Correlations of Sonographical, Surgically Found and Morphological Characteristics of Atherosclerotic Plaques in Patients with Asymptomatic and Symptomatic Carotid Artery Stenosis

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Sonographical, surgically found and morphological characteristics of atherosclerotic plaques from 80 patients with stenosis of carotid artery in the asymptomatic (A = 11) and symptomatic (S = 69) course of the disease were compared.

In 20 patients (25%) fibrous or homogeneous and in 60 (75%) heterogeneous plaques were found morphologically and were subdivided into three and five subtypes according to differences in their morphological and sonographical characteristics.

Three subtypes of fibrous or homogeneous plaques (25%) were composed of fibrous cap only (first subtype), fibrous cap and atheroma (second subtype) and fibrous cap, atheroma and a lot of foam cells *(*third subtype*)* were found to have different thickness, and the degree of carotid stenosis was much higher in the third subtype. Complicated homogeneous plaques were found mainly in patients with the S course of the disease. Critical degree of carotid stenosis and slight (less than 2 mm) thickness in complicated homogeneous atherosclerotic plaques is a dangerous sonographical limit to cerebral ischemic stroke correlated with ulceration and fissuring, foam cells, large deposits of calcifications more frequent in S patients.

Heterogeneous plaques consisted of a fibrous cap without atheroma (first subtype*)* or with atheroma (second subtype), both infiltrated with lymphocytes and macrophages or with plasma cell (third subtype) and activated by polymorphs (PMN) and foreign body macrophages (fourth subtype) and a lot of foam cells (fifth subtype). The first subtype was evaluated as an early type of the development of plaques and the others as having chronic inflammation of cellular and humoral immune reactivities and markers of activation of chronic inflammation (PMN), phagocytosis (foreign body macrophages) and atheromatosis (foam cells) and representing a consistent inflammatory sequence of events leading to the development of heterogeneous plaques. A high or critical degree of stenosis and moderate to high mean values of thickness of plaques prevail in most subtypes (with the exception of the first) of heterogeneous plaques.

About 30% in A and 40% in S patients heterogeneous plaques were complicated. Critical degree of stenosis and thickness of plaques less than 2.44 mm in most complicated heterogeneous plaques of the second subtype are a dangerous sonographical limit in A and S patients. Intraplaqueal haemorrhages, chronic inflammation with PMN, foreign body macrophages, and foam cells without or with only small diffuse calcificates in A patients provide favourable conditions for cerebral ischemic stroke.

Heterogeneous plaques are much more dangerous than homogeneous for the development of ischemic cerebral stroke in patients with the both courses of the disease.

Key words: atherosclerosis, a. carotis, sonography, morphology

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INTRODUCTION

Every year thousands of people develop acute ishemic cerebral stroke which is the second leading cause of death according to frequency. A risk of the development of acute ischemic cerebral stroke increases with the degree of carotid artery stenosis which diminishes cerebral perfusion by narrowing the main or by embolising the smaller arteries. Frequently ulcerated and fissured atherosclerotic plaques from the inner carotid wall become unstable and are the main source of microemboles. Therefore a correlation of clinical and morphological characteristics of unstable carotid atherosclerotic plaques is very important for evaluating cerebral vascular disturbances before developing an acute cerebral stroke and can contribute to the prevention of hazardous invalidation and death, especially in patients with the asymptomatic course of the disease.

PATIENTS AND METHODS

Sonographical, surgically obtained and morphological characteristics of atherosclerotic plaques from 80 patients with stenosis of the carotid artery of both courses, *asymptomatic* (A = 11) and *symptomatic* (S = 69), A/S correlation 1:6, were studied. The mean age of patients was 66.8 years, the male/female ratio 3.7:1. The mean age of men was 65.2 and of females 70.3 years, *i.e*. men were 5 years younger. Upon evaluation of patients' complaints and suspecting a narrowing of the carotid artery, double scanning sonography, angiography of extracranial carotids and of aortic arch with its branches were performed and clinically evaluated before surgical treatment. Atherosclerotic plaques removed in endarterectomies were studied morphologically. Fixed in 10% neutral formaline after dehydration, the plaques were embedded into paraffin. Slices 4 microns thick were stained with hematoxyline-eosine, van Giesone and picrosyrius red solutions. Histopathological changes scored separately from 0 (normal) to 3 (severe) points and the frequency of atherosclerotic plaques in A and S patients were evaluated and correlated with clinical sonographical (before) and surgical (found during endarterectomy) data.

RESULTS

Clinical-sonographical characteristics of atherosclerotic plaques in carotid artery

Two sonographical characteristics – the degree of carotid stenosis and the thickness of atherosclerotic plaques in patients with A and S courses of the disease were examined. The degree of carotid stenosis in A and S patients is shown in Table 1.

