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Pathological Study of the Intestinal Infarction -especially Non-occlusive Intestinal Infarction

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SUMMARY

Among intestinal infarctions, there is a relatively high incidence of non-occlusive intestinal infarctions, which have no evidence of apparent mesenteric vascular occlusion. In these cases, etiology and/or pathogenesis are not known, though some authors described congestive heart failure, digitalis intoxication, minute vessel occlusion, vasospasmus and so on as the trigger of the disorders. The purpose of this study is to examine the vascular factors which have not been reported systematically.

Fifteen autopsy cases were used for this study including five cases of vascular occlusive intestinal infarction (two of arterial occlusions, two of venous occlusions and one of strangulation) and ten non-occlusive ones. Specimens for pathological study were obtained from both mesenteries and intestinal walls.

As to the lesions of the intestinal walls, there were some differences between arterial and venous occlusions. Arterial occlusion showed mucosal necrosis and submucosal congestion while venous occlusion showed marked edema and hemorrhage of intestinal walls with less common necrosis of the mucosa.

Ten cases of non-occlusive intestinal infarctions consisted of eight diffuse and two segmental cases. In the latter, in addition to marked stenotic atherosclerosis of the proximal superior mesenteric artery(SMA), the branch of the SMA toward the impaired parts of intestine was also narrowed by arteriosclerosis. Three of eight diffuse infarction cases also had stenotic proximal SMA and one of them had diffuse arteriosclerotic narrowing from proximal SMA to small mesenteric arteries (vasa recta). One of the other five cases presented microthrombi in the intestinal wall, suggesting Disseminated intravascular coagulation (DIC). The remaining four cases had no obvious vascular changes.

In clinical aspects, six of ten non-occlusive intestinal infarction cases had cardiac diseases such as congestive heart failure, myocardial infarction and pericardial effusion. Hypertension was also found in five of ten cases. Hypotension (shock) before intestinal symptoms became manifest was not seen in any cases.

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INTRODUCTION

Circulatory disturbances of the digestive tracts, especially of intestines, are one of the fatal disorders even nowadays when medical science has progressed rapidly. Strangulation ileus and mesenteric vascular obstruction have reportedly been the main clinico-pathological features of intestinal infarction. In recent years, circulatory disturbances of intestine with no evidence of vascular occlusion have attracted considerable attention, and clinical and experimental reports have increased in number. Some authors estimated that systemic circulatory disturbances, i. e., cardic disease, shock, etc., are the important etiologic factors, and others attached importance to microthrombi of the intestinal wall. However, unanimous concordance has not been attained.

Many of the studies in the literature dealt with large intestinal ischemia, i. e., ischemic colitis mostly using surgical materials without systematic pathological studies of mesenteric vessels. As to the small intestines, non-occlusive intestinal infarctions were reported mainly in 1960's but systematic pathological studies of mesenteric vessels were not performed. These authors suggested that vasospasmus occurring at systemic circulatory disturbance was the pathogenetic factor.

In the cases of non-occlusive intestinal infarctions, pathophysiological conditions such as advanced age, heart failure and hypotension were pointed out by many authors as important etiologic factors. These conditions are readily acceptable. Using autopsy cases whereby the mesenteric vessels as well as intestines could be examined, I examined non-occlusive intestinal infarctions and also the intestinal changes in occlusive and non-occlusive intestinal infarctions, to investigate the vascular changes for the factors of non-occlusive intestinal infarctions.

MATERIALS AND METHODS

From the autopsy cases of the Nagasaki University School of Medicine and its related hospitals, intestines which had mesenteries together were reexamined to possible extent, paying much attention macroscopically to erosion, ulcer, hemorrhage and infarct. Excepting etiologically evident cases such as intestinal amebiasis and fungus infection, intestines seemingly with circulatory disturbances were collected. Moreover intestinal infarction cases were picked up from autopsy protocols and Annual of the Pathological Autopsy Cases in Japan and some of them were added to the material after microscopical reexamination. The cases wherein intestines had no mesenteries or whole bowels were not preserved were excluded from this study because the relation between infarcted bowels and mesenteric vessels could not be examined.

Macroscopical observation of intestinal walls and cross cut surfaces of mesenteric vessels were made, and then as shown in Fig. 1, nine specimens of mesentery, three of mesocolon, three to six of small intestine and three of large intestine were taken as a rule. When further examination was needed, more specimens were prepared accordingly.

Specimens for histopathological study were embedded in paraffin and sliced into 3 to 5 μ sections. Hematoxylin-EOSIN stain, Elastica Van-GIESON stain and Azan-MALLORY stain were performed as a rule, and other special stains were performed as needed. Intestines and mesenteric vessels were examined by light microscopy.

Clinical findings were taken from medical charts and partly from autopsy protocols.

RESULTS

In 289 autopsy cases randomly selected and examined macroscopically, 63 had intestinal lesions such as congestion, hemorrhage and ulcers. From these, 15 cases in all wherein both intestines and mesenteries could be examined were collected as the materials of this study.

Etiologically these 15 cases consisted of five vascular occlusive intestinal infarctions (two of arterial occlusion, two of venous occlusion and one of strangulation) and 10 vascular non-occlusive intestial infarctions (Table 2 & 3).

(1) Age and sex

Table 1 presents age distribution. All cases were older than 50 years old. The age of arterial occlusion cases was particularly advanced. The average age of 10 non-occlusive infarction cases was 64.9 years. The cases of strangulation and venous occlusions were not so old when surgical cases were included.

The sex distribution was one male and one female in arterial occlusions, two females in venous occlusions and one male in strangulation. In non-occlusive infarctions, males were more numerous than females (M : F=8 : 2).

(2) Occlusive intestinal infarction

a) *Arterial occlusion*

The both cases of arterial occlusive infarctions (Table 2; cases 1 & 2) were due to the occlusion of the orifice of superior mesenteric artery (SMA) with mural aortic thrombi based on atherosclerosis. Infarctions were distributed from the jejunum to the right colon coinciding with the blood supply of SMA (Fig. 2). The main histological changes were mucosal necrosis and submucosal congestion (Table 2; Fig. 7).

b) *Venous occlusion*

The both cases of venous occlusive infarctions (Table 2; cases 3 & 4) were occured

Table 1: Age Distribution

Age	50—	60—	70—	80—	90—	Total
Arterial occlusion				1	1	2
Venous occlusion		1	1			2
Strangulation			1			1
Non-occlusive	2	5	2	1		10

Table 2: Pathological findings of vascular occlusive intestinal infarctions

Case No.	Sex Age	Cause	Site of lesion	Mucosa			Submucosa				PM		Mesentery	
				N.	C.	H.	C.	E.	H.	N.	H.	N.	C.	H.
1	M 93	Arterial thrombus	Jej.-Asc.	+	+	+	++	++	−	++	+	−	−	−
2	F 89	〃	Jej.-Trans.	+	−	−	+	−	−	−	−	−	−	−
3	F 67	Venous thrombus	Jej.-Ileum.		++	+	+	−	++	−	++	−	+	+
4	F 73	〃	〃	+	+	++	+	−	++	±	++	+	±	+
5	M 79	Strangulation	〃		+	+	++	−	++	−	++	−	+	±

N: Necrosis C: Congestion H: Hemorrhage E: Edema PM: Propria muscle

by thrombi of the superior mesenteric vein (SMV), which existed continuously to the portal vein. In case 3, SMV thrombus was complicated with liver cell carcinoma based on liver cirrhosis, and in case 4 (Fig. 3), venous thrombus was considered to be primary one though liver showed mild fibrosis.

