

THE DEFIBRINATION SYNDROME ARISING DURING MITRAL VALVOTOMY

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Edge and Bottrill (1959), in their recent analysis of 170 patients submitted to pulmonary resection, mention one death from uncontrollable haemorrhage, in which there was evidence of a clotting defect. The development of acute and sometimes fatal coagulation deficiencies during chest operations is well documented in the French and American literature (Mathey, Daumet, Soulier, Le Bolloch, and Fayet, 1950; Baumann, 1952; Coon and Hodgson, 1952; Soulier, Mathey, Le Bolloch, Daumet, and Fayet, 1952; Penn and Walker, 1954) although it has not received emphasis in papers from this country. Nevertheless, personal discussion suggests that British thoracic surgeons may be encountering such cases, and a further, mild, example is presented to draw attention to the possibility of this occurrence.

CASE REPORT

A woman, now aged 47 years, without any previous history of abnormal bleeding, had undergone valvotomy in 1952 for mitral stenosis; 2 pints of blood were given at this operation. Early in 1957 cardiac failure recurred, and after three periods in hospital a second valvotomy was undertaken on February 3, 1959. Anaesthesia was induced at 9 a.m.; the chest was opened at 9.25 a.m. and blood transfusion started. Adhesions from the previous operation necessitated about an hour's dissection to free the lung and to strip the pericardium. Up to now bleeding had been slight, but at this point three attempts to open the mitral valve by retrograde dilatation from the left ventricle led to blood loss and, at 10.40 a.m., to cardiac arrest. The heart was massaged during the next 50 minutes and finally valvotomy was successfully performed with a finger knife. Spontaneous heart beats now resumed; by this time 6 pints of stored blood had been given. Over the next hour there was a general oozing of blood into the wound, but since no bleeding point could be identified, a basal drain was inserted into the pleural cavity and the chest was closed at 12.45 p.m. By 3 p.m. 2 pints of blood had collected in the drainage bottle, and a sample of blood, taken to obtain serum for further cross-matching, clotted poorly.

In a second blood sample at 3.55 p.m., the platelet count was 280,000 per c.mm., the haematocrit (estimated in an ungraduated container) was approximately 30%, and the thrombin clotting time was slightly prolonged (patient 10.3, 10.9 sec.; control 8.5, 7.9 sec.) with rather a thin clot. A rapid fibrinogen determination (Ingram, 1952, omitting the hot air process but applying an empirical correction) showed a concentration of 0.18 g./100 ml. plasma, about half the average normal for the patient's age (and probably less than half the pre-operative reading, since the E.S.R. had been 17 mm. in one hour by Westergren's method on January 12). Serial thrombin clotting times made on plasma samples which were being incubated at 37° did not show any prolongation through a period of 36 minutes, thus providing no evidence of fibrinogenolysis (Wilhelm, Miles, and Mackay, 1955), a process noted in several of the published cases. The activity of antihæmophilic globulin (assay of Biggs, 1957) was 90% of average normal, but that of factor V, assayed by the ability of the patient's plasma, adsorbed with alumina, to correct the prothrombin time of aged, oxalated plasma, was 36%. A combined assay of factor VIII and Stuart factor, based on the ability of the patient's serum to correct the prothrombin time of Seitz-filtered ox plasma, gave an activity of 95%; but the activity of the Christmas factor, assayed by the ability of the patient's serum to correct known Christmas serum in the thromboplastin generation test (Biggs and Douglas, 1953), was only 12%.

The third blood sample, taken at 6.30 p.m., showed a haematocrit of 33% and the same fibrinogen concentration as at 3.55 p.m. The bleeding from the chest was now less and had virtually stopped after a further three hours, so that purified fibrinogen, although made available, was not given.

A fourth blood sample taken on February 5, when the drain was removed, showed the same haematocrit. The thrombin clotting time was normal (patient 8.5, 8.5 sec.; control 8.2, 9.9 sec.); the factor V activity was 118%; the fibrinogen concentration was now 0.45 g.%; but the Christmas factor activity had risen only to 52%. On February 11 a fifth sample again gave high values for factor V activity and fibrinogen concentration (130% and 0.64 g.% respectively) and showed 81% of control Christmas factor activity.

COMMENT

The occurrence of abnormal bleeding, together with a mixed coagulation defect, suggests the syndrome now well known in obstetric literature as "defibrination," in which it is supposed that tissue substance(s) gain access to the circulating blood and induce a slow, intravascular coagulation, as demonstrated experimentally by Wooldridge (1886) and others. Since lung has been found to be relatively rich in coagulant substance (Gutmann, 1914; Seegers and Schneider, 1951), it might be that in our case the injury to the lung during the dissection of adhesions exuded this material into the blood vessels. In three of Coon and Hodgson's (1952) cases coagulation defects followed periods of cardiac arrest, and they suggested that the consequent hypotension and anoxia might be a provocative factor. It is difficult to estimate the diluting effect of the transfusion of stored blood (in which various clotting factors may have lost activity), but a number of authors have suggested that this may aggravate the condition.

The particular pattern of clotting defects that we observed cannot at present be explained, but varied abnormalities have previously been reported, although not, so far as we know, a fall in the Christmas factor. Deficiencies are usually found among those components that are consumed during normal clotting (fibrinogen, prothrombin, factor V, and antihæmophilic globulin), thrombocytopenia is common, and fibrinolysin may be activated; rarely, heparin may be released. Of the "serum" factors, only factor VII has previously been implicated (Masure and Schockaert, 1954; Coon and Duff, 1958).

It is also still difficult to decide what degree of deficiency merits the infusion of purified fibrinogen. Clearly, this always scarce material should not be given unless the plasma fibrinogen

concentration has been estimated and found to be significantly reduced; otherwise, fresh whole blood or fresh plasma should be given, since other clotting factors might be at fault. On the other hand, when a severe depletion of fibrinogen has been demonstrated, the purified material must be given if serial readings over a few hours show a falling concentration or if bleeding continues (and the concentration does not rise) despite adequate transfusion with fresh blood. There is, however, a strong indication for making available 5-6 g. of the material whenever fibrinogenopenia is found, on the understanding that it will not be used as a panacea.

These recommendations also emphasize the importance of requesting the co-operation of the pathologist as soon as there is reason to suspect the development of an abnormal bleeding tendency, so that a blood sample may be tested at an early stage to provide readings on which treatment may be planned and for later comparisons.

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