Table 1. **Degree of carotid stenosis in asymptomatic (A) and symptomatic (S) patients**

Degree of stenosis %	A patients	S patients	A/S correlation
50–59 ≥50	2/11 (18.2%)	2/69 (2.9%)	6/1
60–69 ≥60	0/11 (0%)	7/69 (10.15%)	0/10
70–79 ≥70	2/11 (18.2%)	8/69 (11.6%)	1.6/1
80–89 ≥80	1/11 (9%)	14/69 (20.3%)	1/2.25
90–99 ≥90	2/11 (18.2%)	25/69 (36.2%)	1/2
99 ≥100	4/11 (36.4%)	13/69 (18.8%)	2/1

A 50% stenosis does not induce any symptoms, and only very sensitive patients (2.9%) had symptoms (S). The symptoms were expressed when carotid stenosis reached more than 60% in S patients (A/S 0/10), therefore not a small group with a high (70–80%) and critical (90–100%) degree of carotid stenosis (54.6%) without symptoms (A patients) was found (A/S correlation in patients with such a degree of stenosis was about the same, Table 1). So, the degree of carotid stenosis was found to be more severe in S patients, but there is not a small group of patients with a high and critical degree of stenosis (54.6%) that have no symptoms (A patients), especially when the atherosclerotic disease is diffuse.

Thickness is another sonographical characteristic of atherosclerotic plaques. The thickness of 3.1–4 and 5.1–6 mm of atherosclerotic plaques prevailed in S patients, while in A patients plaques less than 2 up to 3 mm thick were dominanted (Table 2).

An exception was a plaque 7.9 mm thick in the carotid artery of a 52-year-old A patient in whom four arteries (renal, aorta, carotid and hip) were operated on because of stenosis caused by diffuse atherosclerotic disease. Thus, atherosclerotic plaqu-

Table 2. **Thickness of atherosclerotic plaques in carotid artery in patients with asymptomatic (A) and symptomatic (S) stenosis**

Thickness of atherosclerotic plaque, mm	A patients	S patients	A/S correlation
up to 2	3/11 (27.3%)	22/69 (32%)	1/1
2.1–3	6/11 (54.5%)	18/69 (26%)	2/1
3.1–4	0/11 (0)	17/69 (24.7%)	0/25
4.1–5	1/11 (9%)	7/69 (10%)	1/1
5.1–6	0/11 (0)	4/69 (5.8%)	0/6
6.1–7	0/11 (0)	1/69 (1.4%)	0/1
7.1–8	1/11 (9%)	0/69 (0)	9/0

es are thicker (3–7 mm) in S patients and thinner (1–3 mm) in A patients, except very thick plaques in A patients with a diffuse atherosclerotic process in many arteries. A high degree of stenosis in the carotid artery and atherosclerotic plaques less than 2 and up to 3 mm thick are not always associated with symptoms and do not prevent A patients from an increased risk of cerebral stroke.

Clinical-surgical characteristics of atherosclerotic plaques in carotid artery

As revealed by surgical examination, heterogeneous atherosclerotic plaques very often (75 from 80 patients in the study cohort) were found in both courses of the disease and distributed almost equally in A (10/11, or 90.9%) and in S patients (65/69, or 94%), A/S = 1:1. Only 5 homogeneous plaques from 80 patients determined upon surgical examination (in A 1/11, or 9.1% and in S 4/69, or 5.7% patients) were found in carotid arteries (correlation of homogeneous/heterogeneous plaques in A/S patients was 1:1.5). Ulcerated plaques (16/80) were prevailing in S patients (15/69 /, or 21.7%) and in A (1/11, or 9%), A/S correlation 1/2.4. Fissuring plaques (5/80) were found only in S patients (0/6). Both characteristics (ulcerations and fissuring) were observed in complicated plaques (Table 3).

So, according to surgeon's evaluation heterogeneous atherosclerotic plaques were predominant in both courses of the disease, but heterogeneous pla-

Table 3. **Surgical characteristics of atherosclerotic plaques in the carotid artery of patients with asymptomatic (A) and symptomatic (S) course of the disease**

Surgical characteristics	A patients	S patients	A/S
Ulceration	1/11 (9%)	15/69 (21.7%)	1/2.4
Fissures	0/11 (0)	5/69 (7.2%)	0/7
Homogeneous	1/11 (9%)	4/69 (5.7%)	1.6/1
Heterogeneous	10/11 (91%)	65/69 (94%)	1/1

