COLLOID CARCINOMA ARISING WITHIN FISTULAE IN THE ANO-RECTAL REGION

by

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IN MOST CASES of cancer of the ano-rectal region clinical examination reveals the presence of an obvious tumour or ulcer. Occasionally, however, the primary tumour may be atypical in appearance taking the form of a stricture without much obvious growth on the mucosal surface. These atypical tumours may occasion difficulties in diagnosis, but in the end the presence of a primary of anal or rectal origin can generally be established.

A much more difficult diagnostic problem arises when the presence of carcinoma is found in the perirectal tissues without any evidence whatever of any primary tumour in the mucosa or submucosa of the rectum or anal canal, in spite of the most thorough examination by proctoscopy, sigmoidoscopy and biopsy. Such cases are rare but have been reported by Rosser (1931 and 1934), Yeomans (1936), Gabriel (1948), and Skir (1948). Since almost invariably they have been associated with fistulae of the ano-rectal region they have usually been described as instances of carcinoma developing in or spreading along a fistulous track. The manner of origin of the cancer has been obscure and no satisfactory explanation of its pathology has been offered.

At St. Mark's Hospital we have had the opportunity of making a detailed study of ten of these cases, in eight of which a diagnosis of colloid carcinoma was definitely established in spite of the fact that no primary tumour was found within the rectum. In two other cases multiple fistulous tracks containing mucoid secretion were present but these showed no evidence of malignancy. We shall describe these ten cases and then discuss their possible explanation and give reasons for attributing the lesions to a developmental anomaly.

DETAILS OF CASES

Case 1. Mr. A. S., aged 65 years, first seen 1st February, 1955, with a 10-year history of discharge and intermittent swellings around the anus. One-and-a-half years previously he began to get anal pain. Examination showed a large indurated mass, with multiple fistulous openings exuding colloid material, involving the whole left buttock and extending forward to the perineum and scrotum (Fig. 1). A biopsy proved that this was a colloid carcinoma invading the subcutaneous tissues, though no tumour was palpable or visible within the rectum. Perineal excision of the rectum with a wide excision of perianal skin and perirectal tissues was carried out in two stages by Mr. W. B. Gabriel. The postoperative course was uneventful.

Dissection of the operation specimen revealed that a large cystic tumour about three inches in diameter was situated mainly in the left ischio-rectal fossa, and that this growth had extended upwards in the extra-rectal tissues. Colloid material could be expressed from many fistulous openings on the skin one of which led to a larger fistulous track communicating internally with the

Fig. 1. The perianal condition in Case 1 showing the multiple fistulous openings. (Left lateral position).

rectum on the left side, two inches above the dentate line. The mucosa at this point was puckered, but otherwise the surface of both the rectum and anal canal appeared normal.

To trace the course of these peculiar fistulous tracks a series of transverse slices were cut across the whole operation specimen. In these the main tumour appeared as large cystic spaces filled with colloid material, from which several fistulous tracks, surrounded by what appeared to be fibrous tissue, could be traced upwards, laterally and downwards. Microscopic examination showed that these were lined by mucus secreting columnar epithelium often with well formed crypts of Lieberkuehn (Fig. 2). Surrounding this epithelium in some

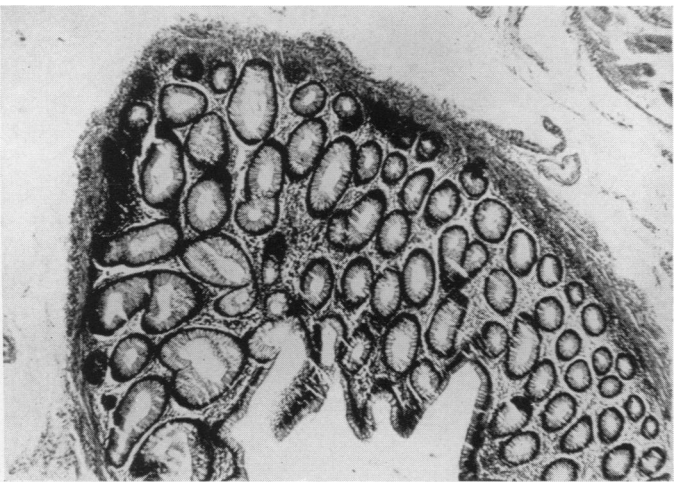

Fig. 2. Photomicrograph of one of the tracks showing the benign columnar epithelial lining with crypts of Lieberkuehn (Case 1). × 15.

