INTESTINAL LESIONS IN MALIGNANT HYPERTENSION

WITH REPORT OF A CASE

BY

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[WITH PHOTOGRAPHURE PLATE]

Although pathological studies of the widespread arteriolar lesions in hypertension have been made, and their frequency in the spleen, kidney, adrenals, pancreas, and gastro-intestinal tract noted, the clinical implications have not been so fully considered (Fishberg, 1934; Moritz and Oldt, 1937; Morlock, 1939; Foa, Foa, and Peet, 1943; Klemperer and Otani, 1931). Fishberg found in his series that only 9% of those with hypertension showed involvement of the gastro-intestinal vessels, while Moritz and Oldt found 15% in a similar group of cases. A study of the literature has failed to reveal any report of the clinical picture produced by such lesions, although it is apparently known that ulceration, haemorrhage, and even perforation with peritonitis may occur. In the present case the intestinal lesions were of great severity and had caused partial infarction of the ileal wall leading to ulceration, haemorrhage, and peritonitis. Clinical symptoms were noted, but they were overshadowed by those of the more serious hypertensive attacks and by the action of the sedatives which the attacks necessitated.

Case Report

A married woman aged 44 was admitted to hospital on July 29, 1946, complaining of severe morning headaches and vomiting. There was a two-weeks history of mistiness of vision, morning headaches associated with persistent retching and vomiting, and dyspnoea on exertion. She had lost 28 lb. (12.7 kg.) in weight over an unspecified period of time. She had had five children, all of whom were alive and well. During two of her pregnancies she had suffered from toxæmia (1931 and 1938), but neither had to be terminated. Recovery in each case was apparently uneventful.

On examination she was found to be pale, thin, and slightly pigmented. Gross bilateral papilloedema was present, and the heart showed clinical enlargement. Blood pressure was 270/170 and haemoglobin 82% (Haldane).

The vomiting remained very persistent, and haematuria, menorrhagia, and rectal bleeding soon followed. By Aug. 11 the haemoglobin had fallen to 42%, the blood urea was 100 mg. per 100 ml., and the urea clearance gave an average figure of 16%. Cystoscopy revealed bleeding from each ureteric orifice, and rectal examination was tender on pressure in the pouch of Douglas. The patient complained of epigastric pain, which was not accompanied by rigidity, and soon afterwards had a sudden attack of cough and tightness in the chest, which was relieved by morphine. On Aug. 12 there was still some abdominal pain and distension, and hiccup proved troublesome.

For the next eleven days the clinical picture was one of persistent vomiting, gradually increasing abdominal distension, obstinate constipation, and a slowly falling pulse, although there was no associated rise of temperature. On Aug. 23 she had a typical hypertensive fit, which lasted for five minutes and ended in coma; a gradual recovery of consciousness followed. The neck veins were distended, the liver extended to three finger-breadths below the costal margin, and the blood pressure had fallen to 210/130. Further attacks occurred, and the patient died in coma on Aug. 25.

Post-mortem Examination

The body was pale, thin, and wasted, with marked abdominal distension, and weighed 6 st. 11 lb. (43 kg.). Internal appearances were as follows. Brain: Congested and oedematous;

marked atheroma of the basal vessels. Spinal column: pronounced scoliosis; cord not examined. Heart: Weight, 400 g.; left ventricular hypertrophy and dilatation; both auricles dilated; tricuspid ring admitted tips of four fingers, the mitral orifice three fingers; heart muscle of fair quality. Coronary arteries: Slight generalized thickening of wall, but lumen not obviously diminished. Aorta: Moderate degree of atheroma, especially in the abdominal portion. Lungs: Air passages contained much fine froth, while the lungs showed acute oedema and congestion. Peritoneum: About 100 ml. of turbid yellow fluid was present in the general peritoneal cavity, and about 50 ml. of pus in the pelvis; several coils of ileum were loosely adherent and showed plaques of fibrin on the peritoneal aspect. Stomach, duodenum, and jejunum were normal. Mesenteric vessels: Careful examination showed no macroscopic abnormality.

