Middle Articles

FOR DEBATE . . .

Intra-abdominal Adhesions as a Manifestation of a Fibrotic Diathesis

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Summary: In 81 patients with fibrous intra-abdominal adhesions there was a high incidence of other lesions in which there was a substantial element of fibrosis. These included chronic peptic ulceration, ovarian cysts, fibrous stenotic lesions, and thickened scars. It is suggested that in some patients a generalized fibrotic tendency as well as local factors may play a part in the pathogenesis of adhesions.

Introduction

Experience shows that the fibrinous adhesions of the early days after abdominal operations tend to be absorbed and that probably only a minority will persist as fibrous adhesions.

The persistence of adhesions is often determined by local factors, such as peritoneal contamination or prolonged inflammation and ileus, and Ellis (1962) has shown the importance of local tissue ischaemia. Even so, some patients seem particularly prone to develop adhesions. This raises the question whether the formation of intra-abdominal adhesions might sometimes be determined by a generalized tendency to fibrosis. This idea is not without precedent in a more limited sphere. There is a high incidence of intestinal obstruction due to adhesions after operation for polyposis coli, and Lockhart-Mummery (1967) suggested that this might be due to an increased tendency for fibrous tissue and adhesions to form in these patients.

Patients with fibrous intra-abdominal adhesions for which operation had been required were therefore reviewed regarding other lesions that contained a large fibrotic element, and for any conditions with an unexpectedly high incidence in which there might be an abnormal deposition of fibrinous or fibrous tissue.

Patients and Methods

The Westminster Hospital records for 1962-8 were searched for cases of intra-abdominal adhesions, which were usually indexed only if presenting with pain or obstruction. Patients were excluded if the adhesions were (a) not proved by operation, (b) found less than two weeks after peritonitis or operation, and (c) due to neoplastic deposits.

By the above criteria 81 patients (29 men and 52 women) were available for study. These figures suggest that adhesions might be more common in women, but there may have been more women in the population at risk. Forty-two patients had presented with acute intestinal obstruction, 18 with recurrent subacute obstruction, 18 with chronic pain, and 3 with per-

sistent intestinal fistulae proximal to adherent loops of bowel, two of these being associated with Crohn's disease.

Twenty patients had undergone more than one operation for their adhesions. The lesions responsible for the first known adhesions were broadly grouped as follows: appendix 29, gastroduodenal 10, biliary or pancreatic 5, intestinal 14, gynaecological 12, and 11 fell into a miscellaneous group. Forty-six had had either "dirty" operations or much peritoneal inflammation.

Findings and Comments

An explanation is given, where it seems necessary, why various lesions described below are regarded as having a fibrotic element.

Chronic Peptic Ulceration

The fibrotic element is usually obvious at operation for chronic peptic ulceration, with scarring commonly visible on the serosal surface.

The series included 25 cases (31%) of proved chronic peptic ulceration, the diagnosis of which was confirmed by operation, or there was an appropriate clinical history together with positive radiological findings. In two more there was a typical history of ulcer dyspepsia with negative barium studies. The distribution according to sex and type of ulcer is shown in the Table; juxta-pyloric ulcers are classified as of duodenal type. The incidence was high in both sexes, and no fewer than 14 of the 29 men had a history of proved chronic peptic ulceration.

Distribution of the 25 Peptic Ulcers, with Juxta-pyloric Classified as Duodenal

	No. of Cases	Duodenal Ulcers	Gastric Ulcers	Total Ulcers
Males	29	13 (44.8%)	1 (3.4%)	14 (48.3%)
Females	52	7 (13.5%)	4 (7.7%)	11 (21.2%)

This high incidence did not merely reflect the proportion of abdominal operations carried out previously for peptic ulceration, because in only nine patients (eight men and one woman) were the adhesions causing trouble attributable to ulcer operations. Even if these nine were excluded the incidence of chronic peptic ulceration was 22.2% (28.6% in males, 19.6% in females). On the other hand, though it is conceivable that chronic intestinal obstruction due to adhesions might have led to motility or secretagogue disturbance predisposing to peptic ulceration, in 13 cases the ulcer had been diagnosed before the adhesions could have occurred.