In the mesentery, venous thrombi were seen from the main trunk of SMV to small mesenteric veins, partly to the intramural vein, though not occupying the whole mesenteric veins. Non-thrombotic areas still existed on both sides of the thrombotic mesentery. Thus, intestinal infarctions were limited to the small intestines, and proximal jeiunum and distal ileum were free from infarction. Macroscopic findings of infarcted bowels were thickening and purple-red discoloration (Fig. 3). Histologically, marked edema and hemorrhage were seen in the whole layers of intestinal walls (Fig. 8(a)) and in related mesenteries. Mucosal epithelium was not necrotic. Epithelium of the crypts were kept intact though that of the villi dropped out (Fig. 8(b)).

c) *Strangulation*

Case 5 was strangulation of the small intestine due to fibrous band originated from abdominal operation (gastrectomy) 20 years previously. Histologically, the intestinal wall disclosed marked hemorrhagic lesion resembling that of venous occlusion.

(3) Non-occlusive intestinal infarction

In Tables 3 to 6, clinical aspects and pathological changes of non-occlusive intestinal infarctions are tabulated. First of all, case reports are presented.

[**Case 6**] A 62-year-old female. About nine months before death, sigmoidectomy and colostomy were performed because of sigmoid cancer. Since then, having been followed up using chemotherapy, she became pancytopenic and developed high fever and hypotension for three to four days before she died. Two weeks before death, she suffered from epigastralgia and watery diarrhea, but the onset time of intestinal infarction was not clarified. Autopsy revealed diffuse small intestinal infarction. Metastasis of sigmoid cancer was not found in either intestines or mesenteries.

[**Case 7**] A 67-year-old male was pointed out one week before death to have heart failure

because of cough and stridor. Three days after he was ambulanced because of epigastralgia, vomiting and diarrhea. In his hospital days, he had high fever and leucocytosis, and then gradually became hypotensive. He died four days after developing abdominal symptoms. Autopsy revealed infarction of the small intestine and right colon. Though a clot of blood was obtained from the SMA, it was not thought to be thrombus as it was pulled out easily.

[**Case 8**] A 63-year-old male, being admitted because of mitral regurgitation and stenosis, had meteorismus complicated with hypotension, high fever and positive occult blood for a week before he died. At autopsy, diffuse intestinal infarction was found extending from the small intestine to the caecum. In spite of left atrial thrombus, SMA did not present any vascular occlusive lesions such as thrombi and emboli.

[**Case 9**] A 61-year-old male was admitted because of orthostatic disturbance, and further examination revealed thrombotic obstruction of the lower abdominal aorta, and a diagnosis of LERICHE's syndrome was made. Angiography was performed then but obstruction of SMA was not observed. He died next day showing ileus, hypotension, high fever and tarry stool. At autopsy, intestinal infarction extending from the ileum to the ascending colon was observed. Thrombo-emboli were not found in SMA or SMV.

[**Case 10**] A 53-year-old male was admitted because of heart failure and atrial fibrillation. He had hypertension in the past history, but after admission, blood pressure gradually dropped and he died. Abdominal signs and symptoms were not noted clinically. At autopsy, diffuse acute and old myocardial infarction was found. Also in intestines, diffuse infarction extending from the small intestine to the large intestine was observed. There were mural thrombi in the abdominal aorta under the orifice of renal arteries. Hematologically, there was hemoconcentration, but thromboembolism was not found in mesenteric vessels.

[**Case 11**] An 84-year-old male died three days after admission because of heart failure and bronchopneumonia. Abdominal symptoms were not recognized. Autopsy revealed old myocardial infarction and myocardial hypertrophy. Diffuse infarction of the small intestine and focal infarction of the large intestine were also found.

[**Case 12**] A 72-year-old male, being admitted because of liver cirrhosis, developed ileus and died after 14 hours. At autopsy, hemorrhagic infarction measuring about 30 cm in length was observed in the jejunum.

[**Case 13**] A 52-year-old male, being admitted because of lung cancer, died of respiratory failure. Abdominal signs and symptoms were not noted. At autopsy, two segmental infarctions, about 20 cm and 25 cm in length, were found in the center of small intestine (Fig. 4).

[**Case 14**] A 61-year-old female was operated for pancreatic abscess five years before. A half year ago, an abnormal shadow of chest X-P was pointed out. Further examination revealed cholangiocarcinoma, and then chemotherapy was commenced. It was complicated with DIC, pleural effusion and pneumothorax. Three days before death, severe abdominal pain and melena occurred. She also suffered from shock, renal failure and DIC

again, and then died. At autopsy, small and large intestines showed infarction.

[**Case 15**] A 74-year-old male had received drug therapy for arteriosclerotic heart disease and hypertension for four years. He was admitted because of heart failure four months ago and discharged after hospital therapy. Three days before death, he was admitted again because of abdominal pain and asthma attack. Abdomen became distended and blood pressure gradually dropped before he died. At autopsy, ischemic change was found in small and large intestines in addition to adenocarcinoma of the lung and general congestion.

a) *Background factors* (Table 3)

Of the ten cases of non-occlusive intestinal infarction reported in this paper, three cases (case 8 with left artial thrombus and cases 9 and 10 with abdominal aortic thrombus) had a possibility of SMA thromboembolism. However, careful examination revealed no thrombus nor embolus in the mesenteric vessels.

Cardiac diseases were found in six cases (60%; three of heart failure, two of myocardial infarction and one of pericardial effusion). Systemic circulatory disturbance was suspected to be the genesis of intestinal infarction. Table 4 shows pathologic findings of the liver and kidneys as the parameters of systemic circulatory disturbance. Congestive centroacinar necrosis of the liver was seen in four cases (all of them had cardiac disease), acute tubular necrosis of the kidney in one and acute tubular dilatation of the kidney in five. Thus the concurrent occurrence of circulatory disturbance in the liver and kidneys was relatively frequent.

Hypertension was seen in five of ten non-occlusive cases, but no hypotension im-

Table 3: Clinical aspects of non-occlusive intestinal infarctions

Case No.	Sex Age	Primary Disease	Cardiac Factor	Hypertention	Atherosclerosis of aorta	Abdominal Sign (Duration)
6	F 62	Sigmoid cancer	/	−	+	Diarrhea (2w)
7	M 67	Cardiac failure	Cardiac failure	+	±	Abd. pain Vomitting (3d)
8	M 63	MSR**	Cardiac failure	−	+	Meteorismus (1w)
9	M 61	Lerich's synd.	/	−	++	Ileus (1d)
10	M 53	MI*	MI*	+	++	None
11	M 84	MI*	MI*	+	+++	None
12	M 72	Liver cirrhosis	/	−	+	Melena Ileus (1d)
13	M 52	Lung cancer	Pericard. effusion	+	+	None
14	F 61	Cholangio-carcinoma	/	−	+	Abd. pain Melena (3d)
15	M 74	Lung cancer	Cardiac failure	+	+	Abd. pain (4d)

* Myocardial infarction ** Mitral stenosis & regurgitation

mediately before the onset of abdominal symptoms. In five non-hypertensive cases, hypotension was not seen immediately before the onset of intestinal infarction. There was a trend that intestinal infarction resulted in hypotension and subsequent death. Though digitalis was used in almost all cases in this study at least in the agonal period, digitalis intoxication was not observed.

Atherosclerosis of the aorta was noted corresponding to their ages, but it was not peculiar to this group.

