

Technetium-^{99m}Tc-HMPAO brain SPECT in antiphospholipid syndrome — preliminary data

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Abstract

BACKGROUND: Antiphospholipid syndrome (APS) is defined as the presence of repeated episodes of arterial or venous thrombosis, recurrent spontaneous abortions and thrombocytopenia in patients with elevated antiphospholipid antibodies. An important feature of APS are cerebrovascular disorders of thrombotic origin. The aim of the study was to assess cerebral blood flow changes utilising brain SPECT HMPAO scanning.

METHODS: Brain SPECT ^{99m}Tc-HMPAO scanning was performed in 20 patients with APS: 12 with systemic lupus erythematosus, 4 with Sneddon's syndrome, 2 with Sjögren's syndrome, 2 with primary APS. 30 healthy volunteers served as a control group.

RESULTS: 19 studies were abnormal, 1 normal. Abnormalities consisted of multifocal perfusion deficits and diffuse decrease of regional blood flow. The average number of focal perfusion deficits was 4.8 ± 1.7 . In 7 patients diffuse hypoperfusion of frontal lobes was seen, in 1 patient additionally hypoperfusion of temporal and occipital lobes. There was a correlation between the number of focal perfusion deficits and cognitive impairment in this group of patients. Correlation between SPECT images and clinical data was moderate in cerebellar syndrome and paresis, weak in persistent headache and vertigo.

CONCLUSIONS: Those results indicate the high utility of CBF brain SPECT scanning in antiphospholipid syndrome.

Key words: antiphospholipid syndrome, cerebrovascular circulation, single photon emission computed tomography

Introduction

Antiphospholipid syndrome comprises arterial and venous thrombosis, repetitive miscarriages and thrombocytopenia. This is accompanied by an increased serum level of antiphospholipid antibodies in IgG and IgM class. Those antibodies comprise anticardiolipin antibodies and so called lupus anticoagulant with specificity against phosphatidylserine and phosphatidylinositol (1). The diagnostic criteria of APS are listed in the table below.

APS may be diagnosed when at least one clinical and one serologic criterion are fulfilled at the same time. Elevated antiphospholipid antibodies level should be stated at least twice in an interval no longer than 8 weeks. In APS a decrease in prostacyclin synthesis, disturbances in antithrombin III, C and S proteins activity are seen, there may be a false-positive Wassermann's test. APS is seen in systemic lupus erythematosus and collagen tissue diseases (secondary APS) or without accompanying diseases (primary APS) (1). APS increases the risk of arterial and venous thrombosis by aggregation of platelets and decrease of fibrinolysis. Therefore antiphospholipid antibodies titers should be established particularly in children and young patients with stroke, also in cerebral sinuses and peripheral venous thrombosis.

APS, although relatively rare, is an important factor of cerebrovascular diseases. In SLE it doubles the risk of stroke. A part of brain infarctions in APS may be silent and mild, resulting in subtle signs of brain injury such as headache, depression, memory loss, and personality disorders (2, 3). A parallel involvement of many vascular beds is frequently seen. APS may also be responsible for peripheral polyneuropathy. Brain HMPAO SPECT might be a useful diagnostic tool in this group of patients. Brain MRI proved useful in patients with APS and severe neurologic manifestations such as stroke and epilepsy (4), but in mild CNS involvement MRI may be negative (5).

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The aim of the study was to assess cerebral blood flow changes utilising brain SPECT HMPAO in a group of patients with primary and secondary APS.

Material and methods

The study involved 20 women with APS: 12 with systemic lupus erythematosus, 4 with Sneddon's syndrome, 2 with Sjögren's syndrome, 2 with primary APS. Mean age was 42 ± 13 years, range 20–74 years. Arterial hypertension, renal insufficiency, congestive heart disease, chronic alcoholism and medication with the possible influence on cerebral perfusion were the exclusion criteria. The project had the approval of the Local Medical Ethics Committee.

Procedure

Brain SPECT studies were performed approximately 1 h following the intravenous injection of ^{99m}Tc -HMPAO (Ceretek; Amersham, Little Chalfont, U.K.), mean activity 740 MBq (20 mCi). Scanning was performed on a triple-head gammacamera Multispect-3 (Siemens, Erlangen, Germany) using a low-energy, ultra-high resolution collimator.

The data were collected into a 128 x 128 matrix, 4.8 mm per pixel. The raw data were smoothed with a Butterworth filter, cut-off frequency 0.35. Chang attenuation correction was not performed. The images were reoriented in the axial, coronal and sagittal planes. The data were displayed on a 10-grade colour scale. Focal perfusion abnormalities were read twice by two independent observers. Their depth was assessed utilising an asymmetry index (AI): $\text{AI} = \text{R} - \text{L}/(\text{R} + \text{L})/2 \times 100\%$, where R and L are mean counts/pixel values in the right and left hemisphere, respectively (6).

