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Dual Isotope Carotid Scintigraphy in Patients with Amaurosis Fugax Attacks

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Summary. A new dual isotope scintigraphic (DISC) examination of the carotid arteries consisting of simultaneous injections of ^{111}In-labeled platelets and ^{99m}Tc-labeled red cells was performed on eight male patients suffering from amaurosis fugax attacks. In concordance with the angiographically proven high percentage of significant extracranial carotid disease in patients with amaurosis fugax, six of the eight patients examined had an increased platelet accumulation in the carotid artery clinically affected. In one patient with normal angiography and one amaurosis fugax attack the platelet scintigraphy even revealed a pathological platelet accumulation in the ipsilateral carotid artery. These findings confirm the hypothesis that most amaurosis fugax attacks are due to arterio-arterial emboli originating from atherosclerotic plaques of the carotid bifurcation.

Key words: Amaurosis fugax attacks – TIA – ^{111}In platelet scintigraphy – Dual isotope carotid scintigraphy

Introduction

According to the definition of Fisher, an amaurosis fugax attack (AFA) consists of a "periodic blindness in which the principle derangement is an interruption of the retinal blood flow, usually in one eye only" [4]. In most cases such an attack is a symptom of carotid artery disease. Numerous ophthalmoscopic observations have shown that a white or yellowish bright thrombus material occludes the retinal vessels during an AFA [5,6,7]. Histological examination of the thrombi has revealed that they consist either of a platelet-fibrin mass [14] or of cholesterol [2]. Harrison et al. [8] were able to show that aspirin decreases the frequency of AFA. A large number of AFA patients—98% according to Ramirez-Lassepas et al. [17] and 88.8% according to Mungas et al. [15]—exhibit atherosclerotic lesions of the ipsilateral internal carotid artery which have been suspected of being the source of arterio-arterial emboli. Other suggested causes of AFA include decreased blood flow behind a stenosis of a retinal artery, cardiac emboli, spasms and Raynaud phenomena of the retinal vessels [1,12]. In addition, papilledema due to raised intracranial pressure may mimic the clinical picture of AFA [1].

In general, AFA can be regarded as a pathogenetic model for hemispheric transient ischemic attacks (TIA) and is accordingly accompanied by a high risk of a completed hemispheric stroke [13]. From this point of view, the question of the pathogenetic mechanism of AFA still remains important.

We have developed a dual isotope scintigraphic (DISC) technique for evaluating pathological platelet accumulations in the carotid arteries. This technique consists of a simultaneous injection of ^{111}In-labeled platelets and ^{99m}Tc-labeled erythrocytes. Details were reported in a recent paper [11].

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Patients

All eight patients involved were male, and Table 1 shows their clinical and angiographical characteristics. In all patients cardiac embolism was excluded by echocardiography and various clinical criteria. All patients gave their informed consent to take part in the study.

Methods

Cell Labeling Procedure

The platelet labeling procedure according to a modification of the technique described by Thakur [21] has been reported elsewhere [10]. Briefly, a compact platelet pellet of 60 ml of venous blood was obtained by differential centrifugation (180 g for 15 min, 1500 g for 7 min), and labeled with 1000 μCi of a ^{111}In oxine solution (pH 6.5), the labeled platelets were resuspended in 5 ml of the patient's plasma and reinjected i.v. The red cells were marked with a commercially available ^{99m}Tc-tin-albumin labeling unit as described by Schwartz and Krueger [20].