Table 4: Microscopical findings of liver and kidneys in non-occlusive cases

Case No.	Central liver necrosis	Renal tubular necrosis (N) (dilatation (D))
6		+ (D)
7		
8	+	± (D)
9		
10	+	+ (N)
11	+	± (D)
12		
13		
14		+ (D)
15	+	+ (D)

b) *Lesions of the intestinal wall*

Histopathological findings of the intestinal wall are shown in Table 5. In this group, intestinal lesions varied from marked edema and hemorrhage resembling venous occlusion (Figs. 5 & 9) to necrosis and congestion resembling arterial occlusion (Figs. 6 & 10). All the cases showed only acute changes without any ulcers or cicatricial stenosis.

c) *Vascular findings*

In this group, there were no organic obstructive lesions in either SMA or SMV. However, vascular stenosis was present in some cases. Table 6 shows the degree of stenosis of SMA. At proximal site of SMA, five of 10 cases showed marked stenosis with atherosclerosis (about 70 to 80% narrowing; Figs. 11, 12(a), 13(a)).

About the branches of SMA (Fig. 1, M4-6), two cases of segmental infarction (cases 12 & 13) presented unusual stenotic figures in the arteries toward the infarcted parts of intestine. In case 12, fibrous thickening of the intima with vascularization in me-

Table 5: Degree of microscopical changes of small intestines

Case No.	Mucosa			Submucosa				PM		Mesentery	
	N.	C.	H.	C.	E.	H.	N.	H.	N.	C.	H.
6	+	+	±	±	±	‡	−	+	+	−	+
7		+	+	+	+	‡	−	+	+	±	+
8	+	+	+	+	−	−	+	−	+	+	−
9		+	−	±	−	+	‡	−	±	−	−
10		+	+	±	−	−	−	−	−	−	−
11		−	−	±	−	−	−	−	−	−	−
12		+	+	‡	‡	‡	+	+	+	±	+
13	+	±	−	+	−	+	−	−	−	−	−
14	+	±	+	+	−	+	−	+	+	−	−
15		+	+	+	−	−	−	−	−	−	−

N: Necrosis, C: Congestion, H: Hemorrhage, E: Edema, PM: Propria muscle

dia caused stenosis of one artery. Elastic fibers of the intima were hardly present in this case (Fig. 12(b)). In case 13, fibrous thickening with proliferation of elastic fibers of the intima and the vascularization in the media were seen (Fig. 13(b)). In this case, arterial narrowing was found in only one branch of SMA toward one of two segmental infarctions. These two arterial changes mentioned above were somewhat different from each other and also from common arteriosclerosis. Suspecting post-vasculitic changes, other organs were examined carefully but no vascular changes of this kind were found anywhere.

Table 6: Degree of arteriosclerosis of SMA

Case No.	M1	M2, 3	M4−6	M7−9	S1−6
6	+	±	±	−	−
7	+	+	+	±	−
8	±	±	+	±	−
9	±	±	+	−	−
10	##	±	+	±	−
11	#	+	+	±	−
12*	##	#	±(##)**	±	−
13*	#	##	±(#)**	−	−
14	±	±	±	−	−
15	##	#	#	+	−

* Segmental infarction
** Arteriosclerosis of one branch of SMA

Most of the 8 cases with diffuse intestinal infarctions showed only mild intimal thickening of the branches of SMA, but one case (case 15) showed relatively marked narrowing of the lumen due to arteriosclerosis (Figs. 14(a)).

In case 15, peripheral mesenteric arteries (Vasa recta) also presented moderate to marked fibrous intimal thickening (Fig. 14(b)). The other nine cases, including both diffuse and segmental infarctions, presented no intimal thickening or mild one (Fig. 15), if any.

There were no vascular changes in the vessels of the intestinal wall in any cases. Mucosal and/or submucosal microthrombi were seen in three cases (Fig. 16). In case 14, microthrombi were also seen in other organs, suggesting DIC. The other two cases (cases 7&8) showed them only in the intestinal walls.

DISCUSSION

Circulatory disturbance of intestines is a disease of poor prognosis if any appropriate therapy is not provided. Intestinal infarction was already reported as mesenteric vascular occlusion in the 19th century (VIRCHOW; 1847, FLLIOT; 1895)[1]. In Japan, according to HAYASHI[2], the first intestinal infarction case was reported by FUJII in 1915.

Recently, among intestinal infarctions, non-occlusive infarction with no organic vascular obstruction had been paid much attention, and a number of reports were presented mostly in 1960's. The concept of ischemic colitis introduced by BOLEY (1963)[3] and MARSTON (1966)[4] has become common clinically, and much efforts were made to elucidate the etiology and/or pathogenesis clinico-pathologically and experimentally[6][10][11][23]. However, there has been no report on systematical pathological studies of vascular changes in relation to intestinal ischemia.

In this report, relations between non-occlusive intestinal infarction and its vasculature were studied, using autopsy materials in whih both intestines and mesenteries could be examined systematically. In addition to this, intestinal lesions were compared between occlusive and non-occlusive infarctions. Fifteen cases were collected for this study.

1) INCIDENCE

MAEZAWA, *et al.*[5] selected 307 cases of intestinal infarction from the Annual of the Pathological Autopsy Cases in Japan in a decade from 1962 to 1971. This figure reportedly represented 0.15% of total autopsies in each year on an average. MIYAJI, *et al.*[6] reported that intestinal disorders due to circulatory disturbance were found in 5.5% of the serial autopsies at a medical center for aged persons. Except for the aforementioned aged group, intestinal infarctions are not thought to be so numerous among autopsy cases but there must be more cases if non-autopsied and surgically treated cases are included. More attention should be paid as MAEZAWA said. Furthermore, it is anticipated that incidence of intestinal infarction would gradually increase with the advancement of age in the society.

The incidence of non-occlusive intestinal infarctions among whole intestinal infarctions varies by author; 10 to 52% in the literature by MCGREGOR, *et al.*[7], 21% by BERGER and BYRNE[9], 50% by PIERCE, *et al.*[8] and OTTINGER[10], 67% by MIYAJI, *et al.*[6] and 26% by HORIE, *et al.* Thus the incidence of non-occlusive cases among intestinal infarctions seems to be relatively high. Although this study is not appropriate to estimate the incidence because materials were not collected from serial autopsies, non-occlusive cases were more than occlusive ones as far as the number is concerned.

2) AGE AND SEX

Concerning the age at onset of intestinal infarctions, almost all authors agreed that this disease occurs in old-aged persons. OTTINGER and AUSTEN[10] classified intestinal infarctions by pathogenesis and estimated the average age to be 77 in arterial thrombus, 68 in arterial embolus, 72 in venous thrombus and 75 in non-occlusive intestinal infarction. There seem to be no significant difference among the groups. In non-occlusive intestinal infarctions, the average age of onset reportedly was 69 by BERGER and BYRNE[9], 64 by MUSA[12] and 67 by HEER, *et al.*[13].

In this report, all 15 cases, especially arterial occlusion cases, were old. As to the 10 non-occlusive cases, the average age was 64, which was not different from that in the previous reports.

The ratio of male to female in the non-occlusive series showed no definite tendency in previous reports. MUSA[12] presented 31:0 in favor of males, while OTTINGER and AUSTEN[10] presented more females than males (39:28). In this study, eight were males and two were females.

3) LESIONS OF INTESTINAL WALL

a) *vascular occlusive infarction*

In the two cases of venous occulsive infarctions in this report, the intestinal wall showed marked thickening and purple-red discoloration macroscopically, and marked hemorrhage and edema microscopically. In spite of severe intestinal lesions mentioned above, the mucosal epithelium remained intact at crypts and dropped out at villi due to hemorrhage. This means that the mucosal epithelium itself was not necrotic.