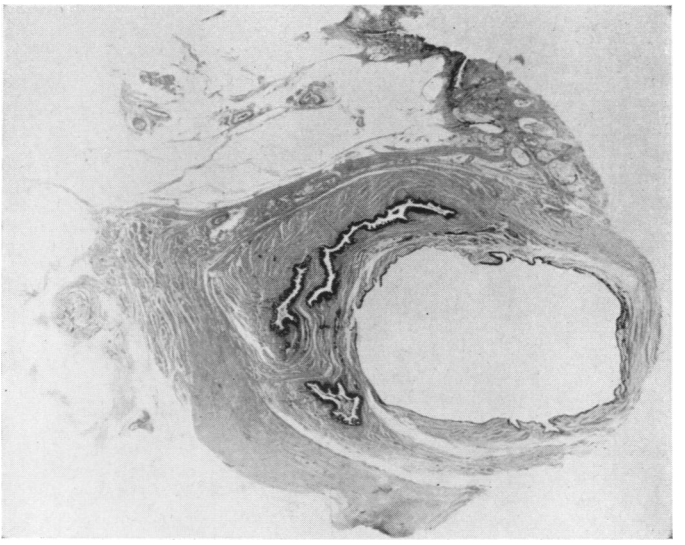

Fig. 3. Photomicrograph of a transverse section of the upper end of the specimen showing the tracks lying to the left of the lumen of the rectum. Note the continuous smooth muscle coat (Case 1). Low power view.

regions was a clearly recognisable muscularis mucosa and external to this a smooth muscle coat, continuous with that of the rectum (Fig. 3). Proximally some of these extraordinary tracks appeared to reproduce the rectum in miniature. More distally some of them united for a short distance, and then separated again before eventually joining the main tumour (Fig. 4). This had the histology

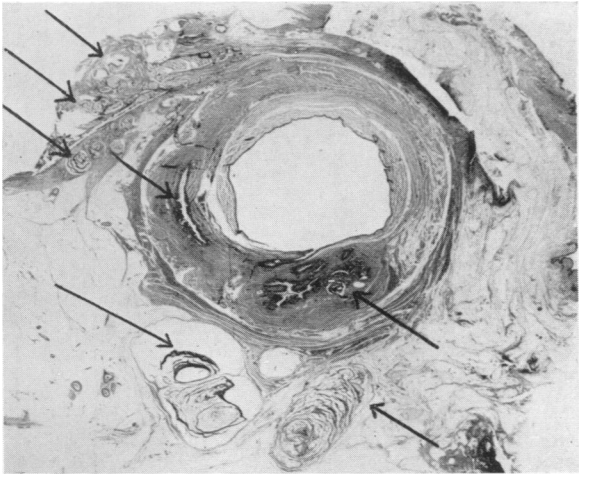

Fig. 4. A transverse section from ano-rectal junction showing fistulous tracks embedded in circular muscle and other tracks containing colloid carcinoma extending widely in the extra-rectal tissues. (Tracks marked by arrows.) Low power view.

of a rectal colloid carcinoma of low grade malignancy. It had spread in the anal sphincter muscles, and also extended along the fistulous tracks. No lymphatic metastases were found.

Case 2. Mr. B. W., aged 59 years, transferred from another hospital where treated for multiple syphilitic ulcers of lower abdomen, scrotum and penis, and multiple perianal fistulae and sinuses in the perineum. On admission to St. Mark's Hospital, 30th September, 1953, gave a history of fistulae and recurrent abscesses around anus and rectum since the age of 15. Examination showed a

Fig. 5. The perianal condition presented in Case 2. The patient is lying in the left lateral position.

brawny indurated swelling on both sides of the anal canal, and extending into both buttocks and scrotum, with multiple fistulous openings discharging colloid material (Fig. 5). *Per rectum,* a hard indurated mass could be felt extra-rectally on the right side at the finger tip ; this bulged into the rectum but did not involve the mucous membrane. Numerous healed syphilitic lesions noted on abdomen, scrotum, and chest. W.R. and Kahn test both positive. Frei test and C.F.T. tests negative. Since the scarring over the abdomen and genitalia resembled a healed gummatous process, and since the rectal lesion did not improve with anti-syphilitic treatment it became clear that this was of a different nature. This was confirmed by biopsy which, as in the former case, revealed colloid carcinoma arising in a fistulous track. A synchronous combined excision was performed by Mr. C. Naunton Morgan, with a wide excision of the perianal tissues extending laterally to both ischial tuberosities and anteriorly to the base of the scrotum and bulbus urethra. After operation the patient developed right hemiplegia and auricular fibrillation and died on the fourth day. Autopsy did not lead to the discovery of any intestinal tumour.