Image Processing

A medium energy parallel hole collimator was used to produce gamma-camera images 1 h and 24 h after injection of both isotopes. Due to the different energy spectra of ^{111}In and ^{99m}Tc it is possible to obtain separate gamma-camera images, thus arriving at the calculation of the ratio ^{111}In/^{99m}Tc for different neck segments. It is then possible to substract the circulating blood pool and to eliminate both false positive results, for example due to overlapping of two blood vessels, and false negative results, when small thrombi remain undetected because of the higher activity of circulating platelets. After subtraction of the red cell image a pure thrombus formation could be seen in the case of a pathological scan. Figure 1 shows one example of a

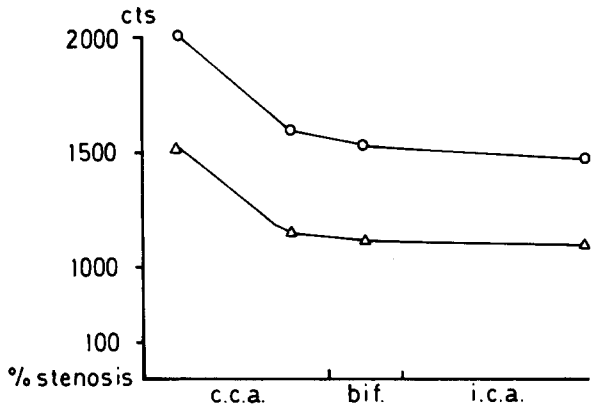


Fig. 1. Activity distribution curves for ^{111}In (△——△) and ^{99m}Tc (○——○) in different neck segments in a case with normal DISC. The ratio $^{111}In/^{99m}Tc$ remains constant at about 0.7. *Abbreviations:* c.c.a. = common carotid artery; bif. = bifurcation; i.c.a. = internal carotid artery

normal activity distribution in the various carotid segments. The ratio $^{111}In/^{99m}Tc$ remains constant at approximately 0.7.

Results

Table 1 shows the angiographical findings in the eight AFA patients. In five patients we found stenoses of the extracranial internal carotid artery, one patient showed an occlusion of the internal carotid artery, one a stenosis of the carotid siphon and the ophthalmic artery, and another had a normal angiogram. Six of the eight patients showed a pathological DISC. In all six of these patients the pathological platelet accumulation was visible on the side clinically affected. In two patients DISC was normal but the angiography pathological. One of them showed a tight stenosis of the internal carotid artery, the other an ulcerated carotid siphon stenosis.

The following case reports may serve as illustrations for elucidating the pathogenesis of AFA due to carotid artery disease.

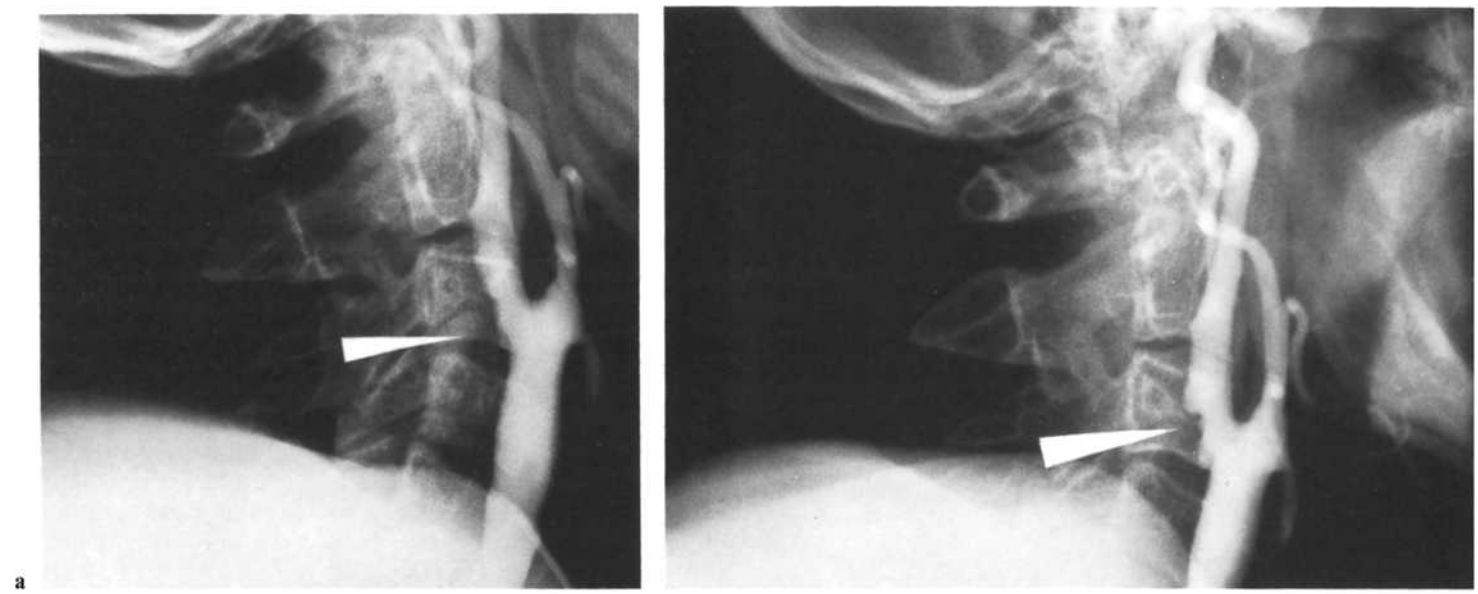
Case 1 (Patient 1 in Table 1)