On the other hand, in the two cases of arterial occlusive infarctions, mucosal necrosis and submucosal congestion were the main microscopical findings while thickening of the intestinal wall, edema and hemorrhage were not notable. Mesenteries were involved in circulatory disturbance in venous occlusion but not in arterial occlusion. Thus differences of intestinal and mesenteric lesions between arterial and venous occlusions were observed but no such difference could be found in previous reports. Since hemodynamic mechanism of ischemia is different between them involving complicated factors such as degree and duration of ischemia, period of examination, etc., it is readilly recognized that intestinal lesions mentioned above might also be different.

MARCUSON, *et al.*[14] examined changes of the colon due to venous occlusion in dogs and estimated that mucosal necrosis was rare in venous occlusion being different from arterial occlusion, and that venous occlusion produced stagnant hypoxia while arterial occlusion produced ischemic hypoxia.

b) *Non-occlusive infarction*

In 10 cases of non-occlusive intestinal infarctions in this paper, the degree of intestinal lesions varied from marked hemorrhage and edema resembling venous occlusion to submucosal congestion like in arterial occlusion. In general, intestinal lesions in non-occlusive infarctions were reported to be limited to the mucosa. PIERCE and BROCKENBROUGH[8] described that the detph of the diseased bowels had no difference between occlusive and non-occlusive infarctions, though MING's description showed more superficial lesions in nonocclusive infarctions. On the other hand, HEER, *et al.*[13] observed two cases of mesenteric involvement in 36 non-occlusive infarction cases.

4) BACKGROUND FACTORS

FOGARTY, *et al.*[16] attributed the genesis of non-occlusive intestinal infarction to 1) congestive heart failure, 2) digitalis intoxication and 3) hemoconcentration, after examination of their 18 cases.

Cardiac diseases, especially heart failure, arrythmia and myocardial infarction, were the important background factors in many previous reports. They were presented in 30 of 31 cases by MUSA, *et al.*[12], 9 of 10 cases by GROSH, *et al.*[15] and 21 of 23 cases by BERGER, *et al.*[9]. BERGER, *et al.*[9] stated that heart failure produced low cardiac output and then compensatory mesenteric arterial vasospasmus might have occurred to maintain the blood flow of the vital organs, such as the brain and the heart, resulting in intestinal ischemia. They also stated that intestinal ischemia led to spasmus of the intestinal wall and further decreased blood flow of the intestine, and that intestinal in-

farction produced shock state and subsequent systemic circulatory disturbance, which in turn decreased the blood flow of the intestine.

GROSH, *et al.*[15] raised a question in their report whether mucosal necrosis of the intestines induced by heart diseases was due to increased portal venous pressure or to mesenteric vascular angiospasmus, but they are of the view that angiospasmus of the arterioles in the intestinal wall was an important factor, quoting the examination by CORDAY and others.

Digitalis is considered to produce intestinal ischemia by its pharmacological effect of constricting the mesenteric arteries. HOBBOUSHE, *et al.*[17] reported a patient administered with digitalis because of mitral stenosis and heart failure, whose angiography before laparotomy for intestinal infarction disclosed segmental spasmus of the medium and small sized mesenteric arteries.

As mentioned above, angiospasmus is considered in many reports as an important etiologic factor of non-occlusive intestinal infarction. In this paper, cardiac diseases might be considered as background factors being found in 6 of the 10 cases (60%; two of myocardial infarction, three of congestive heart failure and one of pericardial effusion), though angiospasmus could not be demonstrated in histopathological examination Digitalis was used in almost all cases but digitalis intoxication was not found even in heart failure patients. Other background factors mentioned in previous reports were diuretic agents, vasopressors, hypertension and arteriosclerosis.

However, OTTINGER, *et al.*[10] described that about one-fourth of patients showed no background diseases in non-occlusive intestinal infarctions like in two patients of this paper. It is felt that more efforts are required to elucidate other etiologic factors of this disease.

5) VASCULAR FACTORS

Reports on non-occlusive intestinal infarctions associated with vasculature of SMA are scarce. FOGARTY and FLETCHER[16] observed chronic occlusive changes of SMA in 14 cases among the 18 non-occlusive intestinal infarctions, but no case of over 50% narrowing of the lumen. OTTINGER and AUSTEN[10] observed sclerosis and/or stenosis of SMA in 10 of their 67 cases. HEER, *et al.*[13] observed atherosclerosis in 33% and emphasized the importance of vascular factors in non-occlusive intestinal infarctions. In these reports, the vascular changes were seen only in proximal region of SMA. We also observed marked stenosis in the same region in three cases of diffuse infarction and two of segmental infarctions.

Arterial lesions in the branches of SMA (Fig. 1; M4-6) were not reported previously. In the two cases of segmental intestinal infarction in this study (cases 12 & 13), unusual stenotic changes were seen in the branches of SMA toward the diseased bowels. Although these arterial lesions themselves might be exceptional changes being uncommon arteriosclerosis, they were suspected to be valuable cases in terms of the relation between intestinal infarctions and vascular changes. The other branches of SMA in these cases and all branches of SMA in the cases having diffuse infarction, except case 15, presented

mild arteriosclerosis and these changes were not stenotic enough to decrease blood flow and were not considered to be related to intestinal infarctions.

There have been some reports concerning the relation between small mesenteric arteries (vasa recta; Fig. 1, M7-9) and intestinal infarctions. AROSEMENA and EDWARDS[19] studied mesenteric arteries in 32 unselected autopsy cases and found six cases of non-occlusive segmental intestinal infarctions. All of these six cases had small mesenteric arterial lesions; intimal fibrous hyperplasia in three cases and atheromatous or thrombotic occlusions in the other three. They described that these vascular changes were related to intestinal infarctions. ABOUMRAD, *et al.*[20], MCGREGOR, *et al.*[7], HANSEN, *et al.*[21] and GOODING and COUCH[22] also reported non-occlusive intestinal infarctions having marked intimal thickening of small mesenteric arteries. In this study, only case 15 presented marked intimal thickening of many small mesenteric arteries which possibly descreased the blood flow of the intestines. Some other cases (cases 7, 8, 10, 11, 12) showed mild intimal thickening of the vasa recta, but suggested no relation to intestinal ischemia.

Some authors described that microthrombi played an important role in non-occlusive intestinal infarctions or ischemic colitis[23)-25)]. WHITEHEAD[24] observed mucosal and submucosal microthrombi in the ischemic intestines as well as in other organs such as the kidney and lung in 20 autopsy cases, suggesting that ischemic enterocolitis was a part of DIC. MARGARETTEN and MCKAY[25] also found microthrombi in 62 of 80 intestinal infarction cases. MIZUSHIMA, *et al.*[23] experimentally produced ischemic intestinal lesions by microthrombi. They produced erosion, ulcer and perforation in the colon of dogs by intravascular injection of Gelform, and described the importance of minute vessel occlusions of the intestinal wall as the pathogenesis of ischemic entercolitis. In this study, microthrombi of mucosa and/or submucosa were observed in three cases. One of them (case 14) was complicated with DIC as in WHITEHEAD's cases. In the other two cases (cases 7, 8), only a few microthrombi existed scatteredly and the possibility that these microthrombi were secondary products can not be denied.