Ileum: At about its middle a length of some 4 ft. (1.22 metres) showed areas of haemorrhagic mucosa in which superficial ulceration could be clearly seen; the ulceration had no particular distribution. Large intestine, normal. Liver: Weight 1,420 g.; cut surface pale, otherwise normal. Spleen: Weight, 90 g. Dark, firm, congested. Kidneys: Weight, left 96 g., right 100 g. Both showed similar appearances; the capsule stripped with some difficulty, leaving an irregular, finely granular surface; the cut surface showed the kidney pattern to be preserved, while the average thickness of the cortex was 6-7 mm.; the blood vessels in the marginal zone were unduly prominent. Bladder: Contained about 50 ml. of purulent urine. The interior appeared normal except for a superficial ulcer, 1 cm. in diameter, which was covered with whitish necrotic material.

Histological Report

In order to classify the retrogressive changes sections were stained by haematoxylin and eosin, Sheridan's elastic stain with Van Gieson, Mallory's phosphotungstic acid haematoxylin and the picromallory method (McFarlane, 1944). The results are given below.

Heart.—The muscle fibres show evidence of marked hypertrophy, and there are in addition several areas of degeneration and replacement fibrosis.

Cerebral cortex.—Brain tissue normal. Arterioles in overlying meninges show some medial hypertrophy.

Striated muscle (pectoralis major).—Small areas of replacement fibrosis only.

Lung.—Congestion of alveolar capillaries, with a small amount of eosinophil material and some "heart failure" cells in a number of the alveoli.

The most marked changes were seen in the kidney and ileum, where degeneration and necrosis were prominent. On the other hand, the medial hypertrophic changes seen in hypertension were present in all the sections taken. These changes have been classed as:—(1) Intimal fibrosis: Staining reaction is pale pink with Van Gieson's method and blue with picromallory. (2) Fibrinoid degeneration: Reddish-orange with picromallory, bluish-purple with Mallory's phosphotungstic acid haematoxylin. (3) Arteriolar necrosis: Here the disintegration of the wall can be seen with haematoxylin and eosin.

Ileum.—Sections show superficial ulceration of the mucosa with secondary infection (Plate, Fig. 1). The most striking change is in the arterioles of the submucosa, where (a) the lumen shows great diminution as a result of intimal fibrosis (Fig. 2); (b) well-marked fibrinoid degeneration is present; and (c) in some vessels there is disruption of the vessel wall with surrounding inflammatory-cell reaction (Figs. 3 and 4).

Kidney.—Considerable narrowing of the interlobular and afferent glomerular vessels is present. In each case there is marked intimal fibrosis, but in addition the afferent glomerular arterioles show fibrinoid degeneration. Some glomeruli show focal degeneration of the tuft (Fig. 5), the affected portion giving a similar staining reaction to that of fibrinoid degeneration in the arterioles. In addition many glomeruli show thickening of Bowman's capsule with an occasional adherent tuft.

Adrenals.—Marked intimal fibrosis of capsular arterioles with early fibrinoid degeneration.

Liver.—Some increase in the portal tract connective tissue, together with intimal fibrosis and early fibrinoid degeneration of the hepatic arterioles.

Bladder.—A small area of superficial ulceration is present. While the arterioles show definite diminution of the lumen as a result of

intimal fibrosis, the change is not comparable in severity to that seen in the ileum.

Uterus.—Arterioles of uterine wall show considerable narrowing as a result of intimal fibrosis.