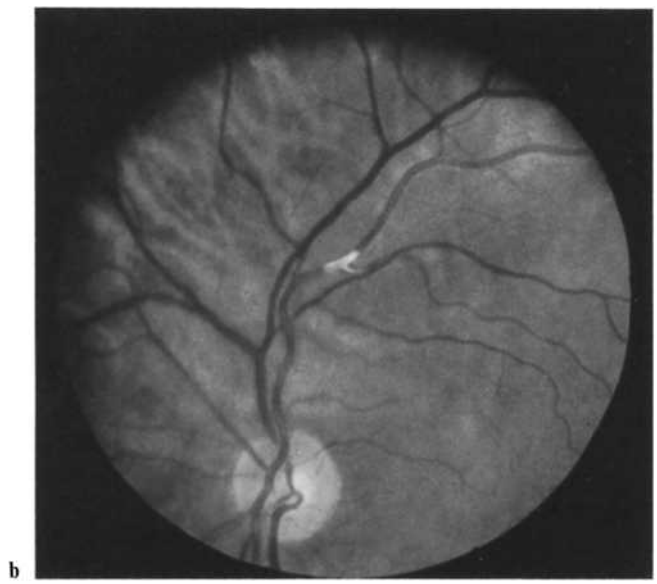
This 57-year-old man was admitted to hospital for the first time in July 1982 because of recurrent attacks of right-sided hemiparesis and sensory disturbance of the right side. Neurological examination revealed only a slight motor disturbance in the right hand; angiography of the left carotid artery showed only slight atherosclerotic lesions in the area of the carotid bifurcation (Fig. 2a). The patient was treated with 1000 mg aspirin daily and discharged from hospital.

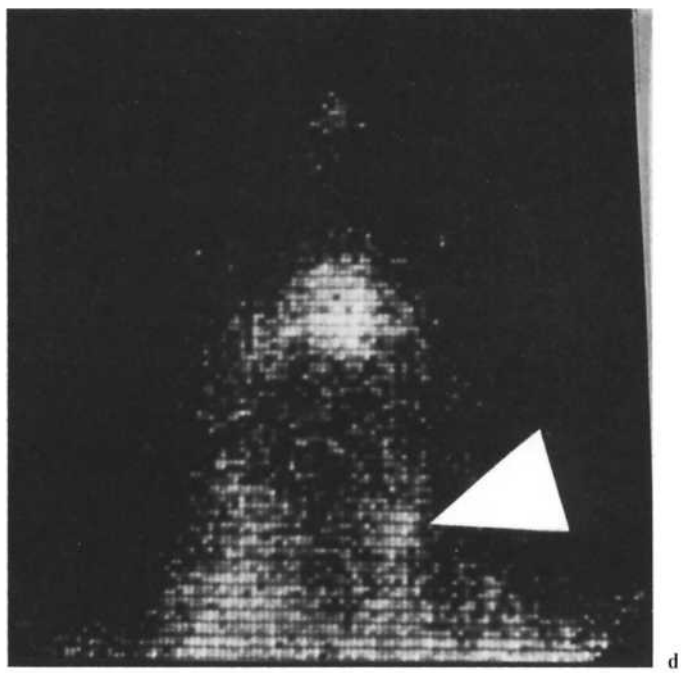
Hospitalisation became necessary 2 months later because of two AFAs in the left eye, and following a third AFA the vision of the left eye was permanently reduced, though no other neurological signs were observed at this stage. The visual acuity was 5/4 in the right eye and 5/20 in the left. With an ophthalmoscope a white thrombus could be observed in one retinal vessel (Fig. 2b). Blood pressure was normal at 120/80 mm Hg, erythrocyte sedimentation rate was increased at 17/46 and blood fasting glucose levels were also increased at 210%–307 mg%. All other laboratory findings were normal. Repeated left caro-

