It is strongly recommended that, with the reagents we used, any flush extending beyond the needle puncture should be recorded as positive.

To increase herd immunity only Schick-positives should be immunized, all pseudoreactors being treated as immune.

The second reading of Schick tests showed a closer correlation with the level of circulating antitoxin than the first, but the first must not be omitted owing to the danger of missing pseudoreactors.

It is possible, though of little practical value, to detect many of the pseudoreactors who have low antitoxin titres.

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NEPHROTIC SYNDROME ASSOCIATED WITH RENAL VENOUS THROMBOSIS AND BRONCHIAL CARCINOMA

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The recognition of an association between long-standing renal venous thrombosis and persistent albuminuria has existed for over forty years (Rowntree *et al.*, 1913; Shattock, 1913). Blainey *et al.* (1954) describe three cases of the nephrotic syndrome, in one of which renal venous thrombosis was confirmed at necropsy. They point out that, while in many cases the aetiology of the syndrome is obscure, it may be caused by interference with venous return from the kidney. Most cases—for example, Derow *et al.* (1939), Moschowitz (1948), and Bell (1950)—have shown involvement of the inferior vena cava.

Thrombophlebitis (often of migratory type) has been known to be associated with malignant disease since

Trousseau (1877) drew attention to its occurrence in visceral carcinoma. Williams (1954) describes three cases of thrombophlebitis migrans associated with bronchial carcinoma, and points out that up to 1951 Gross *et al.* found only nine such cases so associated.

The following case presents an association of the nephrotic syndrome, renal venous thrombosis, and bronchial carcinoma. The inferior vena cava was not involved.

Case Report

A fireman aged 39 was admitted to hospital on December 28, 1954, with a history of dull backache for a fortnight, followed a week prior to admission by marked swelling of

FIG. 1.—Chest x-ray film taken on January 28, after aspiration of chylopleurothorax.

the legs and feet, and moderate swelling of the face, hands, and abdomen. There had been oliguria, headache, and tightness of the chest for a similar period. His previous medical history was limited to chronic dyspepsia of about eight years' duration. A barium-meal x-ray examination in 1949 had shown chronic gastritis. There was no significant family history.

On examination his general condition was fairly good, with slight pallor and slight puffiness of the face, and marked pitting oedema of the whole of both legs. He had moderate ascites and the liver was just palpable and tender, but the spleen was not felt. There was no cardiovascular abnormality and his B.P. was 140/90. There were signs of fluid at the base of the left lung.

The following investigations were carried out during the week immediately following admission. Urine: protein ++++, with numerous hyaline casts and a few pus and red cells, and sterile on culture. Blood urea, 90 mg. per 100 ml.; urea clearance, 4.5% normal; total plasma proteins, 4.4 g. per 100 ml. (albumin 3 g., globulin 1.4 g.), A/G ratio 2.14:1; blood cholesterol, 310 mg. per 100 ml. A blood count showed: Hb, 119%; W.B.C., 11,400 per c.mm. (neutrophil polymorphs 87%, eosinophils 1%, lymphocytes 9%, monocytes 3%); E.S.R., 11 mm. at one hour (Wintrobe); normal morphology of red and white cells. Serum sodium 139 mEq/l.; serum potassium, 6.1 mEq/l.; serum chlorides, 101 mEq/l. Blood W.R. and Kahn tests negative.

He was given 2 pints (1,140 ml.) of dextran intravenously on January 3, 1955, with no diuretic effect, but repetition of a similar transfusion on January 8 resulted in a diuresis of 76 oz. (2.16 litres). A further 2 pints (1,140 ml.) of plasma was given on January 11, but caused no diuretic effect. In spite of these transfusions his total plasma proteins

never exceeded 4.4 g./100 ml., and in fact fell to 3.3 g. on January 13, with albumin 2.2 g. and globulin 1.1 g. (A/G ratio 2 : 1).

A chest x-ray examination on January 24 showed the appearances of a left hydropneumothorax, with some consolidation in the right mid-zone next to the hilum. Aspiration of the left chest showed that the condition was a chylopneumothorax, milky opalescent fluid being withdrawn. The stained deposit showed polymorphs, eosinophils, and lymphocytes in approximately equal proportions and a few endothelial cells, and also strongly sudanophilic isotropic droplets. No pyogenic bacteria or acid-fast bacilli were seen and cultures were sterile. The total protein content was 600 mg. per 100 ml. and the pH 7. A chest x-ray film taken on January 28 (Fig. 1) showed an increase in size of the tumour shadow in the right lower zone.

The blood-urea level gradually rose to 284 mg. per 100 ml. on January 31, and the patient died on February 3 at 2 p.m.