Regional cerebral blood flow was assessed semiquantitatively by calculating the index of regional mean counts/pixel values divided by those in cerebellum.

As significant were considered focal perfusion deficits with asymmetry index values exceeding 2 standard deviations (SD) below the mean for the control group. As significant were considered regional cerebral blood flow deficits with regional/cerebellar ratio values 2 SDs below the mean in the control group (12). Statistical analysis was performed utilising Kruskal-Wallis test and non-parametric Spearman's test. A P -value < 0.05 was considered significant.

Results

Clinical data

In our group of patients persistent headache was seen in 12 patients, including migraineous in 6, vertigo in 9, cognitive impairment in 6, cerebellar syndrome in 3, depression in 3, blurred vision in 3, paresis in 3, epilepsy in 2, hypoacusis of central origin in 1. 1 patient had no neurological or psychiatric symptoms and signs.

Brain SPECT scanning

The results of control group brain perfusion SPECT scanning is shown in Table 1.

In APS group normal pattern of CBF was seen in 1 patient, focal perfusion deficits in 19 patients. Altogether 91 deficits were seen. Those changes were mostly multifocal: one focal perfusion

Table 1. Diagnostic criteria of APS

Clinical criteria	venous thrombosis arterial thrombosis repetitive miscarriages thrombocytopenia
Serologic criteria	anticardiolipin IgG antibodies anticardiolipin IgM antibodies lupus anticoagulant

Table 2. Inter- and intrahemispherical differences of ^{99m}Tc -HMPAO uptake in control group, values are expressed as the percent of tracer's uptake

Asymmetry index (AI) (mean \pm SD)	Regional uptake/cerebellar uptake (mean \pm SD)	
	Right hemisphere	Left hemisphere
Frontal lobe	2.6 ± 2.0	93.6 ± 3.5
Temporal lobe	3.0 ± 1.7	93.8 ± 4.4
Occipital lobe	3.7 ± 2.4	95.4 ± 6.5
Parietal lobe	3.8 ± 2.5	96.3 ± 7.6
Basal ganglia	3.5 ± 2.8	87.6 ± 5.1
Thalami	4.6 ± 2.5	88.7 ± 7.5

defect was seen in 1 patient, two in 6 patients, three or more in 11 patients. The mean number of focal perfusion deficits per patient was 4.8 ± 1.7 . Those deficits were localised mostly in frontal lobes (52 deficits), occipito-parietal border (11) temporal lobe (10), parietal lobe (10), cerebellum (3), basal ganglia (2), thalamus (1). Some typical images are shown in Figures 1–2.

A significantly higher number of focal perfusion deficits was found in patients with cognitive impairment: 8.7 ± 2.2 (52 deficits). Diffuse decrease of regional cerebral blood flow was seen in 8 patients: in 7 bilateral hypoperfusion of frontal lobes (hypofrontality), in 1 patient additionally bilateral hypoperfusion of temporal lobes. However, when this group was compared as a whole with controls, a significant decrease of regional cerebral blood flow was found in frontal and parietal lobes, also in thalami. The results are shown in Table 3.

Clinical brain SPECT correlations

There was a good topographical agreement between SPECT results and clinical data in patients with cerebellar syndrome (in all 3 patients), in paresis (2/3 patients), weak in patients with blurred vision, vertigo and persistent headache, except migraineous ones, where the mean number of focal perfusion deficits was slightly higher than the average of the group (6.7 ± 2.6) vs. 4.8 ± 1.7 . In 2 of 3 patients with depression diffuse hypoperfusion of frontal lobes was seen, in patient with hypoacusis of central origin a perfusion deficit in auditory cortex was found.