Table 1

Patient	Clinical findings	Angiography	Disc
1 (58 years)	Recurrent TIA with right hemiparesis and sensory disturbance of the right side, three AFA in the left eye	Left carotid angiography: slight atherosclerotic lesions of the internal carotid artery (ICA), reangiography 2 months later: ulcerated stenosis	Pathological platelet accumulation in the left ICA
2 (52 years)	Three AFA of the right eye, left-sided hemiparesis, treatment with anticoagulants since 1980	1980: normal carotid arteries. Two years later: occlusion of the right ICA	Pathological platelet accumulation in the right ICA
3 (53 years)	One AFA of the right eye, afterwards left-sided hemiparesis	Normal	Pathological platelet accumulation in the right ICA
4 (62 years)	One AFA of the left eye and one TIA with right-sided hemiparesis	50% stenosis of the left ICA	Pathological platelet accumulation in the left carotid artery
5 (61 years)	Four AFA of the right eye	Ulcerated 80% stenosis of the right ICA, additionally a smooth 50% stenosis of the left ICA	Pathological platelet accumulation in both ICA
6 (65 years)	One AFA of the left eye	60% smooth stenosis of the left ICA	Pathological platelet accumulation in the left ICA
7 (54 years)	More than ten AFA of the left eye	Tight stenosis of the left ICA	Negative
8 (60 years)	Recurrent AFA of the left eye	Bif. angiographically normal but 50% ulcerated carotid siphon stenosis left	Negative







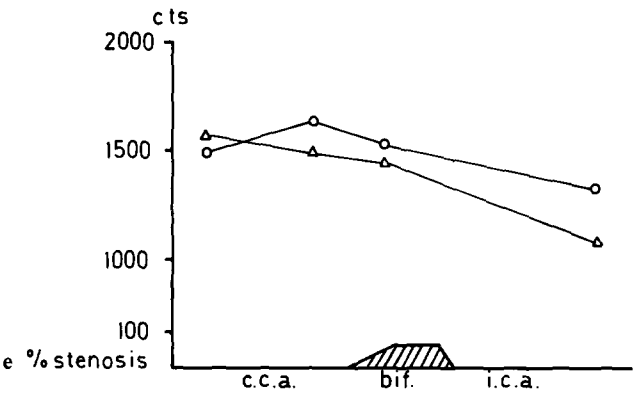
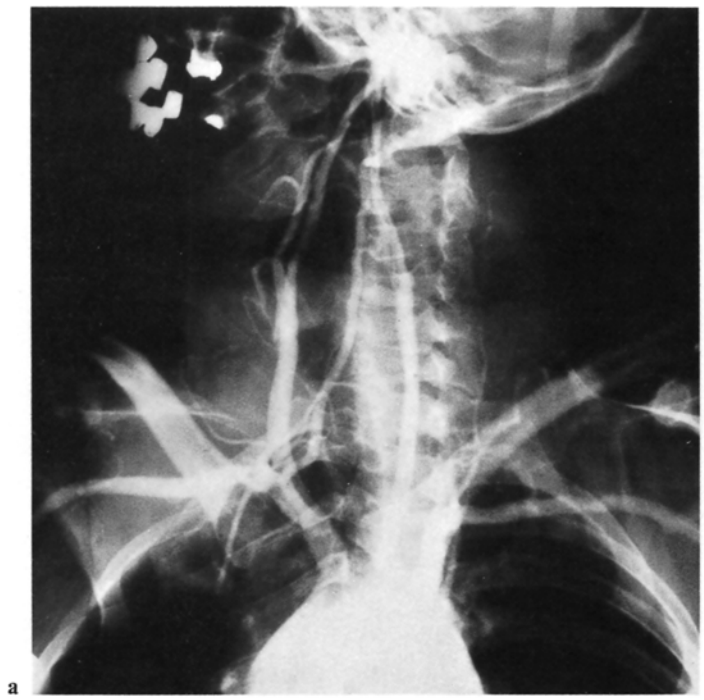