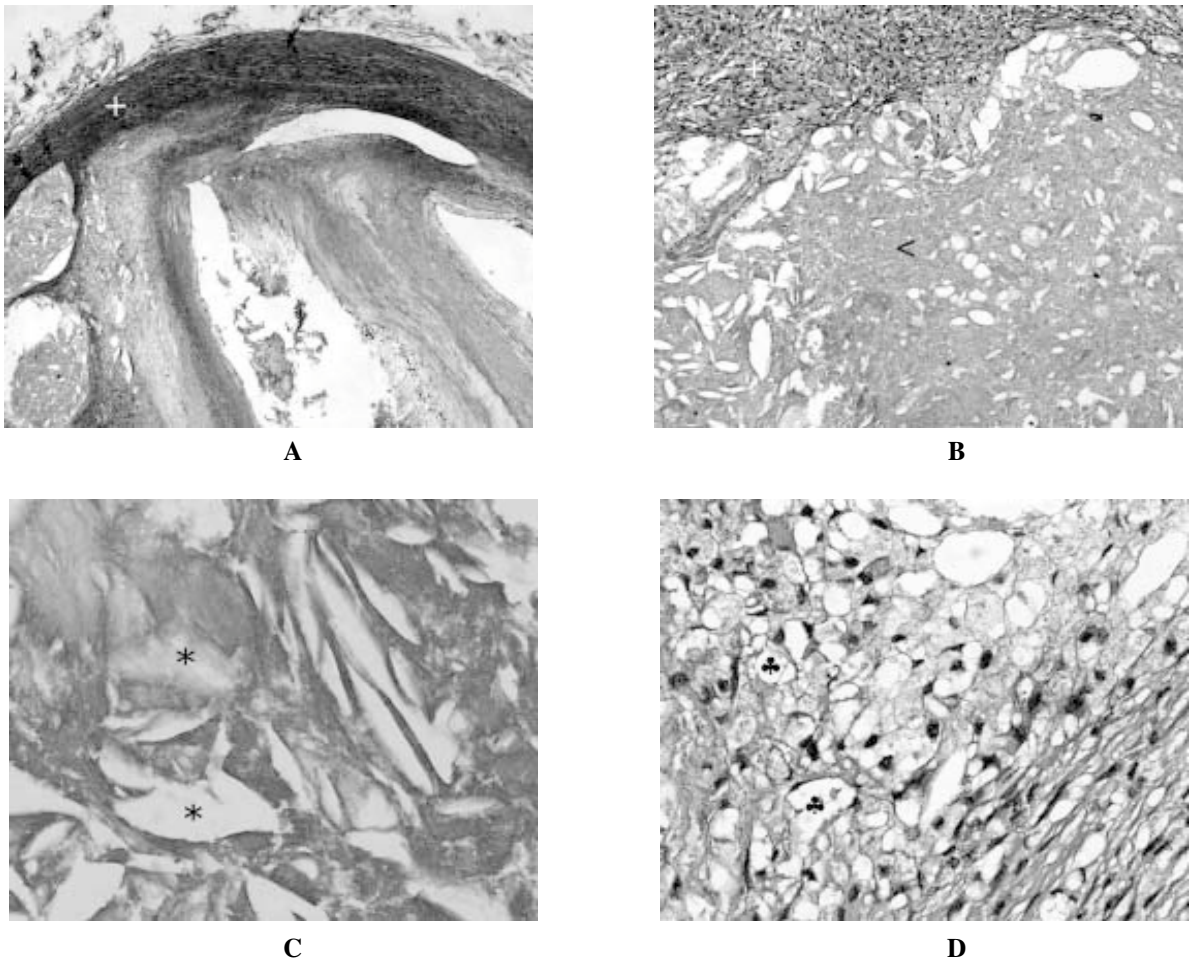

Fig 1. Fibrous or homogeneous atherosclerotic plaques. Fibrous cap (+) without (A) and with (B, C) atheroma (<) and crystals of cholesterol (*) and infiltrated by foam cells (♣) (D). Hematoxylin eosin. × 600

ques with ulcers and fissures were slightly more frequent in S than in A patients. Homogeneous plaques were very rare (5 cases) in both courses of the disease, and ulcer was concomitant only in one A patient. So surgical evaluation of atherosclerotic plaques does not coincide with the morphologically found characteristics of plaques because of considerable interobserver variations in the interpretation of the key characteristics of plaques in predicting stenosis.

Morphological characteristics of atherosclerotic plaques in the carotid artery of A and S patients

According to morphological characteristics, fibrous atherosclerotic plaqu's have a stiff fibrous cap (capsule) consisting of a dense connective tissue matrix with smooth muscle cells and a necrotic core (atheroma) containing dead cells, amorphous lipid masses, crystals of cholesterol, lipid-laden foam cells, plasma proteins and calcificates (Fig. 1, A, B, D).

According to a summary description of morphological characteristics of atherosclerotic plaques, 20 fibrous or homogeneous plaques impregnated by amorphous masses of lipids, crystals of cholesterol, foam cells and diffuse calcificates of 1–2 score without any inflammatory cell were found in our 80 patients (in A 1/20, in S 19/20) and may be ascribed to stable plaques (Table 4).

An other group of plaques that contained a tiny fibrous cap impregnated by atheroma as well as calcificates of average and large depositions (2 and 3 scores) and were infiltrated by chronic inflammatory cells (lymphocytes, macrophages and plasma cells) nearly equally distributed in the carotids of A and S patients were determined as heterogeneous and unstable.

Table 4 shows that histopathological signs of complicated plaques such as ulceration and fissuring, foam cells, large deposits of calcifications were more frequent in S patients. Pathological signs such as intraplaqueal haemorrhages, foreign body macrophages and infiltration with polymorphonuclear cells with no or only small diffuse calcificates were a sign more characteristic of plaques in the carotid artery of A patients. So part of atherosclerotic plaques in S and A patients was complicated and may be ascribed to extremely unstable plaques. Patients having complicated plaques are constantly at risk of developing acute cerebral stroke. Three plaques in S patients were recanalized by angiomatous proliferation.

Subtypes of fibrous or homogeneous atherosclerotic plaques (20 patients)

According to morphological signs, three subtypes of fibrous or homogeneous plaques were found (Table 5), characterized by a different degree of carotid stenosis and thickness of plaques.