Post-mortem Findings

Necropsy was performed 22 hours after death. The changes of most interest were seen in the lungs and kidneys. The hilar region of the right lung was the seat of a white, partly necrotic tumour 4 cm. in maximum dimension, blocking all three lobar branches. There were obstructive infective changes in the peripheral parts, mainly in the lower lobe. Lymphatic spread to the right hilar, tracheal, and upper abdominal lymph nodes had occurred. Neither tumour involvement of the thoracic duct nor a bronchial fistula could be demonstrated. Blood-borne secondary nodules were present in the liver and left adrenal. A small serofibrinous effusion was present in the left pleural cavity, not now demonstrably chyliform.

Further, many pulmonary arterial branches in both lungs contained partly organized thrombi, apparently embolic in type. There was a solitary recent infarct in the left lower lobe.

The kidneys weighed 140 g. each. The capsules stripped easily from smooth pale surfaces. On the cut surfaces there was marked pallor and swelling of the cortical zones. The medullary areas were slightly congested. The tributaries of each renal vein and each main vein contained partly organized thrombus, the medial extremities of which projected slightly into the lumen of the inferior vena cava. The latter channel contained only post-mortem thrombus. The renal arteries and the pelves and ureters were macroscopically normal.

Other findings included fat necrosis of the pancreas and a small active peptic ulcer in the pyloric antrum.

Histologically, the lung tumour was composed of large, somewhat anaplastic, undifferentiated epithelial cells with eosinophilic cytoplasm. The appearances suggested a squamous growth. The stroma was scanty, and foci of necrosis and mitotic figures were numerous. The liver and

adrenal deposits showed a similar structure. Microscopical study of the kidneys showed that thrombi were confined to extrarenal venous channels. Small eccentrically placed fibrin thrombi, not occluding the lumen completely, were seen in venules between 400 and 700 μ in diameter. They were of some duration, being encapsulated and partially penetrated by argyrophilic fibrils springing from the endothelium. In larger vessels (1–2 mm. diameter) the lumen was more severely occluded and more advanced stages of organization were observed, with pronounced condensation of the fibrin (Fig. 2). In the large tributaries and main renal veins, both partially organized and recently formed thrombus material was present, extensively but not completely blocking the lumen.

The cortical zones showed separation of the tubules due to oedema and fine fibrosis. A few pyramidal subcapsular scars with lymphocytic infiltration were present. The glomeruli were slightly swollen. Occasional capillary loops contained small hyaline thrombi, and in others small foci of polymorphs were present. Slight thickening of capillary basement membrane could be demonstrated by the periodic-acid-Schiff technique. The tubular epithelium was generally atrophic. Many tubules contained highly proteinous casts. A few contained granular debris and purulent material. The pelvis showed mild chronic inflammatory changes.

Thrombi were not found in the body apart from those in the renal and pulmonary vessels.

Comment

The occurrence in combination of the lesions described above is of interest on the basis of its rarity alone, as we are not aware of the existence of similar published examples.

A dogmatic opinion cannot be given regarding which lesion came first in time, but the probability is that this is another example of malignant disease presenting as a thrombotic state. The observation of Wright (1952) is important—namely, that a diagnosis of malignancy must be considered when thrombophlebitis persists, or is migratory, despite adequate anticoagulant therapy in adults over 30; or when unexpected bleeding occurs in such patients whose prothrombin times are within the therapeutic range. Although the presence of metastasizing bronchial carcinoma in the present case rendered the final outlook hopeless from the beginning, other cases not induced by any form of malignancy might respond to anticoagulant treatment. Early recognition of the pathogenesis of the nephrotic syndrome in such cases would be essential, if serious impairment of renal functions were not to preclude successful control of such treatment. Renal biopsy would have been of no positive value in establishing the underlying pathogenesis in this case, since thrombi were confined to extrarenal veins, but it might have served to exclude other causes. Further information on the value of this investigation, and of renal venography, would seem desirable. Possibly the only relevant feature in this patient was the rapidity of the process, the blood urea level rising quickly. The picture, we feel, was thus one of a "nephrotic" patient passing unusually rapidly into an azotaemic state.

Summary

A case of the nephrotic syndrome is presented, in which the underlying aetiology was bilateral thrombosis of the renal veins, associated with, and probably attributable to, bronchial carcinoma.

ADDENDUM.—Since the submission of this article for publication, Harrison *et al.* (1956) have recorded 11 cases with radiological or necropsy evidence of renal vein thrombosis. They described in detail two methods of radiological diagnosis. One case is reported in which biopsy showed a carcinoma distal to the orifice of the right upper-lobe bronchus, and in which a subacute glomerulonephritis has been diagnosed for two and a half years. Biochemical changes were typical of the nephrotic syndrome. Inferior caval venography demonstrated blockage of the lower end

FIG. 2.—Hilar region of left kidney ($\times 20$). Elastic van Gieson. Normal renal artery. Medium-sized vein almost completely filled with well-organized thrombus.

of the vena cava, but not the upper limit. There was no necropsy. A case with great similarity to our own has been reported by Brumfitt and O'Brien (1956).