In the operation specimen also no primary tumour was found in the rectum or anal canal but dissection revealed many tracks and small cysts, some containing colloid-like material embedded in the subcutaneous tissues and anal canal muscles. The fistulous tracks were found to be lined by well-differentiated columnar mucus secreting epithelium which appeared to be infiltrating into all adjacent tissues like an invasive carcinoma. The histology was that of a colloid carcinoma of low grade malignancy. No lymphatic metastases were found.

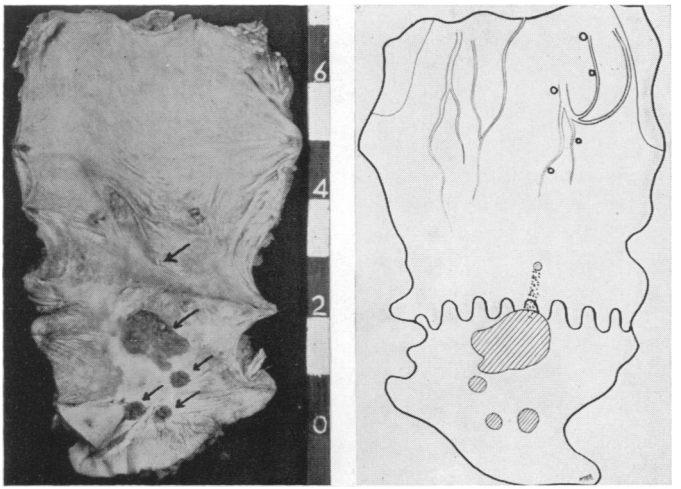

Fig. 6. Operation specimen removed by perineal excision (Case 3). The position of fistulous openings is indicated by arrows, and in the photographs of the gland dissection the upward extension of one track is marked by stippling.

Case 3. Mr. W. P., aged 69 years, had noticed a mucus discharge from the rectum for three years. Five months prior to admission to St. Mark's, he developed an abscess on the left side of the anus. This was treated surgically at another hospital and reported as " malignant." The wound was subsequently diathermised.

Examination at St. Mark's, 3rd October, 1947, showed a tender indurated area posterior to the anal margin, with a scar and granulation tissue extending

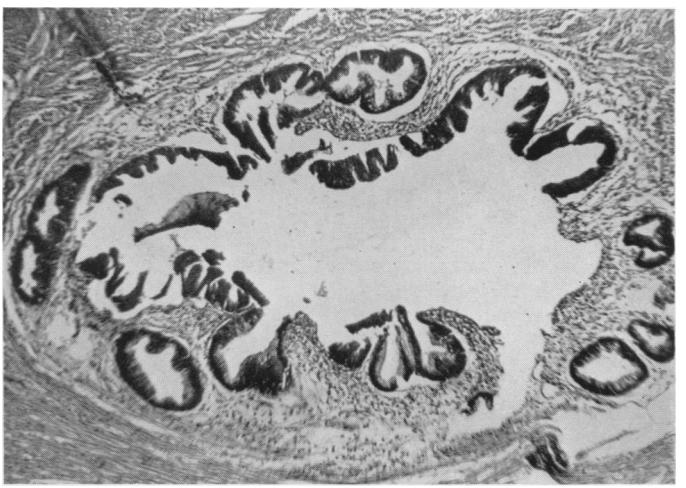

Fig. 7. Photomicrograph showing fistulous track lined by glandular epithelium resembling normal rectal mucosa. This track was found in close proximity to the extra-rectal colloid carcinoma (Case 3). × 70.

across to the left. Biopsy revealed colloid carcinoma. No tumour could be felt *per rectum*. Perineal excision with a wide removal of perianal skin and deeper tissues was carried out in two stages by Mr. C. Naunton Morgan.