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Even assuming a high arbitrary figure of 20% for the hospital incidence of chronic peptic ulceration in all adult surgical patients, the incidence of 31% in this series is significantly high ($P<0.02$).

These findings led to the postulation that, at least in some patients, excessive fibrosis might be a factor in chronicity and recurrence of peptic ulcers.

Simple Cysts of Ovary

Twelve of the 52 women had a history of resection of a simple cyst of the ovary. Four of these also had a peptic ulcer. In seven a cyst had been removed at their first abdominal operation.

Experience suggests that the general incidence of cysts worthy of special mention on grounds of size is probably less than 8%, and when compared with this figure the incidence was significantly high ($P<0.05$). This could be related to a fibrotic tendency. Probably most if not all of these cysts were of the follicular type, and these are thought to be derived from follicles which have failed to rupture (Howkins, 1958). Chronic pelvic inflammation may produce thickening of the ovarian capsule, which is said to hinder rupture of the follicle and lead to the formation of cysts (Haines and Taylor, 1962). Thus there are grounds for regarding follicular cysts as having a large fibrotic element in their pathogenesis.

Fibrous Stenoses

Most stenotic lesions that are not neoplastic are due to post-inflammatory or idiopathic fibrous constriction. The following examples (excluding pyloric stenosis) were recorded: one idiopathic stenosing tenosynovitis (four digits on two hands); one lachrymal duct stenosis; two ureteric stenoses—one idiopathic pelviureteric, one ureterovesical secondary to cystitis; two urethral strictures—one in a woman after several cystoscopic examinations, one in a man with a history of non-specific prostatitis; two short fibrous strictures of the colon of unknown aetiology, of which one required resection; one stenosis of the ampulla of Vater, which soon recurred after sphincterotomy; two ileostomy stenoses (in three cases)—both had required more than one revisional procedure; one mitral valvular stenosis; and two ectopic pregnancies, probably caused by tubal stenosis: both patients also had ovarian cysts removed on separate occasions and one a hydrosalpinx.

There is the impression of an uncommonly high incidence of fibrous stenoses in the series.

Thickened Abdominal Scars

As part of another project mature paramedian or midline abdominal scars had been assessed in 23 of the patients, and in 18 of these the scars were deemed to be abnormally thickened.

Other Lesions

Three patients had cataracts, one presenting at 44 years of age. Two had pronounced pulmonary fibrosis after pneumonia in one and two lobes respectively. Three women had fairly indolent varicose ulcers with much fibrosis. There was one case each of Dupuytren's contracture, otosclerosis, oleogranuloma, and granuloma of the tonsil.

A history of rheumatic fever was found in 7 of the 45 patients aged 50 years or more in 1968, and two had mild mitral valvular disease. The recorded incidence of ischaemic heart disease and thromboembolism was within normal limits, though one man did have a myocardial infarction at 36 years of age.

Eleven women had undergone cholecystectomy, and five of these also had chronic peptic ulceration.

Multiple Lesions

About half the patients had at least two lesions with a large fibrotic element in addition to intra-abdominal adhesions. The following cases illustrate this tendency.

Case 1.—Woman aged 54. Adhesions, thick scars, duodenal ulcer, trigger fingers, ovarian cyst, "very fibrous" gall bladder.

Case 2.—Man aged 59. Adhesions, thick scars, duodenal ulcer, Dupuytren's contracture, lobar pulmonary fibrosis, fibrous stricture of colon.

Case 3.—Woman aged 64. Adhesions, thick scars, lachrymal duct stricture, ileostomy stenosis (three times), history of rheumatic fever.

Case 4.—Woman aged 69. Adhesions, thick scars, gastric ulcer, ovarian cysts, cataracts at age of 44.

