MEDICAL MEMORANDA

Acute Renal Failure in Myelomatosis from Intravascular Coagulation

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Acute renal failure is rare in myelomatosis though some degree of renal insufficiency occurs in 30 to 50% of all cases. In many of the recorded cases of acute oliguric renal failure there is a history of renal contrast radiography—usually intravenous pyelography (Derot *et al.*, 1969)—and in others an infective element has been incriminated (Heptinstall, 1966). In the remaining cases no direct cause can be established (Kjeldsberg and Holman, 1971). Recent reports have shown disturbances in coagulation (Vigliano and Horowitz, 1967), thromboembolic disorders (Catovsky *et al.*, 1970), and abnormalities in fibrin polymerization (Lackner *et al.*, 1970) in association with myelomatosis.

The present report describes a case of myelomatosis in which acute renal failure can be attributed to intravascular coagulation and impaired fibrinolysis.

Case Report

A 59-year-old man was admitted to hospital with anuria for 24 hours and possible oliguria for seven days. Investigations showed: plasma electrolytes normal, blood urea 260 mg/100 ml, creatinine clearance 12 ml/min, haemoglobin 12 g/100 ml, W.B.C. 4,000/mm³, platelets 110,000/mm³, reticulocytes 3%, and E.S.R. 98 mm/hr (Westergren). The peripheral blood film was normal save for the occasional burr cell. The bleeding time was 3½ min, clotting time 9½ min, and the prothrombin time 16 sec (control 13 sec). The urine was sterile on culture but contained 5 red blood cells and 2 granular casts per high-power field. During the first week in hospital the urine output remained minimal and the blood urea rose to 400 mg/100 ml. At that point he began to respond to the Giovenetti diet and fluid restriction, urine output increased, and the blood urea gradually returned to normal.

Investigation of the fibrinolytic-coagulation systems produced markedly abnormal results (see Table). Serum protein electrophoresis showed a discrete M band in the mid-gamma position. On further investigation this was found to be IgG of 2,000 mg/100 ml. The other immunoglobulins were noticeably reduced—IgA 23 mg/100 ml, IgM 11.5 mg/100 ml. Bence Jones protein type K was present in the urine in low concentration. Skeletal survey showed multiple osteolytic lesions and bone marrow aspirate contained atypical plasma cells compatible with a diagnosis of myelomatosis.

Histological Features.—Percutaneous renal biopsy was performed during the recovery phase two weeks after admission. The general architecture of the kidney was normal. In addition to normal age changes some tubules showed a flattened and irregular epithelium with evidence of regeneration. There was no continuing necrosis. Occasional colloid casts were seen. Intravascular plugs of fibrin were present within capillaries of the glomerular tuft (Fig. 1) and in the intertubular capillaries in relation to the flattened and irregular tubular epithelium (Fig. 2). The arterioles were normal and no evidence of major vascular occlusion was found. There was no evidence of pyelonephritis, amyloidosis, or calcification.

Abnormalities found in Fibrinolytic and Coagulation Systems

	Patient's Value	Normal Value
Serum fibrin degradation products (µg/ml) ..	320	0-10
Euglobulin clot lysis time (min) ..	250	60-150
Plasminogen (units/ml) ..	3.2	1.5-4.0
Urokinase sensitivity test (min) ..	120	13-21

FIG. 1—Glomerulus showing occasional capillary loops plugged with fibrin (arrowed). (Martius scarlet blue. ×226.)

FIG. 2—Intertubular capillaries obstructed by fibrin plugs (arrowed). The tubular epithelium is flattened and irregular. (Martius scarlet blue. ×226.)

Comment

Although renal function is often impaired in myelomatosis it is unusual for this condition to present as acute oliguric renal failure.

In the present case there was no history of intravenous pyelography or other contrast radiography. The finding of a

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pronounced increase in the serum fibrin/fibrinogen degradation products suggested either intravascular coagulation or excessive fibrinolysis. The latter, however, could be excluded by the normal plasma plasminogen and the prolonged euglobulin clot lysis time. Intravascular coagulation was subsequently confirmed by the renal biopsy. Although it is likely that the intravascular coagulation caused the tubular necrosis and renal failure in this patient the pathogenesis of the fibrin deposition must remain speculative. Catovsky *et al.* (1970) drew attention to the frequency of thromboembolic disorders in myelomatosis, and Preston and Lee (1972) have shown impaired fibrinolysis in myelomatosis. On admission this patient had a greatly prolonged euglobulin clot lysis time and a prolonged urokinase sensitivity test, both of which indicate some degree of impairment of his fibrinolytic mechanisms.