The first subtype was composed only of fibrous cap (FC) without atheroma (AM), (4/20:1 in A and 3 in S patients), the second consisted of FC with AM (14/20) only in S patients, and the third had FC, AM and foam cells (2/20) in S patients. All subtypes of fibrous plaques contained no inflammatory cells and had a different thickness and degree

Table 4. **Frequency of morphological characteristics of atherosclerotic plaques in carotid arteries of patients with asymptomatic (A) and symptomatic (S) course of disease**

Morphological characteristics of atherosclerotic plaques		A patients	S patients	A/S correlation
Fibrous cap		11/11 (100%)	69/69 (100%)	1/1
Atheroma		11/11 (100%)	61/69 (88.4%)	1/1
Intraplaqueal haemorrhages (thrombus, haemosiderine, siderophages)		6/11 (54.5%)	27/69 (39.1%)	1.4/1
Angiomatosis (neovascularization)		0/11 (0)	3/69 (4.3%)	0/4
Inflammatory cells:	lymphocytes	7/11 (63.6%)	37/69 (53.6%)	1/1
	macrophages	8/11 (72.7%)	38/69 (55.1%)	1.3/1
	foreign bodies macrophages	1/11 (9%)	1/69 (1.4%)	6/1
	foam cells	0/11 (0)	8/69 (12%)	0/11.6
	plasma cells	1/11 (9%)	5/69 (7.2%)	1.25/1
	PMN	1/11 (9%)	2/69 (2.9%)	3/1
	eosinophils	0/1 (0)	1/69 (1.45%)	0/1.5
Score of calcification	1	3/11 (27.3%)	9/69 (13%)	2/1
	2	4/11 (36.4%)	51/69 (74%)	1/2
	3	1/11 (9%)	9/69 (13%)	1/1.4

Table 5. **Degree of carotid artery stenosis and thickness of fibrous atherosclerotic plaques in asymptomatic (A) and symptomatic (S) patients**

Subtype of plaques	Degree of stenosis % (mean)		Thickness mm(mean)		Complicated n		Total n
	A	S	A	S	A	S	
FC	50	77.66	2.8	1.82	0	0	4/20
FC + AM	0	81.21	0	2.15	0	5	14/20
FC + AM + Foam Cells	0	80	0	3.32	0	0	2/20
Total count of fibrous plaques							20/80 (25%)

of stenosis in the carotid as measured sonographically. The first subtype of plaques was somewhat thicker in A patients, but the degree of carotid stenosis in A patients was less than 50%. S patients had thinner plaques, but the higher degree of stenosis in the carotid (about 78%). So, symptoms in patients depended on the degree of stenosis but not on the thickness of plaques, and according to morphological signs the first subtype of fibrous plaques can be evaluated as an early consequence of the development of fibrous plaques. The second subtype that consisted of fibrous cap and atheroma was thicker than the first and had a high degree of carotid stenosis (81.21%) in S patients, but was not found in A patients. The third subtype consisting of fibrous cap, atheroma and a lot of foam cells was thickest (3.32 mm), had a high degree of stenosis (80%) in the carotid of S, but was not found in A patients. So foam cells may be a prerequisite to the thickness of plaques because of their ability to split the complexes of CRP and low density lipoproteins (LDL) circulating in the blood of patients with atherosclerosis.

Five fibrous or homogeneous plaques (25%) with deformations, ulcers, haemorrhages, fresh and older (granules of haemosiderin and siderophages), were evaluated as complicated and were found only in patients with the S course of the disease. According to the functional-morphological status, fibrous or homogeneous plaques represent stable atherosclerotic plaques, but complicated homogeneous plaques were found in S patients at an extremely high risk of ischemic cerebral stroke.

Subtypes of heterogeneous atherosclerotic plaques (60 in 75% of patients)

The second type of heterogeneous plaques in our cohort of patients was found very frequently and correlated in A/S patients as 1/3. It had a very tiny FC and a core impregnated with AM masses, crystals of cholesterol and a lot of lymphocytes (L), macrophages (M), plasma cells (representing chronic inflammation) and polymorphonuclears (PMN) evaluated as markers of the activation of a chronic inflammation (Fig. 2A, B, C, D).

According to the type of infiltrated inflammatory cells, heterogeneous plaques can be subdivided into 5 subtypes: first, FC without AM infiltrated with lymphocytes (L) and macrophages (M) representing cellular immune reactivity; second, FC with AM infiltrated with L and M which represents the prevalence of cellular immune reactivity, too; third, FC with AM infiltrated with L, M and plasma cells representing humoral immune reactivity; fourth, FC with AM infiltrated with L, M, PMNs (markers of the activation of a chronic inflammation) and foreign body macrophages (markers of the activation of phagocyte function induced by viruses); fifth, FC with AM infiltrated by L, M and a lot of foam cells (markers of atheromatosis) which, as mentioned above, are able of splitting the circulating complexes of CRP and low density lipoproteins in the bloodstream. All subtypes of heterogeneous plaques have a different degree of carotid stenosis and thickness of atherosclerotic plaques (Table 6).

As is evident, the first subtype was thinner (mean thickness 1.05 mm) and form a moderate degree of carotid stenosis in S patients only and may represent an early stage of the development of heterogeneous atherosclerotic plaques. All other subtypes with AM and chronic inflammatory cells representing cellular and humoral immune reactivities and morphological signs of activation of the chronic inflammation and phagocytosis as well as atherogenesis formed a high or critical degree of carotid stenosis and had moderate to high mean values of thickness. The thickest were plaques with foam cells (making up to 13% of heterogeneous type) which favour plaque thickening.