Discussion

Although most attention has been devoted to the kidney in the study of hypertensive arteriolar lesions, the widespread nature of the change has been well recognized. Morlock (1939) studied the ratio of the size of lumen to thickness of arteriolar wall in a hypertensive and a control group and claimed to have found significant changes in a number of organs, including the gastro-intestinal tract. Foa, Foa, and Peet (1943) carried out similar measurements in muscle biopsies and compared them with those made in the arterioles of many organs from a series of post-mortem cases. They concluded that the abnormalities found in the muscle biopsies were representative of the general arteriolar changes in the rest of the body. An excellent and very complete study of hypertensive arteriolar lesions throughout the body was made by Moritz and Oldt (1937), who demonstrated that similar mild changes might be found in certain organs in non-hypertensive individuals, although severe changes were rare except in the spleen. When the changes in a hypertensive group were compared the organs most often affected were, respectively, the spleen, kidney, pancreas, adrenals, and gastro-intestinal tract. In these organs the lesions were in many cases classed as severe. It is therefore a very significant fact that two organs—namely, the kidney and the gastro-intestinal tract—should show frequent severe arteriolar lesions in hypertensive cases when no case in the control group showed any severe change in these organs. In contrast there were a number of cases with severe lesions of the splenic arterioles in the control group, and their appearance in hypertensive cases is thus of lesser significance (see Table). They furthermore noted

Table Showing Incidence of Severe Changes (figures from Moritz and Oldt, 1937)

Organs	Severe Changes	
	Non-hypertensive Group	Hypertensive Group
Spleen	21%	55%
Kidney	0%	47%
Gastro-intestinal tract ..	0%	15%
Pancreas	5%	43%
Adrenals	6%	42%

that 38% of those with chronic hypertension showed superimposed acute degenerative, necrosing, and inflammatory lesions in the renal arterioles. This type of lesion was not, however, confined to the kidney, and it is interesting to note that it was found next most frequently in the gastro-intestinal tract. It is now well realized that a small number of patients with chronic hypertension, whatever the aetiology, may develop a terminal malignant hypertension, and the acute lesions described represent this condition. The fact that severe lesions are found more often in benign hypertension in the spleen, kidney, pancreas, and adrenals than in the gastro-intestinal tract is in marked contrast to the incidence in malignant hypertension. Here the gastro-intestinal arterioles are affected next in frequency to the kidney, and it clearly suggests that when severe gastro-intestinal lesions occur they are confined to cases of malignant hypertension. It should not, however, be forgotten that the retinal vessels are not normally examined at necropsy, and probably have the highest incidence of all.

These observations have been amply confirmed in experimental work where the pathological picture was one of malignant hypertension. Wilson and Pickering (1938), producing hypertension in rabbits, noticed especially well-marked acute arterial lesions in the intestine. Wilson and

Byrom (1939) found in their hypertensive rats that, apart from the kidney, the most severe acute lesions were present in the mesenteric arteries, and that these lesions were so acute as to resemble those seen in human polyarteritis nodosa. This is of some interest when it is remembered that the kidney and gastro-intestinal vessels are so often affected in that disease. Pickering and Prinzmetal (1938) found acute arterial and arteriolar lesions in the gut in hypertensive rabbits and described petechial haemorrhages in that organ. This is reminiscent of Goldblatt's (1938) classical hypertensive experiments on dogs, in which he found similar petechial haemorrhages in the gastro-intestinal tract and which he attributed to rupture of a dissecting haemorrhage into the walls of severely degenerated, hyalinized, or necrotic arterioles. This lesion of the arterioles he considered to be identical with that seen in malignant hypertension in man.

There are few references in the literature to gastro-intestinal arteriolar lesions giving rise to pathological changes such as ulceration and haemorrhage in man. This may be due to the fact that the disease has proved fatal before the gastro-intestinal changes have become sufficiently advanced. Klemperer and Otani (1931) described four cases of "haemorrhagic enterocolitis" in malignant hypertension, but gave very few details beyond noting that in one of these cases the lesion was confined to the jejunum and ileum. Jablons (1944) in a clinical study of gastro-intestinal symptoms in hypertension and renal disease found that most cases showed no "demonstrable macroscopic lesions" in the gastro-intestinal mucosa. He mentions, however, that ulcerative lesions occur in malignant hypertension and are often responsible for extensive bleeding. In a series of ten cases he found ulcerative lesions of the large intestine in two. Jablons states that this ulceration may occur anywhere in the alimentary tract from the pharynx to the anus and may cause haematemesis or rectal bleeding at the outset of the disease, although it is commoner as a terminal feature. Professor Clifford Wilson (personal communication) states that he has observed vascular lesions in the bowel in many cases of malignant hypertension, sometimes leading to ulceration and in two cases to perforation and peritonitis. These observations are well in accord with the features of the present case, in which rectal bleeding developed just over two weeks before death, and in which ulceration of the small intestine with peritonitis was found at necropsy although no perforation had occurred. A clinical diagnosis was not made, probably because there was considerable sedative administration to combat the rather severe terminal hypertensive attacks.