Summarizing the vascular lesions of non-occlusive intestinal infarctions in this paper, proximal SMA showed marked atherosclerotic narrowing in five cases, and in two of them the branches of SMA also showed arteriosclerotic narrowing which was thought to be related to segmental intestinal infarctions. Another case had marked arteriosclerosis of small mesenteric arteries. It is highly possible that the blood flow of SMA is lowered than usual by these vascular lesions and much more by additional systemic circulatory disturbance, resulting in ischemic bowel disease. One of the remaining five cases presented microthrombi associated with DIC, and two presented also microthrombi which could not be identified if primary lesions or secondary ones. Minute vessel occlusion mentioned by MIYAJI, *et al.*[6] is also considered to be an important pathogenetic factor.

However, it must be noted that there are such cases as cases 6 & 9 wherein no vascular lesions nor clinical background factors are present. Keeping this in mind, it is essential to make further studies upon collecting more cases.

CONCLUSION

Using autopsy cases wherein mesenteries as well as intestines could be examined, infarctions of the small intestine, especially non-occlusive ones, were studied in terms of 1) pathological changes of the intestinal wall, 2) those of mesenteric vessels and 3) background etiologic factors. The results obtaines were as follows.

1) The author confirmed the existence of non-occlusive intestinal infarction by examination of mesenteric arteries.
2) The background etiologic factors of non-occlusive intestinal infarctions tended to be advanced age, heart disease and hypertention.
3) As to the intestinal lesions;
   a) In occlusive intestinal infarctions, differences existed between arterial and venous occlusions, the latter being severer.
   b) In non-occlusive intestinal infarctions, intestinal lesions varied by case from mild to severe ones.
4) In half of the non-occlusive intestinal infarctions, proximal SMA presented marked stenosis due to atherosclerosis, and one of them also had marked arteriosclerosis of small mesenteric arteries, and two of them had uncommon arteriosclerosis in medium sized arteries (branches of SMA) related to their segmental infarctions. One of the other half presented microthrombi. Thus, vascular factors were suspected to play an important role.
5) Neither vascular change nor clinical background factor was found in two cases of non-occlusive intestinal infarction.

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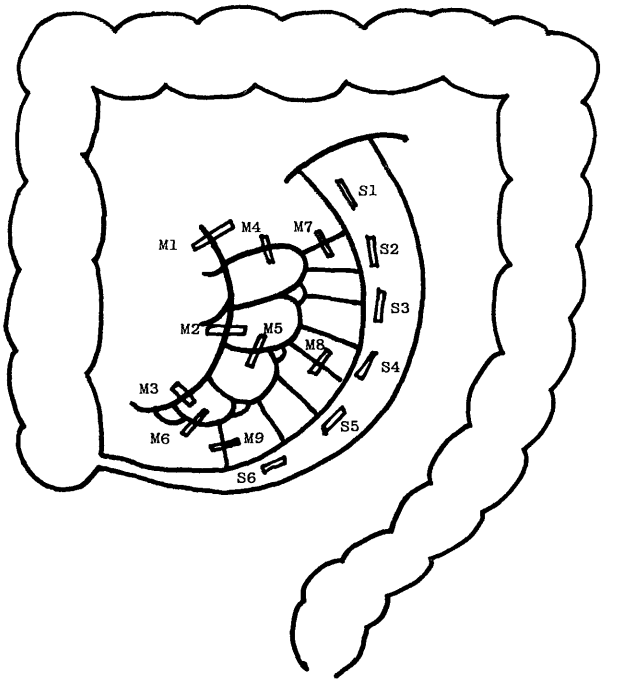

Fig. 1 This illustration shows cutting method of intestine and mesentery.

Fig. 2 Diffuse infarction of the small intestine due to arterial thrombus of SMA (case 1).

Fig. 3 Diffuse infarction of the small intestine due to venous thrombus (arrow) of SMA (case 4). Intestinal wall shows marked thickening and purple-red discoloration.

Fig. 4 Two segmental infarctions are seen in the middle portion of the small intestine (case 13).

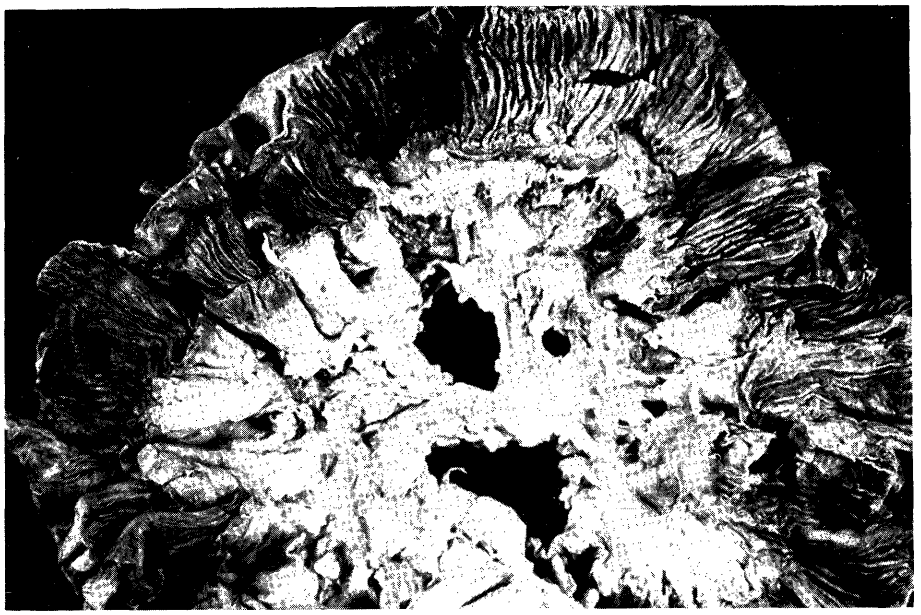

Fig. 5 Diffuse non-occlusive infarction of the small intestine (case 6).

Fig. 6 Diffuse non-occlusive infarction of the small intestine (case 11).

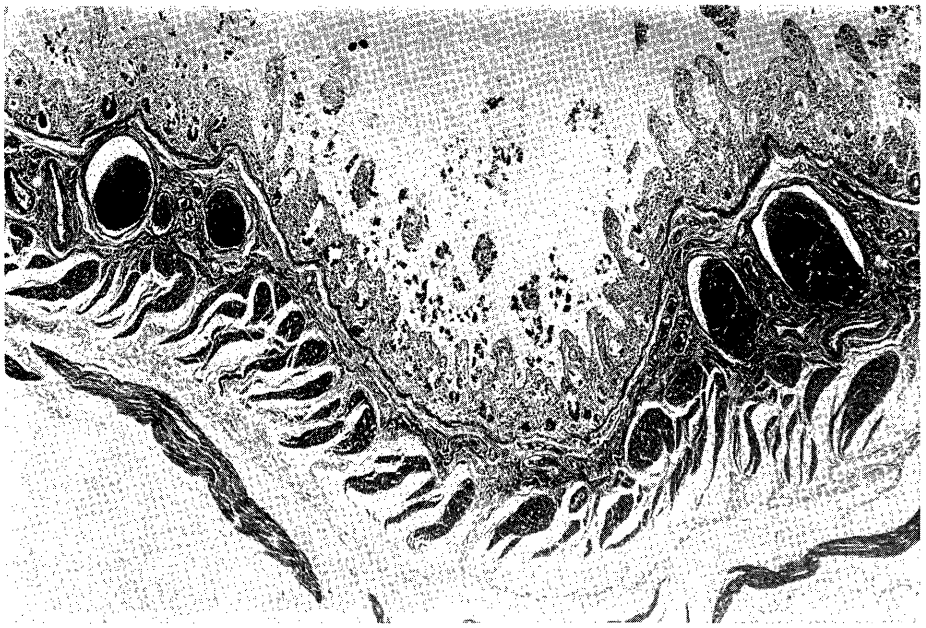

Fig. 7 Intestinal wall of the arterial occlusive infarction. Submucosal congestion is the main feature (case 2) (H.E. ×40).