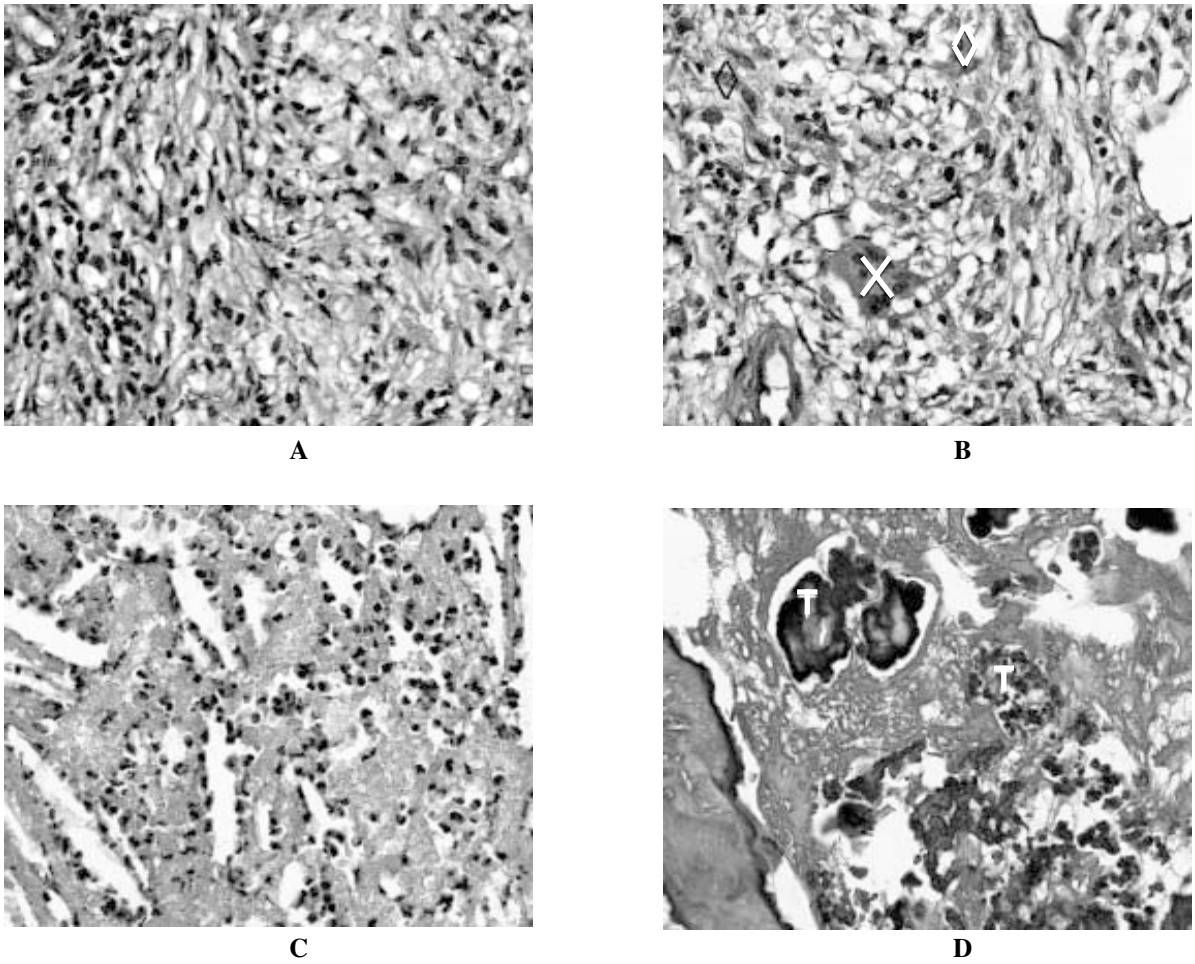

Fig. 2. Heterogeneous atherosclerotic plaques. A – heavy infiltration with lymphocytes and macrophages, B – chronic inflammation activated by foreign body macrophages (×) and siderophages (◊), C – a lot of PMN and erythrocytes, D – large deposits of calcifications (T). Hematoxylin eosin. ×600

Table 6. **Degree of carotid stenosis and thickness of heterogeneous atherosclerotic plaques in asymptomatic (A) and symptomatic (S) patients**

Subtype of plaques	Degree of stenosis % (mean)		Thickness mm (mean)		Complicated n		Total n
	A	S	A	S	A	S	
FC + L + M	0	66.66	0	1.05	0	0	2
FC+ AM + L + M	87.88	88.03	2.22	2.46	3	13	41
FC + AM + L + M + plasma cells + siderophages	0	87.25	0	1.82	0	2	4
FC + AM + L + M + PMN + foreign body macrophages	77	92	1.87	2.74	0	2	5
FC + AM + L + M + foam cell	0	88.88	0	3.22	0	3	8
Total count of heterogeneous plaques	10	50			3(30%)	20(40%)	60/80 (75%)

A lot of complicated plaques were found in the heterogeneous type (with deformations, ulcers, fresh and older haemorrhages), which were almost equally distributed in A (30%) and S (40%) patients.