It is of interest to report that eight months later the patient was readmitted with clinical and radiological evidence of a pulmonary infarct.

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Benzhexol-induced Blindness in Parkinson's Disease

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Benzhexol is a synthetic antiparkinsonian drug with peripheral and central atropine-like effects (Goodman and Gilman, 1970), thus its use in patients with angle-closure glaucoma is contraindicated. We have not found any report in the literature of blindness due to angle-closure glaucoma induced by this drug. Three such cases are reported here.

Case Reports

Case 1.—A 57-year-old man suffering from Parkinson's disease and senile dementia was examined in the eye clinic in December 1965. He had been receiving 15 mg of benzhexol daily for two years. In the right eye the visual acuity was 6/15 and the intraocular pressure was maximal. The cornea was slightly oedematous and the pupil was 4 mm in diameter and did not react to light. There was excavation and atrophy of the optic disc. The visual field was constricted to 5-10° around the centre. In the left eye the visual acuity was 6/15, the intraocular pressure was 50 mm Hg, the cornea was slightly oedematous, and the fundus was normal. The visual field was intact. On gonioscopy the anterior chamber angle seemed closed in both eyes. The administration of benzhexol was stopped, pilocarpine and eserine were instilled every 5 minutes, acetazolamide was given intravenously, and glycerol was administered by mouth. The intraocular pressure in the left eye became normal and the angle opened. In the right eye the intraocular pressure remained high and a filtering iridectomy was performed. Subsequently a peripheral iridectomy was performed in the left eye.

Case 2.—A 70-year-old man suffering from Parkinson's disease and senile dementia was examined in the clinic in March 1966. He had been receiving 15 mg of benzhexol daily for one year. After four months on this medication he had complained of deterioration of vision in the right eye and two months later glaucoma was discovered. When first seen by us the right eye had no light perception because of absolute glaucoma and there was advanced excavation and atrophy of the optic disc. In the left eye vision was 6/9, the intraocular pressure was 64 mm Hg, and there was slight excavation of the optic disc. The visual field was normal. In both eyes the

anterior chamber was shallow and the anterior chamber angle closed. Treatment with benzhexol was stopped. In the left eye the intraocular pressure became normal with conservative treatment and the angle opened. In the blind eye the intraocular pressure remained high. Peripheral iridectomy was performed later in the left eye.

Case 3.—A 55-year-old woman was admitted to the clinic in July 1970 because of high intraocular pressure in both eyes first discovered earlier the same day. She had been receiving 15 mg of benzhexol daily for two years because of paranoia. On examination the right eye was found to be blind from glaucoma. In the left eye vision was 6/9, the intraocular pressure was 43 mm Hg, and the fundus was normal. No glaucomatous field defects were present. The angle was closed in both eyes. Benzhexol medication was stopped and she was treated with miotics and acetazolamide. In the left eye the intraocular pressure became normal and the angle opened. A peripheral iridectomy was performed. In the right, blind eye the intraocular pressure remained high.

Comment

Total blindness of one eye in two patients and practical blindness with tubular vision in one eye of a third patient occurred as a result of angle-closure glaucoma due to long-term treatment with benzhexol. Glaucoma induced by the systemic administration of atropine has been described by several authors (Ulman and Mossman, 1950; Larmande and Toulant, 1951; Duke-Elder, 1969) as a result of subcutaneous injection, suppositories, or during prolonged administration of belladonna by mouth.

Benzhexol has a mydriatic effect which is about one-third as strong as that of an equal dose of atropine systemically (Goodman and Gilman, 1970). Since the therapeutic dosage of benzhexol in Parkinson's disease is from 15 to 30 mg a day its mydriatic effect is many times greater than that obtained through therapeutic use of atropine, which seldom exceeds 2 mg a day. The prolonged cumulative effect of benzhexol tends to cause creeping angle-closure glaucoma—that is, glaucoma without acute symptoms of pain and redness of the eye. This and the mental condition of the present patients account for the delay in the diagnosis of the glaucoma. It is therefore advisable to have gonioscope evaluation in all patients who are to be treated with benzhexol or any related drug.

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