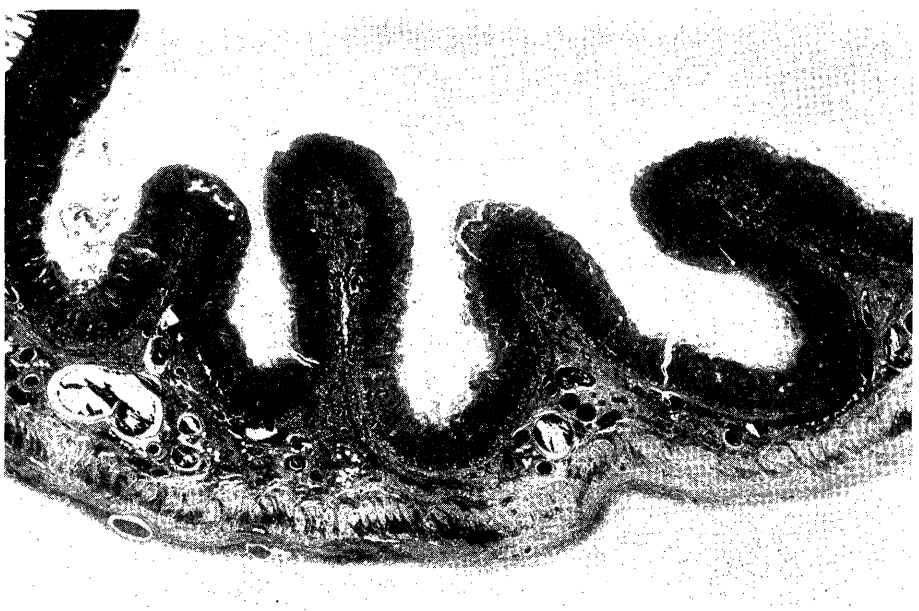

Fig. 8 Intestinal wall of the venous occlusive infarction.
(a) Marked hemorrhage of the mucosa and submucosa (case 4) (H.E. ×20).

Fig. 8 (b) High power view of the same case. Mucosal epithelium of the crypts are kept intact (arrows) (H.E. ×40).

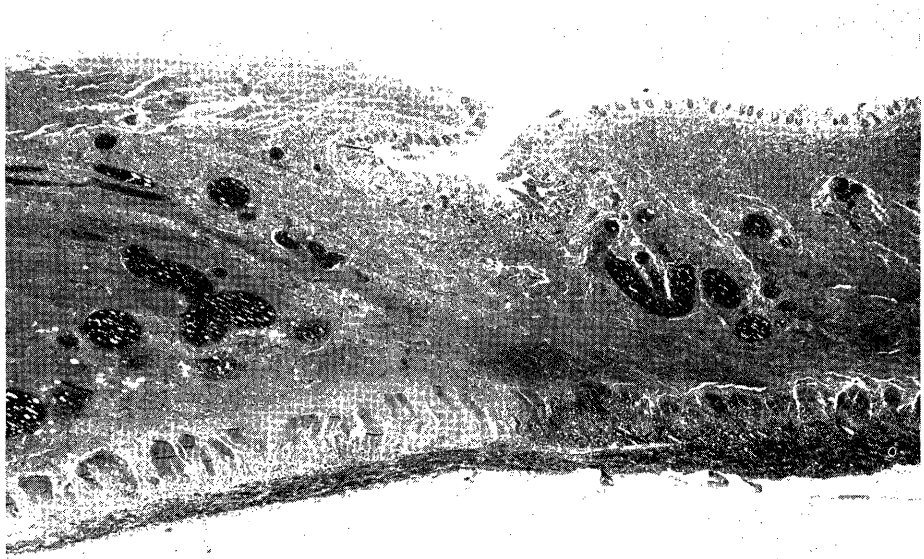

Fig. 9 Intestinal wall of the non-occlusive segmental infarction (case 12). Marked edema and hemorrhage are seen in the intestinal wall (H.E. ×20).

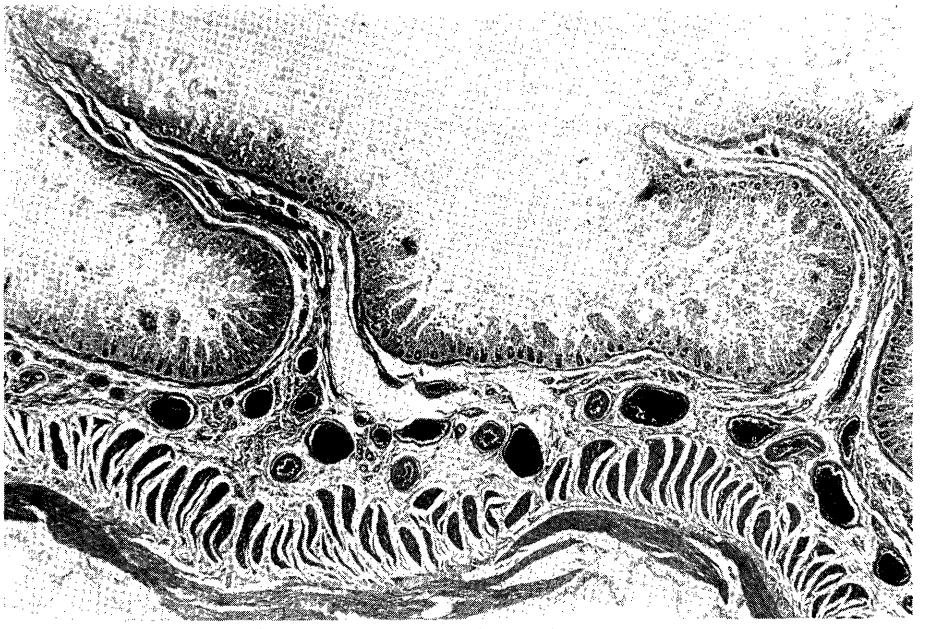

Fig. 10 Intestinal wall of the non-occlusive diffuse infarction (case 11). Submucosal congestion is obvious (H.E. ×20).

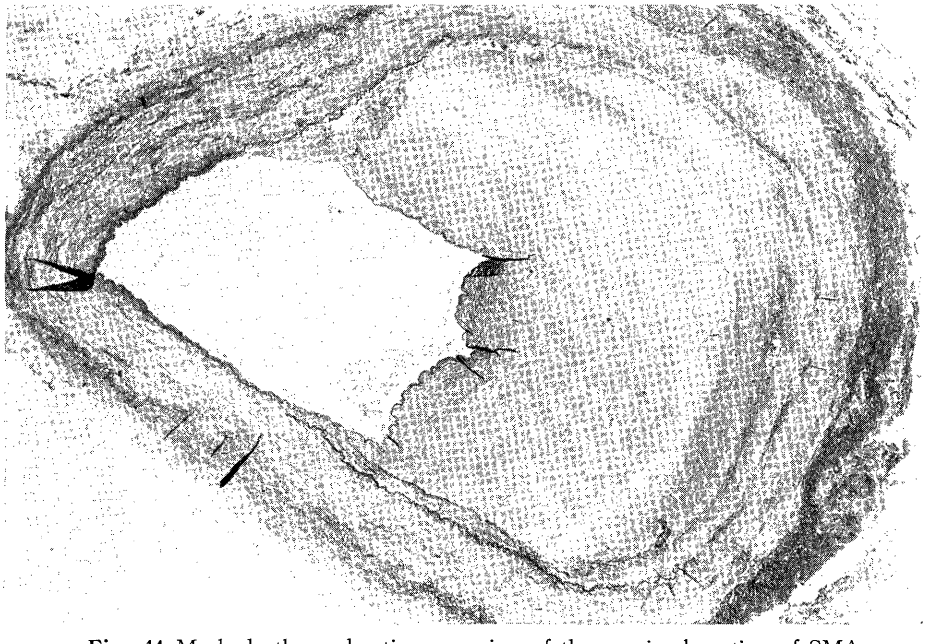

Fig. 11 Marked atherosclerotic narrowing of the proximal portion of SMA in diffuse non-occlusive infarction (case 10) (EVG stain, ×20).