Table 7. **Clinical and morphological characteristics of complicated atherosclerotic plaques in patients with asymptomatic (A) and symptomatic (S) courses of the disease**

Type of plaque/ sonographical characteristics	Subtype of homogeneous plaques			Subtype of heterogeneous plaques					Total n
	1	2	3	1	2	3	4	5	
Stenosis, % (mean)									
A	0	0	0	0	89.7	0	0	0	
S	0	93.75	0	0	90.8	99.5	91.0	89.3	
Thickness, mm (mean)									
A	0	0	0	0	2.46	0	0	0	
S	0	2.0	0	0	2.44	3.05	3.55	2.8	
A patients	0	0	0	0	3/10 (30%)	0	0	0	3
S patients	0	4	0	0	13/50 (26%)	2	2	3	24

Complicated heterogeneous plaques had heavy or diffuse calcifications which appear as very large loadings in all but frequently in the superficial layer. Very often local intraplaqueal thrombi, haemorrhages and medial thinning predisposing of cholesterol microemboli or aneurysm dilatation (deformations) were found. According to summarised morphological characteristics (Table 3), ulcerated (2.4:1) plaques prevailed in S, but fissured ones (O:7) together with intraplaqueal fresh haemorrhages were more frequent in A patients (A/S as 1.4:1). Local thrombi (old haemorrhages with haemosiderin) were equally distributed in A and S patients (1:1). According to functional-morphological characteristics, heterogeneous plaques are unstable plaques, and heterogeneous complicated plaques are extremely hazardous for cerebral ischemic stroke and even death of patients.

To avoid the risk of acute ishaemic cerebral stroke in A and S patients, it is important to compare the clinical (sonographical) and morphological characteristics of complicated plaques (Table 7). Four fibrous or homogeneous plaques 2.0 mm thick, with the critical degree of carotid stenosis and the second subtype of plaques (consisting of FC impregnated heavily with AM) with ulcers, deformations and haemorrhages in S (20%) patients only were ascribed to *complicated*.

Most complicated heterogeneous plaques of the second subtype (Table 6) and almost equally distributed in A (30%) and in S (26%) patients were 2.44–3.55 mm thick, and the degree of carotid stenosis was critical.

The critical degree of carotid stenosis and a slight (below 2 mm) thickness in the complicated homogeneous type of atherosclerotic plaques are dangerous sonographical limits of cerebral ishemic stroke only in S patients.

The critical degree of stenosis and the thickness of plaques over 2.44 mm in most complicated heterogeneous plaques of second subtype are dangerous sonographical limits of cerebral ishemic stroke both in A and in S patients.

Thus a high degree of carotid stenosis observed sonographically, together with core infiltration by atheroma and morphological signs of activation of chronic inflammation, phagocytosis and atheromatosis in plaques, plays a crucial role in the development of complications and instability of plaques, favouring the development of cerebral ischemic stroke.

DISCUSSION

A correlation of clinical and morphological characteristics of atherosclerotic plaques is very important not only for the evaluation of cerebral vascular disturbances before the acute cerebral stroke is developed, but also for determining what type of plaques is more dangerous for the development of complications and instability. In 80 patients of the study cohort the average age was 66.8 years, men prevailed as 3.7:1 and were 5 years younger than the female patients. So atherosclerosis of carotid arteries is a disease of relatively middle-aged patients, mostly men. Therefore in 14% of patients the atherosclerotic disease of carotid arteries is asymptomatic (A = 11), but in 86% it is symptomatic (S = 69), and A/S 1:6. According to sonographical characteristics of carotid arteries we found that atherosclerotic plaques (3–7 mm) were thicker in S patients and thinner (1–3 mm) plaques prevailed in A patients, except very thick plaques in A patients with a diffuse atherosclerotic process in many arteries. According to our data, a high degree of carotid stenosis together with thickness of atherosclerotic pla-

ques 2 and 3 mm thick is not always associated with symptoms and does not prevent A patients from an increased risk of cerebral stroke. So sonographical data such as the degree of stenosis and thickness of plaques are very useful for the selection of patients for surgical treatment.

Clinical surgical evaluation of atherosclerotic plaques so far does not coincide with morphologically found characteristics and has a little value in the characterisation of plaques because of very subjective and not objective criterians of evaluation.

Upon morphological evaluation 20 fibrous or homogeneous (25%) and 60 heterogeneous (75%) plaques were found in 80 patients. The plaques were subdivided into three and five subtypes according to plaque morphology and the difference of sonographical characteristics.

Three subtypes of fibrous or homogeneous plaques composed of fibrous cap only (first subtype), fibrous cap and atheroma (second subtype), and fibrous cap, atheroma and infiltrated by a lot of foam cells *(*third subtype*)* have a different thickness and the degree of carotid stenosis. Both sonographical characteristics (thickress and stenosis) were much higher in the third subtype of plaques infiltrated by foam cells. A recent evidence suggests that CRP circulating in blood displays a calcium-dependent *in vitro* binding to low density lipoprotein (LDL) and induces uptake of native LDL by foam cells. Splitting the complexes of CRP and LDL, foam cells may be responsible for the higher thickness of plaques (1) in A and in S patients, as we found. Fibrous or homogeneous plaques are stable atherosclerotic plaques, but complicated homogeneous plaques were found in them, too (26%), mainly in patients with the S course of the disease. A critical degree of carotid stenosis and a slight (below 2 mm) thickness of atherosclerotic plaques are dangerous sonographical limits of complicated homogeneous atherosclerotic plaques leading to cerebral ischemic stroke found only in S patients. The thickness of fibrous cap and core with lipids may be similar to those of plaques of A and S, but position of the core and a local thinning of the cap may predispose to a fissuring of plaques (11).