It is therefore suggested that gastro-intestinal ulceration, haemorrhage, and perforation occur only in malignant hypertension. In this disease the arteriolar lesions are of necessity much more severe, and the gastro-intestinal vessels are involved in a greater number of cases. The recognition of such a possibility is considered to be of clinical importance, although it is realized that in a number of cases gastro-intestinal complications will occur only as a terminal event.

Summary

A case of malignant hypertension with intestinal ulceration, haemorrhage, and peritonitis is described.

The pathological lesions of the alimentary tract are accounted for by the increased vulnerability of the gut in malignant hypertension.

The possible clinical importance of recognizing such a condition is raised.

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SILICEOUS GRANULOMA DUE TO TALC

A CAUSE OF POST-OPERATIVE PERITONEAL ADHESIONS

BY

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[WITH PHOTOGRAVURE PLATE]

Post-operative peritoneal adhesions have long excited the interest of surgeons and stimulated speculation about their pathogenesis. One is often surprised at operation by the scantiness, softness, and avascularity of intraperitoneal adhesions seen after the resolution in an unopened abdomen of a bacterial inflammation such as an appendicular abscess or a more generalized peritonitis. On the other hand, if it be necessary to reopen the abdomen after an aseptic laparotomy, adhesions may be found that are dense, vascular, and widespread. These findings suggest that laparotomy may on occasion introduce into the abdomen a substance more persistently irritant than bacteria. Observations over the past 15 years have identified one such irritant as talc—a complex magnesium silicate—the substance used almost universally in the preparation of gloves for operation. Two excellent reviews on the harmful effects of talc in the peritoneal cavity have appeared in the past year in America (Eiseman, Seelig, and Womack, 1947) and in this country (Roberts, 1947).

Within the abdomen the irritant action of talc elicits a proliferative response comparable to that found in traumatic siliceous granuloma (pseudotuberculoma silicoticum) (Shattock, 1916; Faulds, 1935). The effects are not limited to the peritoneum, and the implantation of talc at laparotomy may be followed by granulomatous formation in the scar, by sinuses or faecal fistulae, stenosis of entero-anastomotic stomata, and, as Roberts has shown, by chronic fibrosis of the Fallopian tube with consequent sterility. The patient's history and the density of the peritoneal adhesions found at operation may suggest the diagnosis of siliceous granuloma, but the only certain proof is to find, in microscopical sections of the collagenous tissue, doubly refractile material with the appearance of talc closely related to foreign-body giant cells. The use of "polaroid" screens on the ordinary microscope is simple and usually leaves little doubt about the diagnosis, but, unless sections are examined for anisotropic material, cases may easily escape recognition and be diagnosed as tuberculosis, regional enteritis, sarcoidosis, keloid scar, or non-specific foreign-body reaction, although the situation of the granuloma may well occasion comment.

Foreign bodies such as suture material are often surrounded by giant cells and can show in varying degrees

the property of rotating the plane of polarized light, but they are unlikely to be scattered diffusely in the peritoneum, and the structure of talc as seen by polarized light is fairly characteristic (see Plate, Fig. 3). Many years after its implantation in the tissues talc has been recognized in sections prepared by routine histological methods (Roberts, 1947).

