Platelet Stickiness in Patients with Intracranial Tumours

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Brit. med. J., 1967, 4, 25-26

The observation of Nathanson and Savitsky (1952), that patients with active multiple sclerosis have an increased percentage of adhesive platelets in their blood has been fully confirmed (Caspary *et al.*, 1965; Wright *et al.*, 1965; Millar *et al.*, 1966). Indeed, in few disorders associated with abnormal platelet stickiness have the findings been so consistent. The cause of this abnormal platelet behaviour and whether it has a role in the pathogenesis of the disease are unknown. Platelet stickiness was not increased in a variety of chronic neurological disorders, but Nathanson and Savitsky (1952) showed that it was raised in four cases of the Guillain-Barré syndrome and in six of the eight patients with brain tumours that they studied.

Millar *et al.* (1966) have suggested that the increased platelet stickiness encountered in multiple sclerosis may be consequent upon degradation of neural tissue; this is rich in phospholipid, fractions of which have been shown to be potent aggregators of platelets in suspension (Kerr *et al.*, 1965). Since brain tumours can also cause extensive necrosis of nervous tissue it might be anticipated that they would increase platelet stickiness and that the increase would be most pronounced in rapidly growing tumours. In this study platelet adhesiveness has been measured in a series of patients with intracranial tumours and an attempt made to relate adhesiveness to the nature and rate of growth of tumours as evidenced by the length of clinical history.

Material

Fifty-two patients with suspected brain tumours admitted consecutively to the University Department of Neurology in Newcastle or the Regional Neurological Centre were studied. At the time of measuring adhesiveness this provisional diagnosis was the only information available to the investigator. No comatose patients were included and the majority had been ambulant before admission. At the end of the study case notes were examined and the final diagnosis, together with details of the clinical history, was obtained. Blood samples were taken soon after admission and before angiography or air studies had been carried out. The majority were collected between 9 and 10 a.m. and proximity to meals was avoided.

Blood was taken from an antecubital vein by a clean venepuncture into 3.8% sodium citrate in the proportion nine volumes of blood to one of citrate. Platelet adhesiveness was measured by use of a minor modification of Payling Wright's (1941) technique as described by Millac (1967a). Briefly this consists in rotating 2 ml. of citrated blood in a 25-ml. conical flask for 30 minutes at 4 r.p.m.; platelet counts are made before and after this procedure with Nygaard's direct visual method as modified by Hellem (1960).

$$\text{The percentage adhesive platelets} = \frac{\text{Initial—Final platelet count}}{\text{Initial count}} \times 100$$

The standard deviation of replicate determinations is 4.4%

As at present there is no agreed method for correcting the relation between haematocrit and platelet adhesiveness, only patients with a haematocrit within the range 35-48 were included.

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Results

The patients were divided into four groups on the basis of their diagnosis and clinical history.

Group 1.—Intracranial space-occupying lesions were excluded in these patients. Either no cause for their symptoms was found or they had other neurological disorders such as benign intracranial hypertension, aqueduct stenosis, vascular disease, etc.

Group 2.—Included here were patients with benign tumours. These comprised four pituitary adenomas, two meningiomas, a neurofibroma, craniopharyngioma, and one cerebellar haemangioblastoma. Histological verification was obtained in all cases except two pituitary tumours.

Groups 3 and 4.—All these patients had invasive tumours, which were gliomas or intracranial metastases with only two exceptions. These were a medulloblastoma and a carcinoma of the frontal sinus extending intracranially. The primary brain tumours were all histologically verified, apart from a thalamic glioma, diagnosed on the angiographic appearances, and a calcified temporal lobe tumour in a patient with a 10-year history of epilepsy, where a clinical diagnosis of oligodendroglioma was made. In patients with established malignant disease elsewhere in the body an intracranial space-occupying lesion is usually assumed to be metastatic in nature and biopsy not undertaken. For this reason only one of the 10 intracerebral metastases was histologically verified. Patients were

allotted to group 3 if their neurological symptoms had been present for more than three months before admission to hospital, and to group 4 if symptoms were of three months' duration or less.

Details of these groups, including numbers, sex distribution, mean age, mean initial platelet counts, and mean percentage adhesive platelets, are given in the Table. Adhesiveness values are also shown in the Chart. Patients in whom no tumour could be demonstrated (group 1) had a mean percentage of adhesive platelets very close to that obtained by the same

worker in a previous study of 80 healthy subjects (40 males, 40 females)—mean percentage adhesive platelets 40.3, standard error ± 0.9). For the purpose of this study, therefore, these group 1 patients have been regarded as controls, and differences in means have been analysed against them.

