

## Arterial thrombosis and accelerated atheroma in a member of a family with familial antithrombin III deficiency

J. WINTER  
B.Sc., M.B., Ch.B., M.R.C.P.

D. DONALD  
M.B., M.R.C.Path.

B. BENNETT  
M.D., M.R.C.P.

A. S. DOUGLAS  
M.D., D.Sc., F.R.C.P.

*Departments of Medicine and Pathology, University of Aberdeen, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZB*

### Summary

The case is described of a young man with probable familial antithrombin III deficiency, a disorder associated with a marked predisposition to venous thrombo-embolic events. In addition to a history of venous thrombosis and pulmonary embolism, at post-mortem this patient demonstrated widespread arterial thrombosis and atheroma. The probable association of severe arterial thrombosis and atheroma with a clearly definable coagulation disorder predisposing to thrombosis is of interest.

### Introduction

Antithrombin III (ATIII) is the major physiological inhibitor of the coagulation mechanism (Barrowcliffe, Johnson and Thomas, 1978). Patients with familial ATIII deficiency show a marked predisposition to venous thrombo-embolism. The authors describe a young man with probable familial ATIII deficiency in whom recurrent severe arterial thrombosis and atherosclerosis occurred in addition.

### Case report

The patient died in 1970 aged 30 years. In 1962 he had sustained a pulmonary embolism and received anticoagulants. In 1962 and 1966 he developed thrombophlebitis of both legs, and in 1967 right brachial artery occlusion occurred; albuminuria was noted. Bilateral varicose veins were noted in 1968, with stasis ulcers; albuminuria persisted. In 1969 and 1970 pulmonary embolism recurred, chest X-ray showing biventricular enlargement. In March 1970 congestive cardiac failure developed, aortic systolic and diastolic murmurs being noted. In December 1970 severe abdominal pain occurred and he died after a brief admission. His blood pressure and blood sugar were normal throughout; he was a

cigarette smoker. After his death, his mother, 4 of his siblings and others in his family were found to have ATIII deficiency and have been described previously (Mackie *et al.*, 1978).

### Post-mortem findings

The upper half of the body was deeply jaundiced, the lower half paler.

Heart: Both ventricles were enlarged, 2 areas of healed infarction were present, the mitral valve was sclerosed and incompetent, the aortic valve sclerosed and stenosed.

Arteries: There was extensive atheroma of the aorta and vessels arising from it including the coronary arteries. The aorta was totally occluded by thrombus from the coeliac axis to the femoral vessels and partially occluded up to diaphragmatic level. Coeliac, mesenteric and renal arteries were occluded and marked atheroma present in the pulmonary arteries.

Veins: The inferior vena cava was occluded by thrombus at the right renal vein level. Hepatic, splenic, portal and mesenteric veins were occluded by thrombus.

Abdominal viscera: the bowel showed widespread infarction: liver, kidneys and spleen showed numerous infarcted areas, venous thrombi and arterial atheroma.

### Discussion

Hereditary ATIII deficiency is one of the very few biochemically definable states universally accepted as predisposing to thrombosis. The existence of the deficiency in this man cannot be established with certainty now, but the symptoms together with the findings of the deficiency in his mother and siblings suggest strongly that he, too, was ATIII deficient. Previous reports of ATIII deficiency emphasize the

predisposition to venous thrombosis shared by this patient and his relatives (Egeberg, 1965). This man showed, in addition, severe arterial thrombosis not previously recorded except in 2 newborn children of ATIII-deficient mothers (Bjarke, Herin and Blombäck, 1974). Additionally, this man showed widespread severe atheroma at the age of 30 years, in the absence of the commoner predisposing factors such as hypertension or diabetes (his lipoprotein profile is unfortunately unknown). Predisposition to atheroma, like arterial thrombosis, has not previously been recorded in patients deficient in ATIII. Both findings, namely arterial thrombosis and atheroma in association with a plasma abnormality favouring thrombosis, are of interest. Clearly a factor additional to the ATIII deficiency must be invoked to account for the extension of

abnormalities into the arterial tree in this man but cannot be defined retrospectively.

#### Acknowledgments

We are grateful to Professor A. R. Currie of the Department of Pathology, University of Edinburgh, who provided details of the pathology of this patient.

#### References

- BARROWCLIFFE, T.W., JOHNSON, E.A. & THOMAS, D. (1978) Antithrombin and heparin. *British Medical Bulletin*, **34**, 143.
- BJARKE, B., HERIN, P. & BLOMBÄCK, M. (1974) Neonatal aortic thrombosis. *Acta paediatrica scandinavica*, **63**, 297.
- EGERBERG, O. (1965) Inherited antithrombin deficiency causing thrombophilia. *Thrombosis et diathesis haemorrhagica*, **13**, 516.
- MACKIE, M., BENNETT, B., OGSTON, D. & DOUGLAS, A.S. (1978) Familial thrombosis: inherited deficiency of antithrombin III. *British Medical Journal*, **1**, 136.