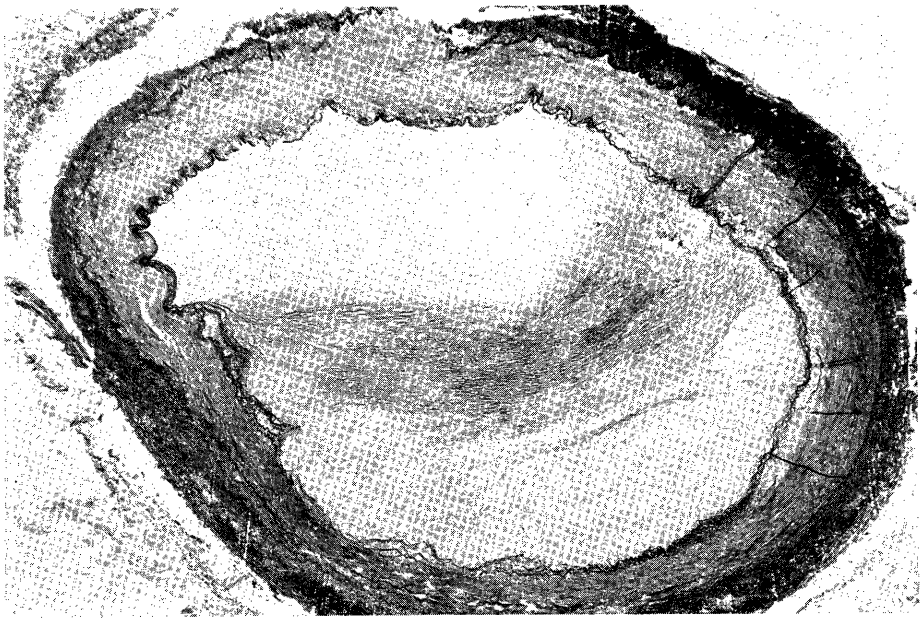

Fig. 12 Mesenteric arteries of case 12.
(a) The proximal portion of SMA shows marked atheromatous narrowing and (b) one branch of SMA shows intimal fibrous thickening and medial thickening with vascularization(arrow). (EVG stain, ×20)

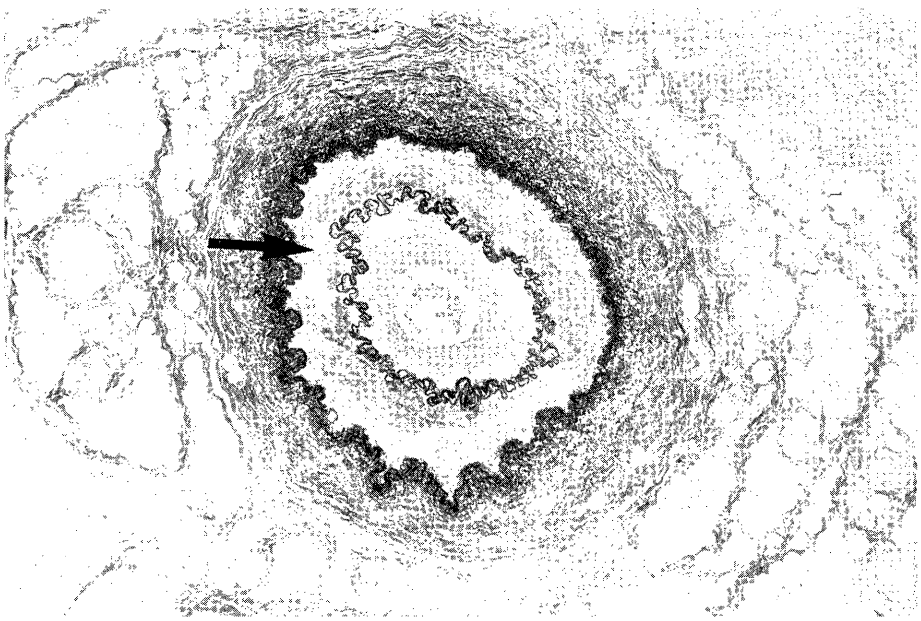

Fig. 12 (b)

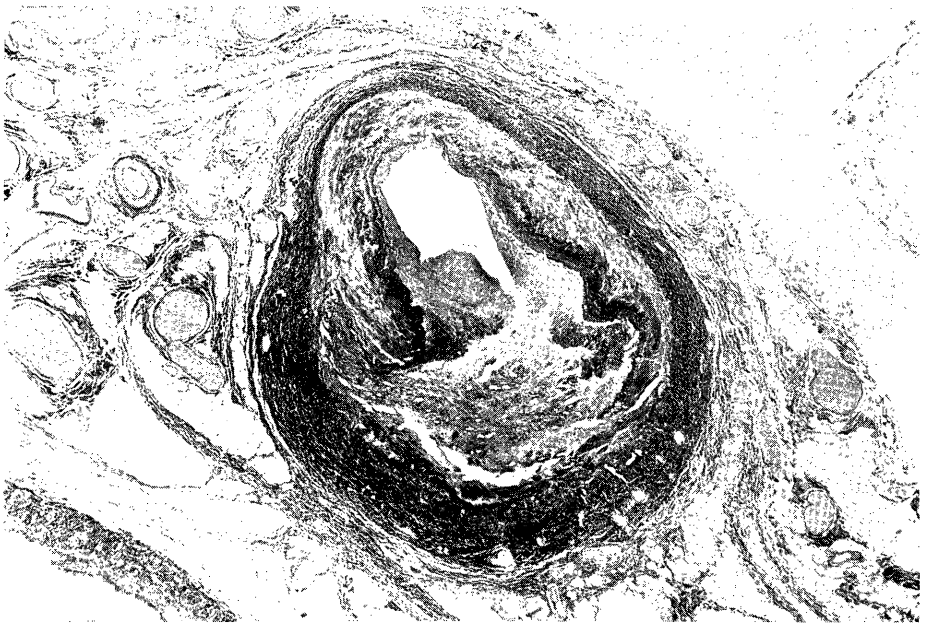

Fig. 13 Mesenteric arteries of case 13. (a) The proximal portion of SMA and (b) one branch of SMA. Fibro-vascular proliferation of media is seen (arrow). (EVG stain, a: ×20, b: ×40)