Multiple Adhesiotomies

In 20 patients more than one operation for obstruction due to adhesions had been carried out. Chronic peptic ulceration had occurred in three out of eight men and in four out of 12 women. Six out of 12 women had a history of ovarian cystectomy. These findings suggest that there may be a more pronounced fibrotic tendency in patients having multiple adhesiotomies.

ABO Blood Group Distribution

In view of the high incidence of duodenal ulceration it seemed of interest to investigate the ABO blood group distribution in intra-abdominal adhesions. In the 75 patients whose blood group was known there seemed a high proportion of group O. To enlarge the series a further 26 patients with substantial but asymptomatic adhesions, collected as part of another study, were added to give 101 cases. Patients were selected without previous knowledge of their blood groups.

The blood group distribution of the combined series was: O, 55; A, 36; B, 9; and AB, 1. Ikin's (1939) figures for the general ABO distribution in the South of England were used as control. This gave a significant excess of group O compared with group A ($P<0.01$).

The results were not biased by the peptic ulcer patients, in whom the O:A ratio was similar to that in the series as a whole, but the series is not large enough for much weight to be attached to this apparent blood group O preponderance in adhesions. Further studies may show whether an association between fibrosis and blood group O offers an explanation of ABO group distributions in chronic peptic ulceration.

Discussion

Evidence for a Fibrotic Diathesis.—The aetiological significance of a generalized fibrotic tendency in some patients would tend to be obscured in a series of intra-abdominal adhesions where the local factor alone would in many cases be sufficient cause. Furthermore, in a retrospective series the concomitant fibrotic lesions would probably be understated owing to incomplete diagnosis or recording, and some patients were likely to develop further lesions in their remaining years. On the other hand, the series is selected in that all the patients had undergone abdominal operations. There is the further difficulty that even an approximate general incidence of some of the lesions described is not known. Even so, it can be stated with reasonable certainty that there was an abnormally high incidence of chronic peptic ulceration in both sexes, and of ovarian cysts in women. The incidence of stenotic lesions and thickened abdominal

scars seemed high, and in the older patients a history of rheumatic fever. In these conditions there is an obvious fibrotic or fibrinous component. Possibly the most striking feature of the series was the large number of patients with a multiplicity of fibrotic lesions. Association does not necessarily mean causation, but the results of this study support the hypothesis that some individuals are particularly prone to intra-abdominal adhesions because of a generalized fibrotic tendency. The tendency may be more pronounced in women. It is thought of as representing one end of a spectrum of fibrosis rather than as a separate phenomenon, and the strength of the fibrotic tendency is probably determined by multiple factors.

Pathogenesis of a Fibrotic Diathesis.—A fibrotic diathesis could arise as an abnormality at substrate, enzymatic, or cellular level. Perhaps most worthy of further investigation are the factors in the fibrin-fibrinolytic system, and such studies are in progress.

Conclusions

The high incidence of lesions with a large fibrotic element in this series supports the hypothesis that in some people there is a generalized fibrotic tendency which plays a part in the

formation of intra-abdominal adhesions. It is suggested that a fibrotic tendency can initiate or modify the natural history of some lesions. Examples of this may include the pathogenesis of follicular cysts of the ovary, the promotion of chronicity in peptic ulceration, a tendency to stenoses, and a tendency to thickened cutaneous scars.

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Trace Element Metabolism in Animals and Man

[FROM A SPECIAL CORRESPONDENT]

The First International Symposium on Trace Element Metabolism in Animals was held in Aberdeen from 14 to 18 July under the joint auspices of the World Association for Animal Production and the International Biological Programme. The meeting was attended by more than 160 participants from 23 countries.