Fig. 2a–e. Patient 1. (**a**) First angiogram of the left carotid artery; slight atherosclerotic lesions in the area of the carotid bifurcation. (**b**) White thrombus in the retinal artery after an AFA. (**c**) Repeated left carotid angiography 2 months later: ulcerated stenosis of the internal carotid artery. (**d**) Pathological platelet accumulation in the left carotid artery. (**e**) The ratio $^{111}In/^{99m}Tc$ tends towards one in this particular segment. (○——○) ^{99m}Tc activity; (△——△) ^{111}In activity. Abbreviations see Fig. 1

tid angiography now showed an ulcerated stenosis of the left internal carotid artery (Fig. 2c). Figure 2d shows the platelet scintigraphy with a pathological platelet accumulation in the particular segment of the left internal carotid artery, and Fig. 2e the activity distributions of ^{111}In and ^{99m}Tc; the ratio $^{111}In/^{99m}Tc$ tends towards an accumulation in the bifurcation segment.

Case 2 (Patient 2 in Table 1)

Because of intermittent claudication, a 45-year-old man was admitted to hospital in 1980, where angiography revealed severe stenoses of both femoral arteries. Because of a carotid bruit on the right side additional angiography of the aortic arch was performed. Figure 3a shows no significant atherosclerotic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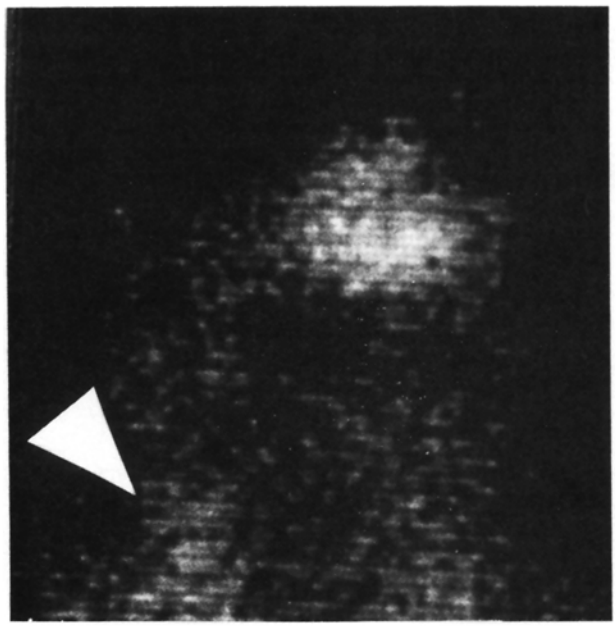
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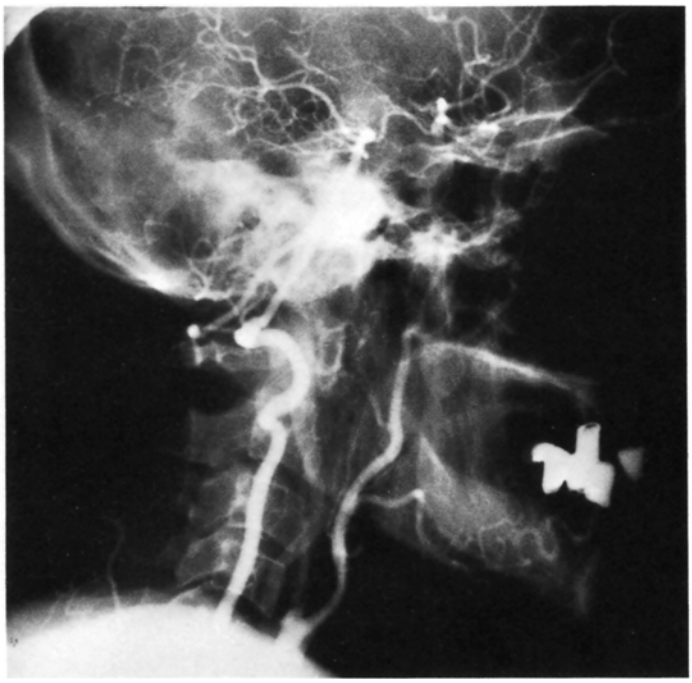
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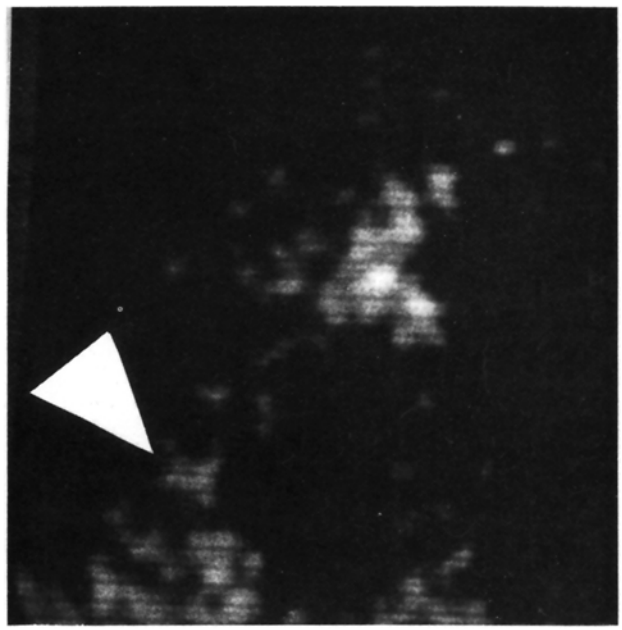
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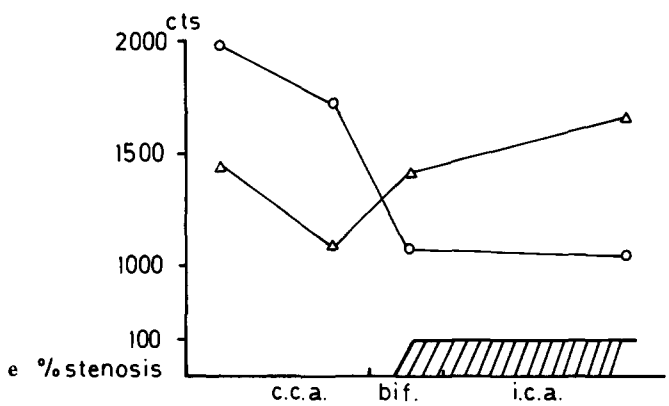