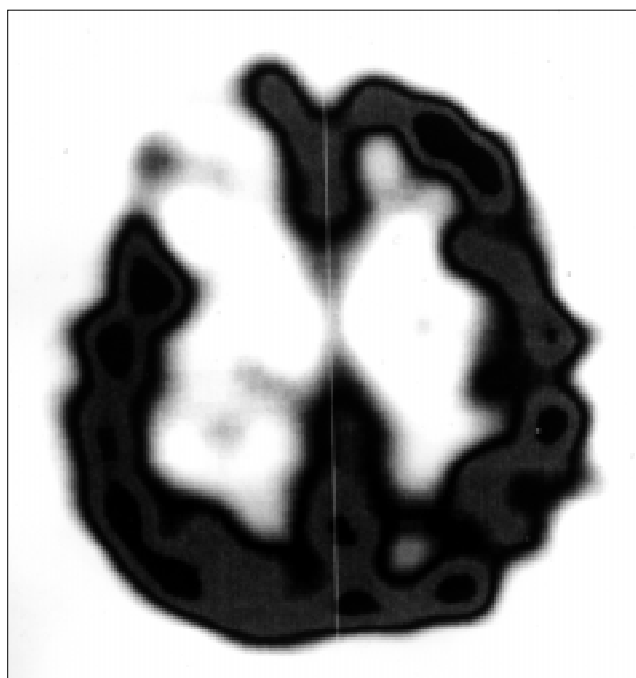


Figure 1. Focal hypoperfusion of right frontal lobe.



Figure 2. Bilateral hypoperfusion of frontal lobes (bilateral hypofrontality).

Table 3. Regional cerebral blood flow (expressed as % of cerebellar perfusion)

Brain region	Control group (n = 30)		APS (n = 81)	
	Right hemisphere (mean \pm SD)	Left hemisphere (mean \pm SD)	Right hemisphere (mean \pm SD)	Left hemisphere (mean \pm SD)
Frontal lobe	93.6 \pm 3.5	92.9 \pm 3.8	88.6 \pm 7.3 *	86.8 \pm 8.7 *
Temporal lobe	93.8 \pm 4.4	93.1 \pm 4.8	92.2 \pm 7.6	91.4 \pm 7.9
Occipital lobe	95.4 \pm 6.5	95.6 \pm 6.6	95.0 \pm 7.3	94.5 \pm 7.7
Parietal lobe	96.3 \pm 7.6	96.4 \pm 7.0	89.9 \pm 7.7 *	87.6 \pm 6.9 *
Basal ganglia	87.6 \pm 5.1	85.5 \pm 5.4	84.2 \pm 8.4	84.0 \pm 8.7
Thalami	88.7 \pm 7.5	85.4 \pm 7.3	80.7 \pm 7.6 *	80.8 \pm 7.4 *

*statistical significance

Discussion

There are few papers on brain SPECT in APS (5, 7, 8). Regarding focal perfusion deficits our findings are consistent with the main theses of previous reports, with even higher incidence of focal perfusion deficits seen in our study. However, we found frontal area the most affected by focal perfusion deficits, in contrast to the previous study performed with ^{99m}Tc -HMPAO, where focal perfusion deficits were most frequent in parietal lobes (5). Relative sparing of cerebellar vascular bed was consistent in all studies.

In studies performed so far a semiquantitative regional perfusion analysis was not performed, although diffuse, bilateral brain involvement was shown by visual analysis in about half of the patients (5). In our group hypoperfusion was shown in frontal and parietal lobes, also in thalami. The reasons for regional hypoperfusion are unclear. Whereas perfusion decrease in frontal lobes may be secondary to the focal perfusion defects, this can hardly

explain diffuse perfusion defects in the other brain areas, particularly in thalami, where focal perfusion defects were rare.

Focal perfusion deficits in APS are probably of thromboembolic origin and the territory of middle cerebral artery (MCA) is at a higher risk for vascular occlusion (9, 10). The explanation might be sought on a ground of pathological findings. In APS arterial fibrin thrombi in different stages of recanalisation, fibrous webs formed across arterial lumen and proliferation of intimal fibrous tissue or myointimal cells are seen (9). Those changes are what might be expected from thrombotic events that have been attributed to antiphospholipid antibodies (APA). IgG APA antibodies inhibit protein C and thrombomodulin — mediated anticoagulant activity (12), also they interfere with platelet aggregation mediated by prostacyclin (13). The prognosis in APS is poor, due to renal complications (14), although immunosuppressive, antiplatelet and anticoagulant therapy in those patients has led to apparent, short-term clinical improvement (15).

Cerebral blood flow SPECT scanning may be an imaging modality of choice in those patients. In other studies on brain vascular lesion in autoimmune diseases rCBF SPECT proved superior to MRI (16, 17, 18), also in patients with primary APS (5). This may be due to the ability of brain CBF SPECT scanning to visualise an incomplete infarction (19) and the zone of ischemic penumbra.

Out of the clinical findings of our study, an increased frequency of focal perfusion defects was found in patients with migraine. This could be consistent with observations and hypotheses attributing an increased incidence of migraine in patients with APS to microembolisation (20). However, an alternative opinion exists, either attributing increased migraine frequency to venous thrombosis in APS (21) or questioning the relationship between migraine and APS at all (22).

Conclusions

These results indicate the usefulness of CBF brain SPECT scanning in antiphospholipid syndrome. rCBF brain SPECT reveals in APS multiple flow defects.

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