Professor E. J. UNDERWOOD (Australia) in the introductory lecture gave a lucid exposition on the recent advances made in this "the second golden era of trace element research," with its increasing awareness of trace element disorders in man. He instanced the widespread occurrence of iron-deficiency states—especially in women in underprivileged groups—the detection of a conditioned zinc deficiency in male dwarfs in the Middle East, the occurrence of osteoporosis and collapsed vertebrae in women and of dental caries in children as consequences of fluorine deficiency, and the increasing evidence that, though chromium could be essential for the well-being of man, it was present in sub-optimal levels in many human diets. He drew attention to the possibility of an increasing incidence of trace element excesses as well as inadequacies, mentioning the accumulation of cadmium, lead, and mercury in the environment as a result of the greater urbanization and industrialization of society. Professor Underwood also stressed the need for a continual reassessment of trace element requirements in humans and animals as a result of the changes in living habits and food production, such as the increasing cleanliness which reduced the contamination of food, the decreasing use of cast-iron and galvanized vessels, the increasing calorie consciousness in women, and the important changes in farming practices. He also mentioned the possibility of the discovery of further trace-element deficiencies in the underdeveloped countries when major disorders such as protein-deficiency and parasitic diseases had been overcome.

Trace Element Deficiency and Excess

Dr. W. J. PORIES (U.S.A.) and Dr. W. H. STRAIN (U.S.A.) presented two papers on the role of zinc in epidermal repair in man. The delay in wound healing associated in humans with zinc deficiency was largely associated with a lack of epidermal migration across the granulations. Oral therapy with zinc salts caused wound healing to progress at a normal rate, and it seemed on the basis of serum zinc levels that zinc deficiency was surprisingly prevalent in humans, even when the diet would have been regarded as containing adequate levels of zinc. A serum zinc level of 100 µg./ml. was suggested as the level below which zinc deficiency might exist. Furthermore, genetic differences, dietary habits, and degenerative changes all appeared to influence the availability of zinc.

The existence of genetic variations in the copper metabolism of sheep and in the incidence of swayback was also noted by Dr. G. WIENER (Edinburgh), thus introducing a further complication to be considered in any comparison of apparent regional variations in trace element requirements. Several papers were presented on the pathology of swayback and copper poisoning in sheep and on the role of manganese in animal nutrition, especially in respect of skeletal development and reproduction.

The mode of action of fluoride in dental caries was described by Dr. G. N. JENKINS (Newcastle). He claimed that the effectiveness of fluoride depended on its unique combination of properties whereby it influenced tooth morphology during tooth formation, reduced the solubility rate of apatite, favoured the remineralization of carious cavities in the intervals between feeding, and reduced the metabolic activity of bacteria on the tooth surface. He also suggested that molybdenum might be effective in controlling dental caries.

Experimental Studies of Trace Element Function

Dr. C. F. MILLS (Aberdeen) pointed out the importance of regulating the pattern of food intake in control animals used for investigating metabolic disorders associated with trace element deficiencies and toxicities. In zinc-deficient rats, for instance, where the appetite was restricted and food intake reduced, it had been found that many of the apparent effects of zinc deficiency on growth, on nucleotide synthesis, and on carbohydrate metabolism were not due to zinc deficiency per se, but to the different feeding habits of the deficient animals compared with those of the controls.

Dr. J. G. REINHOLD (Lebanon) went on to discuss the changes in zinc concentrations and enzyme activities of rat tissues during the initial stages of zinc depletion. Changes in zinc concentration in plasma, liver, and intestine and in the activities of liver alcohol dehydrogenase and intestinal alkaline phosphatase and phytase had been noted within a few days when rats had been maintained on a low zinc diet. Dr. J. M. HSU (U.S.A.) suggested from the results of an investigation of the role of zinc in cysteine metabolism that zinc was essential in the regulation of protein and glutathione synthesis. In carefully controlled experiments with rats in the early stages of deficiency, however, Dr. J. K. CHESTERS (Aberdeen) had found that protein synthesis had been reduced by only a small—though statistically significant—amount in the kidney and the spleen. Synthesis of deoxyribonucleic acid, as measured by ³H-thymidine incorporation, had been reduced in zinc deficiency, but there had been no significant effect on liver nuclear ribonucleic acid synthesis, as measured by ¹⁴C-orotate incorporation.

Dr. J. W. SUTTIE (U.S.A.) in a study of fluorine toxicity in rats also emphasized the