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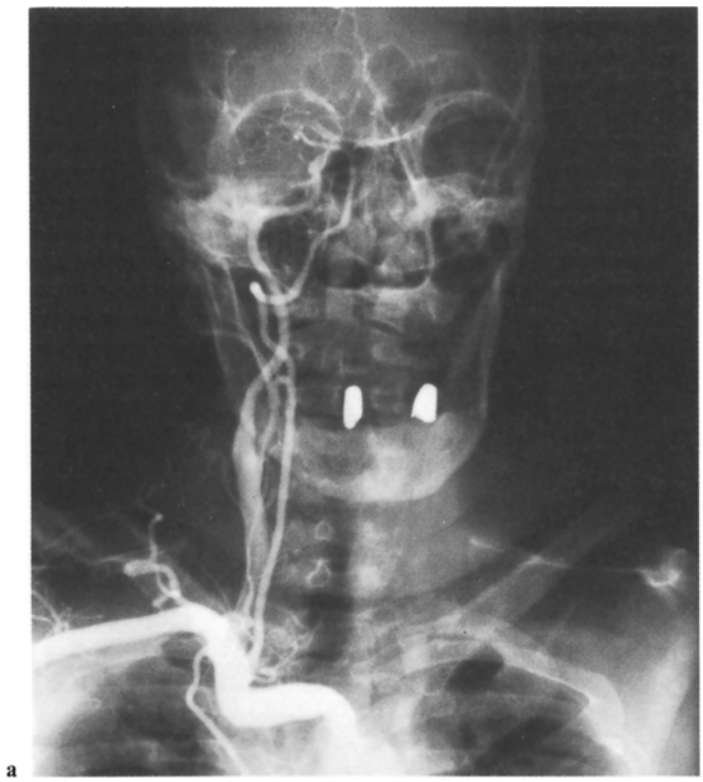
Fig. 3a–e. Patient 2. (**a**) Angiography of the aortic arch in 1980: no significant atherosclerotic lesions of the right internal carotid artery. (**b**) Two years later: occlusion of the right internal artery. (**c**) Pathological platelet accumulation in the right carotid artery. (**d**) After subtraction procedure: thrombus formation in this area. (**e**) Decrease of the erythrocyte bound activity, whereas the platelet bound activity increases. (○——○) ^{99m}Tc activity; (△——△) ^{111}In activity. Abbreviations see Fig. 1



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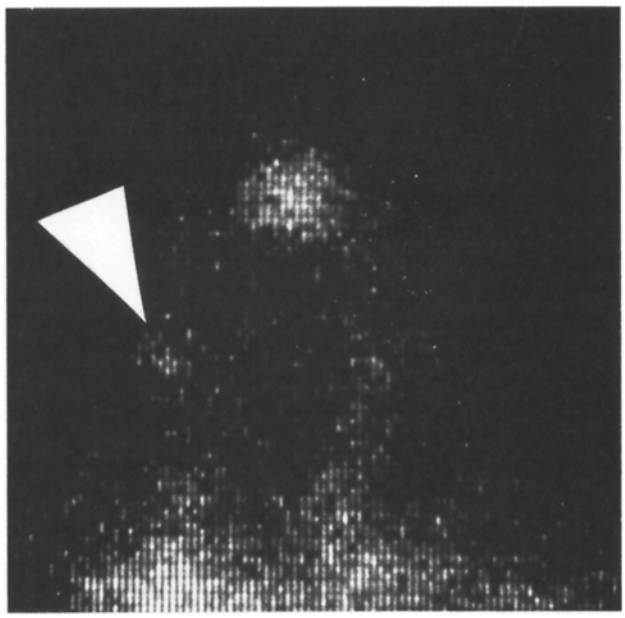

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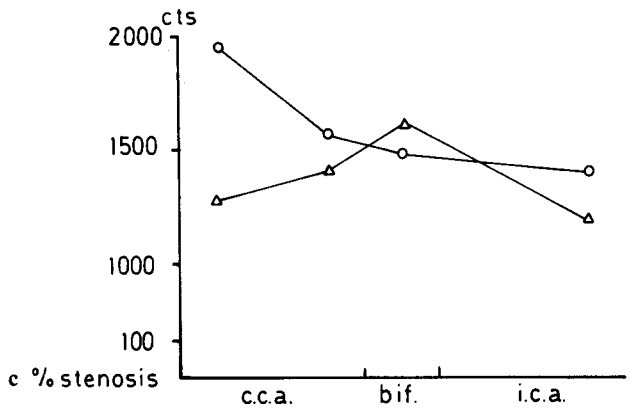

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Fig. 4a–c. Patient 3. (**a**) Normal right carotid angiogram. (**b**) Pathological platelet accumulation in the right carotid artery. (**c**) Increase of ^{111}In activity (△——△) in the area of the right carotid bifurcation indicating a thrombus formation. (○——○) ^{99m}Tc activity. Abbreviations see Fig. 1

changes of both carotid bifurcations at this stage. Since the patient refused operation he was treated with oral anticoagulants (Dicumarol). The prothrombin time during anticoagulant therapy was within therapeutic limits and ranged between 15 and 30s. In January 1981 the Dicumarol medication was reduced for 3 weeks because of an epistaxis but was continued thereafter.