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INTRAHEPATIC CALCIFICATION

BY

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The finding of intrahepatic calcification on routine chest radiography is felt to be unusual enough to arouse interesting speculative discussion as regards aetiological factors. The following case is recorded in view of the relative rarity of the lesion, the absence of symptoms, and the associated diagnostic problem.

Case Report

A white man aged 37 attended for routine medical examination prior to re-enlistment in the Army. On questioning he was completely asymptomatic and admitted to no upset of any individual system. His appetite was good and his weight steady. In particular there were no symptoms referable to the gastro-intestinal system. He smoked 30 to 40 cigarettes a day and drank an average of 2 pints (1.1 litres) of beer a day.

His previous history revealed the following: B.T. malaria in 1943 while in Assam; treated with quinine; none since 1943. Amoebic dysentery and hepatitis in 1945, while in

Assam; he was treated in hospital for one month and received two injections (? emetine) and made an uneventful recovery. He had never worked with dogs or other animals and had never been in Australia or abroad apart from Assam. He had no recollection of ever having jaundice save the attack in 1945, in Assam, and had never suffered from urticaria or skin rashes. The family and social histories revealed nothing relevant.

Clinical examination showed no abnormality in any of the systems; in particular there was nothing to suggest hepatic disease. A routine chest x-ray examination revealed multiple streaks of calcification under the right diaphragmatic leaf, these areas of calcification being arranged in an arcuate manner suggesting the wall of a cyst in the liver area.

A tentative diagnosis of a calcified cyst of uncertain aetiology in the right lobe of the liver was made and the following investigations were undertaken: haemoglobin, R.B.C., and E.S.R. normal; W.B.C., 5,400 (polymorphs 46%, lymphocytes 54%); W.R. and Kahn, negative; liver-function tests and serum protein values normal; M.S.U., normal; examination of stools for cysts, amoebae, ova, and pathogens, negative; Mantoux 1/1,000 positive; Cassoni test negative; complement-fixation test for hydatid disease was positive, titre 1:4.

X-ray examination of the upper abdomen, to show diaphragm and liver area, revealed a rounded calcified shadow about 3 in. (7.5 cm.) in diameter and clearly demarcated (see Fig.). Lateral views showed this to be situated in the posterior part of the right lobe of the liver. Screening added no further information, the lesion appearing solitary. There was no overlying deformity of the diaphragm, which moved equally on both sides, and the right lower zone of the lung fields was clear. Unfortunately it was not possible to perform tomography.

Discussion

Intrahepatic calcification is not common, and raises an interesting diagnostic problem. There are several possible explanations, although none is by any means common. Thus F. W. Konzelmann, in a series of 8,000 necropsies, detected hepatic calcification to any marked extent in only one case (Heilbrun and Klein, 1946).

Hydatid Disease.—This can often give rise to intrahepatic calcification, and is of two types. (a) Solitary, showing on radiography as a smooth, well-defined unilocular lesion, the calcium appearing as reticulated streaks or more solid areas throughout the cyst wall. (b) Alveolar hydatid disease (echinococcosis-bavaro-tyrolienne). This is far less well known, largely because of its fairly limited geographic distribution (South Germany, Switzerland, Czechoslovakia, Tyrol, and East Russia). Walshe (1954) reported what was probably the first case in Britain, occurring in a person who had never been abroad. Opinion is swinging towards the acceptance now that alveolar hydatid disease is due to the same parasite as the common hydatid lesion, the differing pathological process being due to the larval variant. This type of hydatid lesion is far commoner in the right lobe of the liver, and the original "mother" lesion does not encapsulate but evaginates, with the resulting formation of multiple minute cysts in the surrounding liver substance. Each lesion is surrounded by a zone of granulomatous reaction, and the lesion is progressive and of fatal outcome. Because of the progressive nature and its ill-defined limits, this form is not amenable to surgery. The reason for this "alveolar" form as distinct from the commoner hydatid lesion is thought to be its original failure to encapsulate, so allowing leakage of contents and infiltration into surrounding tissues. Spread may proceed via blood and lymphatic channels to any part of the body. In cases where calcification occurs, radiological appearances of the liver show multiple irregular calcified areas around the main original lesion.

Hepatic Abscess.—This may be of pyogenic origin, including subdiaphragmatic foci, or may follow on

Postero-anterior view of upper abdomen.