Case History

Miss B., aged 74, was admitted to the medical wards of the Western Infirmary on Oct. 3, 1947, for investigation of a severe anaemia which had developed over the past four years. She was found to be passing considerable quantities of altered blood in the stools, but intensive clinical, haematological, and radiological investigation failed to establish a source. Transfusion of 9 pints (5.1 litres) of blood over a period of a month scarcely replaced the loss, and her condition remained precarious. The decision to perform laparotomy was taken in the hope of finding the bleeding-point. She had undergone no previous abdominal operation.

First Operation.—On Nov. 26 Prof. C. F. W. Illingworth made a right paramedian incision in the upper abdomen, and his note states that wide exploration of the abdomen was carried out. A Meckel's diverticulum was found attached by its fundus immediately deep to the umbilicus. The diverticulum was not apparently the source of bleeding and so was not removed, though its tip was freed from the abdominal wall. The spleen was enlarged to perhaps twice normal size. The previous haematological investigations having yielded no facts to contraindicate splenectomy, this was carried out and the arteries at the ends of both curvatures of the stomach were divided in the hope that the undisclosed lesion might be in the upper division of the portal system. The patient recovered uneventfully from this operation, but bleeding into the alimentary tract continued. On several occasions aspiration of the stomach was carried out over long periods, but no blood was recovered. By Dec. 9 the haemoglobin level had fallen to 38% and it appeared necessary to explore the abdomen once more. In the absence of Prof. Illingworth the responsibility for this step fell on one of us (W. A. M.). The patient was prepared by transfusion of 4 pints (2.27 litres) of blood.

Second Operation.—This was performed on Dec. 9, 13 days after the first operation. There were dense adhesions of recent origin involving the stomach, omentum, the Meckel's diverticulum, and the anterior abdominal wall. The diverticulum was removed and opened but no ulceration was found. The entire small bowel contained altered blood; nowhere throughout its length could a polyp or ulcer be palpated, but accurate examination of the stomach was prevented by adhesions. The abdomen was then closed; recovery from the operation was satisfactory, and four days later the haemoglobin value was 82%. Bleeding into the alimentary tract, however, continued as before, and to date is unexplained.

Pathological Report.—The specimen consists of a Meckel's diverticulum 3.5 cm. long. The peritoneum is dull and the wall thick and dense. The mucosa has a normal velvety appearance. Histological sections show zones of thickly woven collagenous connective tissue external to the muscularis and extending into it here and there for a short distance. This tissue replaces most of the subserous fat, is responsible for the increased thickness of the wall, and forms the outer surface of the diverticulum at several places (Plate, Fig. 1). Imbedded in it lie many foci of macrophages and foreign-body giant cells, arranged in some instances in the form of poorly defined follicles. These cells surround brownish crystalline doubly refractile particles of an average length of 15 μ and of a shape identical with surgical talc (Figs. 2 and 3). Similar material is seen underneath the serosa in varying concentrations in all parts of the diverticulum. The mucosa is of normal small-intestine type and no areas of gastric heterotopia are present.

Comment

There is no doubt that these lesions had their origin in the first operation, 13 days before the specimen was removed. It is comparatively rarely that the opportunity occurs to examine tissue removed from the abdomen such

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FIG. 1.—Low-power view of one of the many ulcers found in the ileum at necropsy.

FIG. 2.—Extreme diminution of arteriolar wall. Overlying mucosa can be seen at the top of the picture ($\times 150$).

FIG. 3.—Arteriolar necrosis. Vessel on left shows disintegration of its walls and cellular infiltration ($\times 100$).

FIG. 4.—Arteriolar necrosis. Larger vessel shows disintegration of wall. Lumen identified only by presence of a few red cells ($\times 160$).

FIG. 5.—Glomerulus showing adherent tuft in which focal necroses can be seen ($\times 150$).

K. DAMODARAN: THE LIVER IN INFECTIVE HEPATITIS

FIG. 1.—Acute necrosis ($\times 170$).

FIG. 2.—Early fibrous reaction ($\times 80$).

FIG. 3.—Post-mortem autolysis ($\times 180$).

FIG. 4.—Subacute hepatic necrosis ($\times 30$).

FIG. 5.—Subacute hepatic necrosis ($\times 170$).