In January 1982 three AFAs occurred, each with total blindness in the right eye for several minutes, and after developing a left hemiparesis the patient was admitted to hospital. The motor disturbance disappeared within 1 week. On admission the prothrombin time was 21s, the serum lipids were increased (triglycerides 240mg/100ml, cholesterol 362mg/100ml), and CAT scan and ophthalmoscopic examination were normal. Angiography of the right brachial artery revealed a total occlusion of the internal carotid artery and a stenosis of the external carotid artery (Fig. 3b). Doppler sonography showed a retrograde flow in the right ophthalmic artery, and DISC examination revealed a pathological platelet accumulation in the area of the right carotid artery (Fig. 3c and 3e). The activity distribution in this particular segment showed a significant ^{111}In excess in this vessel segment accompanied by decreased red cell bound activity (Fig. 3e). Under aspirin medication no further attacks occurred.

Case 3 (Patient 3 in Table 1)

A 53-year-old man with longstanding arterial hypertension had an AFA of the right eye in April 1983, and 1 week later a left-sided hemiparesis led to hospitalisation. The first physical examination showed an increased blood pressure of 200/120 mmHg. All laboratory findings were normal, as was the CAT scan examination. Right brachial arteriography showed no evidence of stenoses or ulcerations (Fig. 4a).

Nevertheless, the DISC examination revealed a pathological activity increase in the right carotid artery (Fig. 4b) and the activity distribution curve demonstrated an increase of platelet bound activity in the right carotid bifurcation segment (Fig. 4c).

Discussion

DISC examination of eight AFA patients showed a pathological platelet accumulation in the carotid artery ipsilateral to the affected eye in six of the cases. Angiographic findings in AFA patients generally show significant lesions of the extracranial internal carotid artery more often than in patients with hemispheric TIA [3, 15, 17, 19]. Two of our patients exhibited a normal DISC; one of these can be explained by a stenosis of the carotid siphon and the ophthalmic artery. The other patient was suffering from a tight stenosis of the carotid artery. According to our experiences discussed in a recent paper [9], DISC is less often positive in cases of high degree stenosis.

Patient 1 showed a fast growing ulcerated plaque of the internal carotid artery and scintigraphic analysis revealed a distinct platelet accumulation, suggesting intraluminal embolisation as the underlying pathogenesis. In patient 2 a total occlusion of the internal carotid artery developed within 2 years despite regular anticoagulant therapy. After hospitalisation and aspirin treatment no further attacks occurred, either because of the effect of antiplatelet therapy preventing recurrent distal stump embolisations via ophthalmic anastomosis, or the recurrent attacks stopping because the occlusive process had finally come to an end. DISC showed decreased red cell activity due to the occlusion but an increase in platelet bound activity in the same segment (Fig. 3e). It could be suggested that this particular constellation represents a fresh occlusion in which the thrombus organisation had not been completed. Usually however, patients with a carotid occlusion exhibit normal platelet scintigraphy.

In patient 3, DISC showed the only pathological finding as an explanation for the recurrent ischemic attacks since the angiogram was normal and there was no evidence for embolism. Possibly DISC indicated a small mural thrombus which remained undetected by angiography.

The findings underline the important role played by platelets in the pathogenesis of AFA. The question of whether TIA is caused hemodynamically or is the result of arterio-arterial embolism originating from ulcerated stenoses is currently under discussion [16, 18]. Although both pathogenetic mechanisms seem possible, platelet scintigraphy may help to differentiate between them and therefore may prove useful in therapeutic decisions regarding management of transient ischemic events.

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