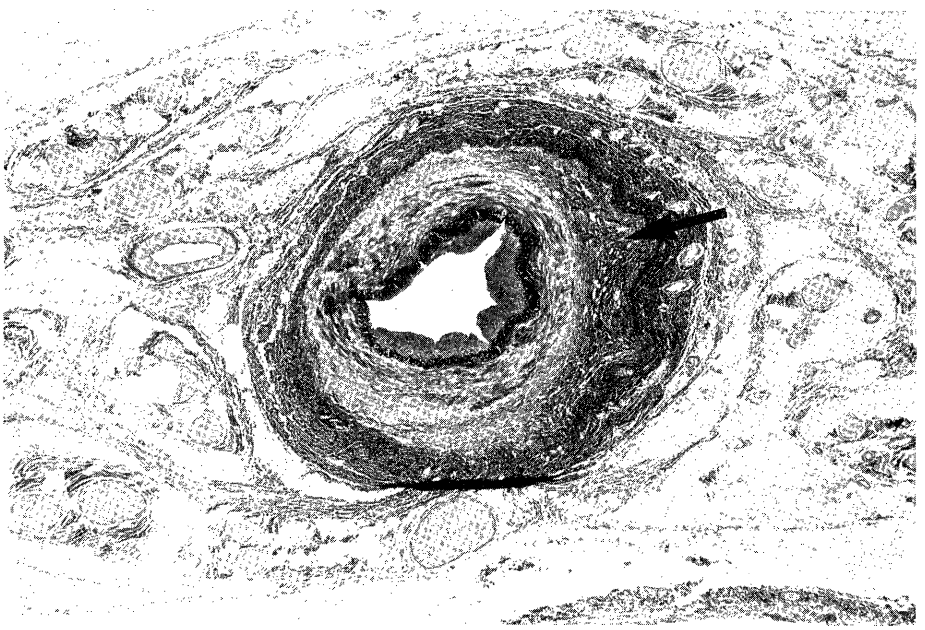

Fig. 13 (b)

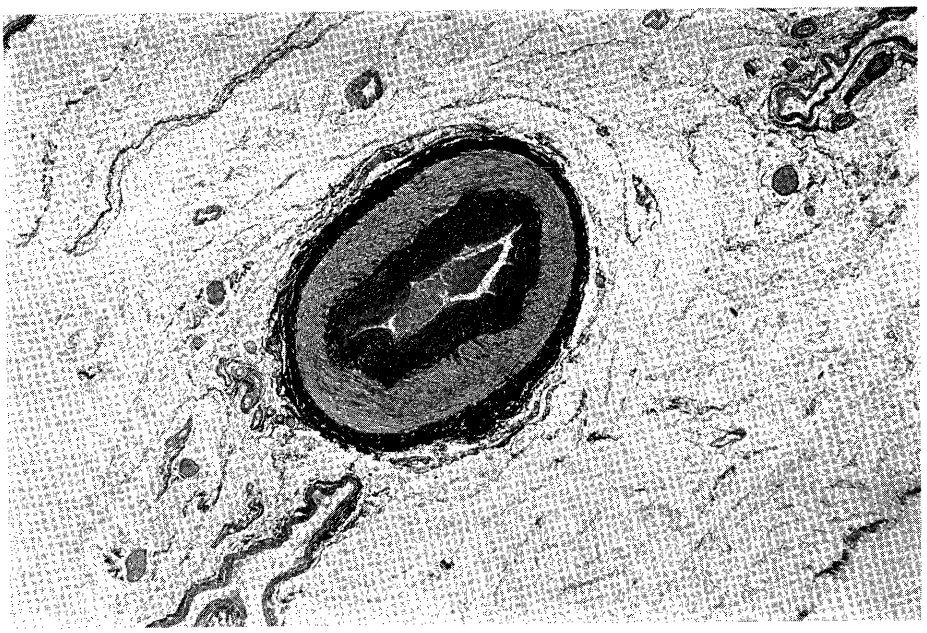

Fig. 14 The branch of SMA (a) and vasa recta (b) show marked to moderate arteriosclerosis (arrows) in case 15. (EVG stain, ×20).

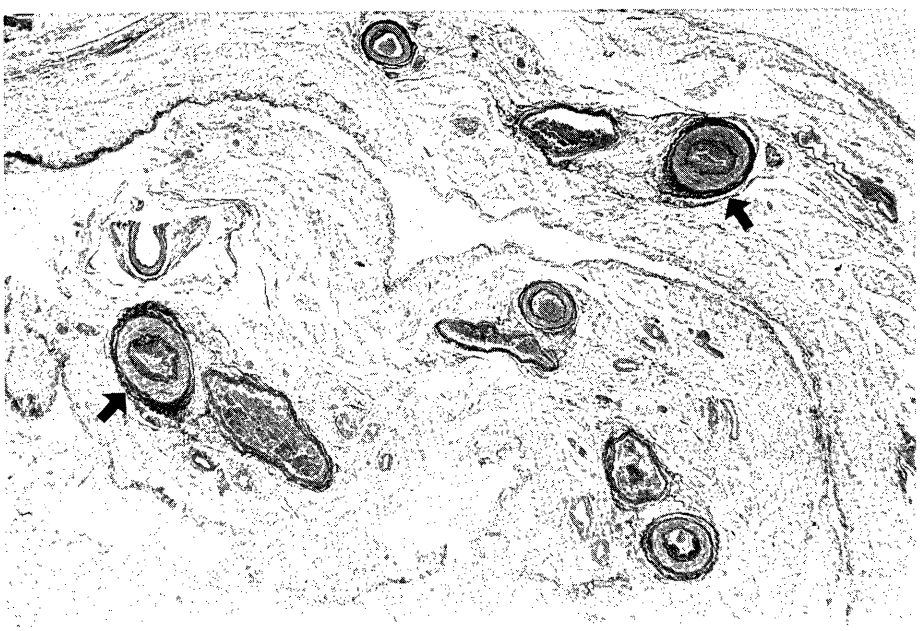

Fig. 14 (b)

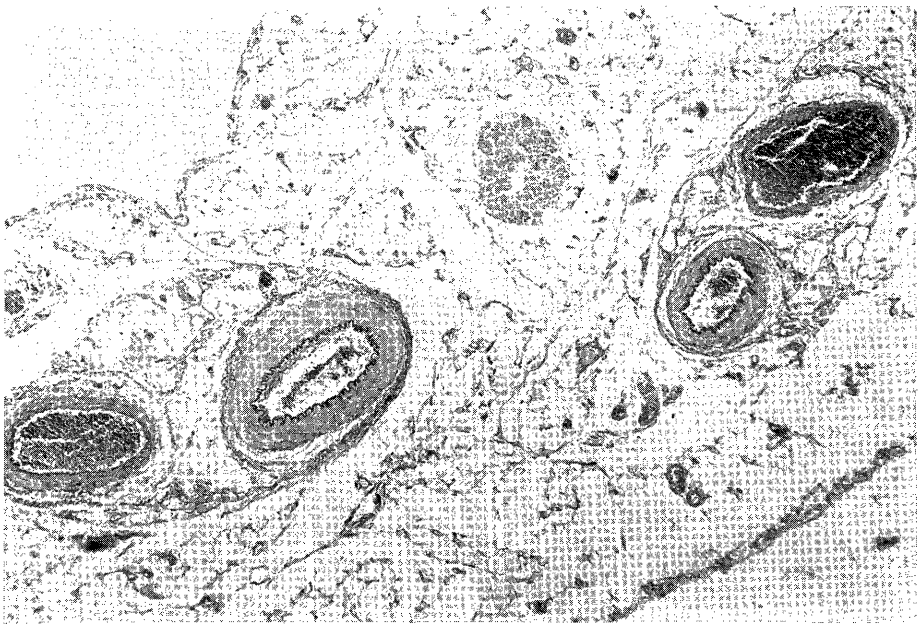

Fig. 15 None to mild intimal thic kening of the small mesenteric arteries (vasa recta) (case 10) (EVG stain, ×50).

Fig. 16 Fibrin thrombi (arrows) in intestinal wall of case 14 (H.E. ×100).

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