteristics of cerebral circulation, using TCD to detect the presence of cerebral emboli in middle cerebral artery (ACM) and to determine the probable source of embolisation in patients with presumed MID and AD.

METHODS

A group of 77 persons was divided into 4 subgroups: 1. subgroup of patients with MID (n=19; 10 male and 9 female); 2. subgroup of patients with AD (n=19; 11 male and 8 female); 3. subgroup of patients with hypertension (without signs of neurodegenerative disease) (n=19; 11 male and 8 female) and 4. sex and age adjusted control group (CG) of 20 persons. The CG did not include patients with either hypertension, diabetes or other serious risk factors. The mean age of patients with MID was 74.32±8.30 years, in the AD group the mean age was 70.37±8.85 years. At the time of examination patients were receiving complex therapy, including besides phamacotherapy also psychotherapy and rehabilitation of physical functions. Patients were examined at early stages and in moderate phases of dementia.

The duplex ultrasonographic examination of extracranial and intracranial circulation was preceded by neurologic, neuropsychological and psychiatric examination. Evaluation of presence of microemboli was carried our according to basic identification protocol (unidirectional/monophasic signal with duration of 300 ms, amplitude higher by 3 dB and characteristic acoustic signal component).

The presence of microemboli was determined using Multi Dop X2 device (maker DWL) during 60 minutes long monitoring. The patient was supervised during the whole period of monitoring to eliminate presence of artifacts, most commonly caused by movements of
the patient’s head. In cases where microemboli were detected, the patient underwent echocardiographic examination. To assess brain structure, all patients underwent brain CT or MRI.

RESULTS

We found significantly higher incidence (68.4%, p=0.5267) of asymptomatic microemboli in ACM in the group of patients with MID compared to the AD group, the group of patients with hypertension and CG (Table 1). The probable source of embolisation in patients with MID was a stenotic process in carotic arteries (n=8), and in lesser extent of cardiac origin (n=5). In the AD group cardioembolism was suspected in one patient, and carotic stenosis in two cases. In the control group and in patients with hypertension carotic stenosis was considered the source of emboli in cases of detected cerebral embolism.

DISCUSSION

Multi-infarct dementia and Alzheimer’s dementia are diseases of higher age. Their ethiopathogenesis is not yet completely understood (Victoroff et al. 1995; Sabri et al. 1999; Skoog et al. 1999; Purandare et al. 2006). Several literary sources hint, that ultrasound examination with implementation of embolidetection has a significance in diagnostics of these diseases. Föerstl and colleagues have already in 1989 assumed an affection of small vessels of brain circulation in patients with MID (Foerstl et al. 1989; Biedert et al. 1993, 1995; Sattel et al. 1996). Italian authors stress changes of vascularity in patients with MID and AD (Matteis et al. 1998). In order to evaluate the impairment of microcirculation Puls et al. recommend carrying out ultrasound examination with assessment of cTT (arteriovenous cerebral transit time), a method, which requires administration of contrast substance (Puls et al. 1999). Presence of cerebral embolisation is considered a prognostic factor of stroke. Embolisation has been seen lately as a causal factor of damages of neuropsychic functions after surgeries on heart and vessels (Declunder et al. 1998; Fearn et al. 2001; Russel 2002; Stygall et al. 2003; Pazderova et al. 2014a,b; Žitkanová et al. 2014). Anatomic pathology studies (Fisher 1969; Liston & La Rue 1986; Hofman et al. 1995; Pasquier et al. 1998; Behrouz et al. 2012) mention multiple occlusions of cerebral microcirculation or its focal dilatation caused by microembolisation. Multiple, especially continuous, “asymptomatic” cerebral microemboli can be also a cause of gradual changes of neuropsychic functions, and can be a risk factor not only for ischemic stroke, but also for cognitive impairment (Russell 2002; Pancák et al. 1996; Pancák et al. 1998).

Results of this work concerning especially patients with MID also confirm these assumptions. In patients with AD a more complicated ethiopathogenesis is presupposed; one in which changes in microcirculation are considered not prominent but rather supplementary.

CONCLUSION

In conclusion it is possible to sum up, that results of this work point to higher incidence of “asymptomatic” microemboli in the middle cerebral artery in patients with multi-infarct dementia. We assume, that the presence of microemboli can present a risk factor for multi-infarct dementia. Possible means of influencing the course of the disease are searching for the source of embolisation, and its treatment.

REFERENCES