In 60 patients (75%) heterogeneous plaques were determined (in 10 A and in 50 S patients*)*. The plaques consisting of fibrous cap without (first subtype*)* or with atheroma (second subtype), both infiltrated with chronic inflammatory cells (macrophages and lymphocytes) representing cellular or (with plasma cell) showing humoral immune reactivities (third subtype), with polymorphs (PMN) and foreign body macrophages (fourth subtype), and a lot of foam cells (fifth subtype) were determined morphologically. The first subtype was evaluated as an early type of the development of heterogeneous plaques and the fourth as having markers of the activation of chronic inflammation such as PMN. Activation of chronic inflammation means a finding of PMN in sites of inflammation. PMN is a cell extremely sensitive to the cytotoxins of various infectious agents and is a universal sign of the activation of chronic inflammation (10). So PMNs in atherosclerosclerotic plaque, together with clinical markers of inflammation such as CRP, might be indicators of an infective process and atherosclerosis may be an inflammatory lesion (2). CRP are intimately involved in one of the major cellular events – in formation of atherosclerotic lesions, namely monocyte infiltration (1). Recent publications have suggested a potential role of *Chlamydia pneumonia* and adenoviruses (herpes simplex virus type 1) in the development of immune inflammation, mechanisms and transport of infectious agents into the vascular wall and an important role of infective agents in the pathogenesis of atherosclerosis (3). Evidence for this includes a direct demonstration of the pathogen in atherosclerotic arteries (aorta, coronary, carotid, pulmonary, femoral and iliac) and plaques (4) as well as in sera of patients (5) and is implicated also in plaque instability. The adhesion of *C. pneumoniae*-infected circulatory component(s) to endothelium and smooth muscle cells represent the first step in an inflammatory response (6). Not only a viable pathogen, but also *C. pneumoniae* membrane protein was demonstrated in macrophages in advanced atherosclerotic lesions, but not in fatty streaks or normal arteries (7). Authors found similar staining patterns in macrophages in five carotid artery specimens, of which four were positive for *C. pneumoniae* membrane protein. So the presence of macrophages implies an inflammatory response and it is recognised that inflammatory changes could weaken the fibrous cap of plaque, predisposing it to rupture and thrombosis (8). Both types of plaques, homogeneous and heterogeneous, have an atheroma (fatty centre). But the fatty centres of unstable heterogeneous plaques are much larger and softer than those in stable homogeneous plaques, and fibrous caps are much thinner. Unstable plaques are swarming with T cells and macrophages, immune cells that cause inflammation and make these plaques even more unsettled. T cells stimulate smooth muscle cells in the fibrous cap to stop producing collagen and macrophages to produce enzymes that degrade collagen. This two-side attack on collagen thins off the fibrous cap until it breaks (9). The fibrous cap of heterogeneous unstable atherosclerotic plaques in S patients almost always is thinner, and the necrotic core infiltrated by lipids is located nearer to the fibrous cap. So, unstable plaque theory seems more likely to affirm many of the existing approaches, as our results do.

C. pneumoniae is a common respiratory pathogen which causes pneumonia, bronchitis and sinusitis (9) and can regionally spread to carotid and other arteries. Literature data show that the immune and microbial factors may play a role in the pathogenesis of atherosclerosis and cell proliferation in the injured vessel wall (5). The present data on the morphological and clinical (sonographical) characteristics of heterogeneous atherosclerotic plaques in the carotid artery of patients agree with the inflammatory sequence in morphologically determined subtypes leading to the development of unstable heterogeneous atherosclerotic plaques.

CONCLUSIONS

1. Sonographical, surgical and morphological characteristics of atherosclerotic plaques from 80 patients with carotid stenosis in asymptomatic (A) and symptomatic (S) courses of the disease were studied (A/S 1:6). The mean age of patients was 66.8 years, the mail/female ratio was 3.7:1, and men were on average 5 years younger than women.

2. The degree of carotid stenosis was more severe in S patients, but 30% of patients with high and critical degrees of stenosis and complications had no symptoms (A patients). Thicker atherosclerotic plaques (3–7 mm) had S while thinner (1–3 mm) had A patients (except very thick plaques in A patients with diffuse atherosclerotic disease). The high degree of carotid stenosis together with plaque thickness 1 to 3 mm is not always associated with symptoms (A patients).

3. Surgical evaluation of atherosclerotic plaques so far does not coincide with the morphological characteristics of homogeneous and heterogeneous plaques and is of a low value in their characterization.

4. Twenty fibrous or homogeneous (25%) and 60 heterogeneous plaques (75%) were found morphologically and subdivided into three and five subtypes according to differences in morphological and sonographical characteristics.

5. Three subtypes of fibrous or homogeneous plaques composed of fibrous cap only (first subtype), fibrous cap and atheroma (second subtype) and fibrous cap, atheroma and a lot of foam cells (third subtype) were found to be of different thickness, and the degree of carotid stenosis was much higher in the third subtype.