Those subjects found to have benign tumours (group 2) did not differ in their mean adhesiveness from those in group 1, though the mean initial platelet count in this group was significantly lower than in the others. In patients with invasive

patients could account for the variation in platelet adhesiveness shown. There appears to be no explanation for the low mean initial platelet count in the group of patients with benign tumours, but the number in this group was small.

Nathanson and Savitsky attributed the increased platelet stickiness found in patients with cerebral tumours to a non-specific effect of malignancy. Yet the occurrence of similar changes in platelet adhesiveness in patients with active multiple sclerosis and rapidly growing brain tumours suggests an alter-

Platelet Stickiness in Intracranial Tumours

	Group 1	Group 2	Group 3	Group 4
No.	15	9	10	18
Proportion of males to females	11:4	5:4	3:7	12:6
Mean age	44.0 $\pm$ 3.2	40.7 $\pm$ 3.9	40.5 $\pm$ 5.2	53.9 $\pm$ 3.3 (P < 0.05)
Mean initial platelet count per cu. mm. $\times 10^3$	250 $\pm$ 10.3	206.3 $\pm$ 13.5 (P < 0.01)	315.1 $\pm$ 36.5	259.2 $\pm$ 15.9
Mean % adhesive platelets	39.8 $\pm$ 1.8	39.9 $\pm$ 2.6	41.5 $\pm$ 2.7	49.4 $\pm$ 2.0 (P < 0.01)

Standard errors follow $\pm$ sign.

P values are given where means differ significantly from those in Group 1.

Group 1: No space-occupying lesion found. Group 2: Benign tumours. Group 3: Invasive tumours; clinical history of more than three months' duration. Group 4: Invasive tumours; clinical history of three months or less.

tumours platelet stickiness was increased. The increase was small and did not reach significance in those with a longer clinical history (group 3), but became more striking and was significant in group 4 patients with a presenting history of three months' duration or less (P < 0.01). The mean age for this group was, however, significantly higher than that of the control patients (P < 0.05).

The mean percentage of adhesive platelets did not differ significantly between patients with cerebral metastases and those with primary brain tumours.

Discussion

These findings support Nathanson and Savitsky's (1952) observation that platelet adhesiveness is increased in brain tumours. In this larger series raised stickiness was found to occur most often in those patients with invasive tumours and a short history of disease, while platelet adhesiveness in patients with benign tumours lay within the normal range. It is recognized that the length of a patient's history may be influenced by many factors, but in general most rapidly growing brain tumours cause the patient to present for investigation within a few weeks of the onset of symptoms, and it is these tumours which are associated with a relatively rapid destruction of neural tissue.

The group of patients showing increased platelet adhesiveness while matched for sex were significantly older than the control patients with negative investigations. However, the effect of age upon platelet adhesiveness is not yet clear. In a previous study (Millac, 1967b) no significant effect of age, within a similar range, on adhesiveness was found in 80 healthy subjects and 82 patients with multiple sclerosis. It is thought unlikely that the difference in age between these two groups of

native explanation. In both these clinical situations there is acute destruction of neural tissue, and it seems possible that degradation products may enter the circulation and bring about the alteration in platelet behaviour.

Summary

Platelet adhesiveness has been measured in 52 patients admitted with suspected brain tumours. Compared with those patients whose investigations turned out to be negative or in whom the neurological diagnosis was other than brain tumour, patients with invasive tumours and a clinical history of three months' duration or less had a significantly increased platelet adhesiveness. In view of the similarity in alterations of platelet adhesiveness in patients with rapidly growing brain tumours and multiple sclerosis it is suggested that these platelet changes are consequent on acute degradation of neural tissue.

I wish to thank Professor Henry Miller and the physicians and surgeons of the Regional Neurological Centre, Newcastle upon Tyne, for permission to study patients under their care.

REFERENCES

- Caspary, E. A., Prineas, J., Miller, H., and Field, E. J. (1965). *Lancet*, 2, 1108.
- Hellem, A. J. (1960). *Scand. J. clin. Lab. Invest.*, 12, Suppl. No. 57.
- Kerr, J. W., Pirrie, R., MacAulay, I., and Bronte-Stewart, B. (1965). *Lancet*, 1, 1296.
- Millac, P. (1967a). *J. neurol. Sci.*, 4, 151.
- (1967b). *Dtsch. Z. Nervenheilk.*, 191, 74.
- Millar, J. H. D., Merrett, J. D., and Dalby, A. M. (1966). *J. Neurol. Neurosurg. Psychiat.*, 29, 187.
- Nathanson, M., and Savitsky, J. P. (1952). *Bull. N.Y. Acad. Med.*, 28, 462.
- Wright, H. P. (1941). *J. Path. Bact.*, 53, 255.
- Thompson, R. H. S., and Zilkha, K. J. (1965). *Lancet*, 2, 1109.