6. Fibrous plaques represent stable atherosclerotic plaques, but complicated plaques were found mainly in S patients. The critical degree of carotid stenosis and slight (below 2 mm) thickness of complicated fibrous plaques are dangerous sonographical limits to cerebral ishemic stroke and correlate with ulceration and fissuring, foam cells, large deposits of calcifications in the plaques.

7. Heterogeneous plaques were composed of fibrous cap without atheroma (first subtype) or with atheroma (second subtype), both infiltrated by lymphocytes and macrophages or plasma cells (third subtype) and activated by polymorphs (PMN) and foreign body macrophages (fourth subtype) and a lot of foam cells (fifth subtype). A high or critical degree of stenosis and moderate to high mean values of thickness prevailed in most subtypes of heterogeneous plaques (with exception of the first).

8. The first subtype was evaluated as early and others as having a consistent inflammatory sequence with markers of activation of chronic inflammation, phagocytosis and atheromatosis, which promote the development of heterogeneous atherosclerotic plaques.

9. About 30% of heterogeneous plaques in A and 40% in S patients were complicated. The critical degree of stenosis and the thickness over 2.44 mm were dangerous sonographical limits of complicated heterogeneous plaques mostly of the second subtype. Intraplaqueal haemorrhages, foreign body macrophages and infiltration with PMN without or only with small diffuse calcificates in complicated heterogeneous plaques of A patients favour the development of cerebral ischemic stroke.

10. Heterogeneous plaques represent unstable plaques and together with complications (signs of liability) are much more dangerous than homogeneous plaques in the development of ischemic cerebral stroke in patients of both courses of the disease.

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ULTRAGARSINIŲ, CHIRURGINIŲ IR MORFOLOGINIŲ POŽYMIŲ PALYGINIMAS ATEROSKLEROZINĖSE PLOKŠTELĖSE LIGONIAMS SU BESIMPTOME IR SIMPTOMINE MIEGO ARTERIJŲ STENOZĖMIS

S a n t r a u k a

Ištirtos 80-ies ligonių su besimptome (A) ir simptomine (S) miego arterijų stenozėmis (A/S 1:6) aterosklerotinių plokštelių ultragarsinės, chirurginės ir morfologinės charakteristikos.

20 (25%) homogeniškų ir 60 (75%) heterogeniškų plokštelių radome morfologiškai ištyrę plokšteles ligonių, sirgusių miego arterijų stenozėmis. Pagal plokštelių morfologines ir ultragarsines charakteristikas jos buvo suskirstytos atitinkamai į 3 ir 5 potipius.

Trys fibrozinių ar homogeniškų plokštelių potipiai, sudaryti vien iš fibrozinio dangtelio (pirmasis), fibrozinio dangtelio ir ateromos (antrasis) ir fibrozinio dangtelio, ateromos ir putotų makrofagų (trečiasis), pasižymėjo skirtingu storiu ir stenozės laipsniu didėjančia tvarka (didžiausias – trečiojo potipio plokštelėse). Komplikuotos homogeniškos plonos (iki 2 mm storio) plokštelės ir kritišku stenozės laipsniu miego arterijose, išopėjusios, su plyšimais, putotais makrofagais ir stambiais kalcifikatais buvo pavojingos ribos ischeminio smegenų insulto vystymuisi S ligoniams.

Heterogeniškų plokštelių, sudarytų iš fibrozinio dangtelio be ateromos (pirmasis), su ateroma (antrasis), abiejų infiltruotų limfocitais ir makrofagais arba ir plazminėmis ląstelėmis (trečiasis) ir aktyvuotų PMN bei svetimų kūnų makrofagais (ketvirtasis) ir su daugybe putotų makrofagų (penktasis), potipiai skyrėsi pagal plokštelių storį ir stenozės laipsnį. Aukštas ir kritiškas stenozės laipsnis miego arterijose ir vidutiniškos bei storos plokštelės buvo būdingos daugumai heterogeniškų plokštelių potipių, išskyrus pirmąjį, kurį vertinome kaip ankstyvąjį heterogeniškų plokštelių vystymesi. Kitų potipių heterogeniškos plokštelės buvo infiltruotos uždegimo ląstelėmis, rodančiomis ląstelinio (limfocitai, makrofagai) ar humoralinio (plazminės ląstelės) imuninio uždegimo nuoseklią seką su morfologiniais lėtinio uždegimo aktyvumo (PMN), fagocitozės aktyvumo (svetimų kūnų makrofagai) arba gilios ateromatozės (putoti makrofagai) žymenimis. Apie 30% A ir 40% S ligoniams radome komplikuotas heterogeniškas plokšteles (su labilumo požymiais). Pavojingos ultragarsinės komplikuotų heterogeniškų plokštelių ribos buvo kritiška stenozė ir 2,44 mm plokštelės storis, o morfologiškai dažnas antras plokštelių potipis tiek A, tiek S ligoniams. Intraplokštelinės hemoragijos, lėtinis uždegimas su PMN, svetimų kūnų makrofagais ir putotomis ląstelėmis bei smulkiais difuziškais kalcifikatais ar be jų A ligoniams sudarė palankias ischeminio smegenų insulto vystymosi sąlygas.

Raktažodžiai: aterosklerozė, a. carotis, sonografija, morfologija