The operation specimen showed only a flat ulcer on the posterior part of the anal canal with the openings of several fistulae filled with colloid material

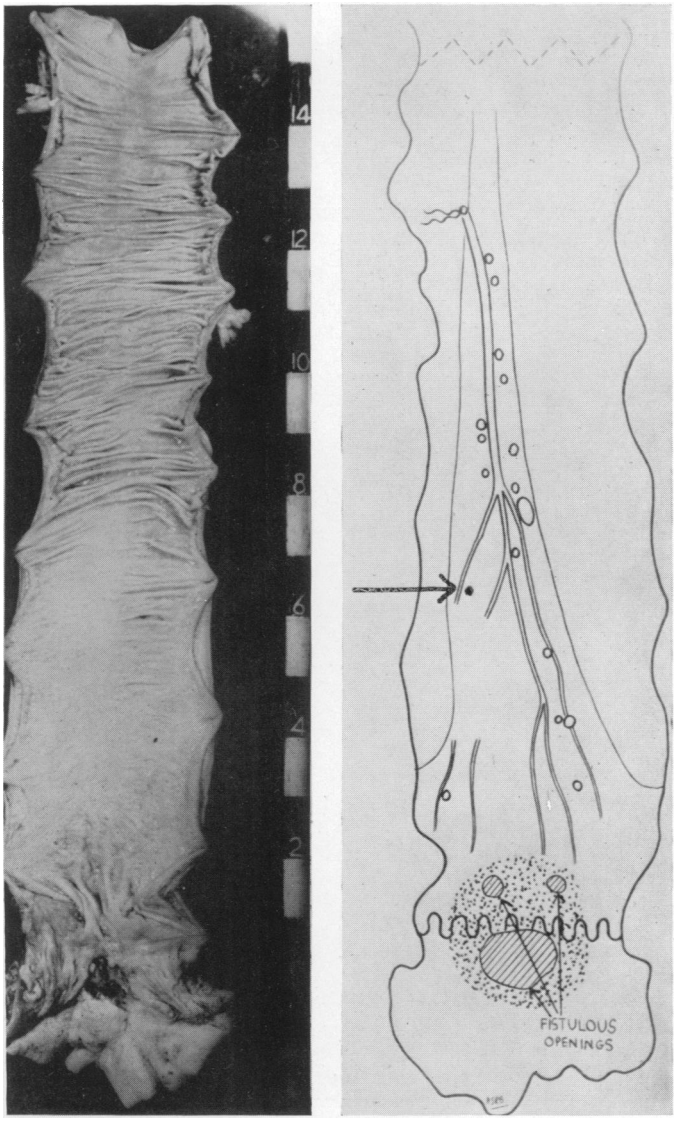

Fig. 8. Operation specimen (Case 4). The position of the various fistulous openings can be seen. The stippling indicates the extent of the colloid infiltration. The position of the solitary glandular metastasis is marked.

(Fig. 6). The upper main fistulous track was lined by apparently normal mucus secreting epithelium (Fig. 7), but at a lower level a mass of colloid carcinoma was found infiltrating the anal muscles and extending along towards the external openings. No primary tumour in the rectum and no lymphatic metastases. For two years there was no evidence of recurrence but he then developed a fracture of the first lumbar vertebra due to a secondary deposit. Deep X-ray therapy given but death two-and-a-half years after rectal excision.

Case 4. Mr. E. C. B., aged 56 years, first seen on 7th October, 1944. Ten years previously he had had an operation for haemorrhoids which was followed by a persistant anal discharge. On examination a chronic perianal abscess, with two external openings, was seen near a right posterior skin tag. The anal canal was distorted and the lumen constricted. Treatment by synchronous combined excision—(Mr. O. V. Lloyd-Davies) with wide excision of perianal skin and deeper tissues.

The operation specimen showed no tumour in the rectum, but all the tissues around the ano-rectal ring were swollen and the lumen of the bowel was much narrowed. Fistulous openings were present in the lower third of the rectum and anal canal (Fig. 8), and one track contained granulation tissue and colloid material. Microscopic examination showed a mass of colloid carcinoma infiltrating the sphincter muscles and growing into the ischio-rectal fat, but not extending into mucosa of rectum or anal canal (Fig. 9). A metastasis was found in one haemorrhoidal lymphatic gland (17 glands examined).

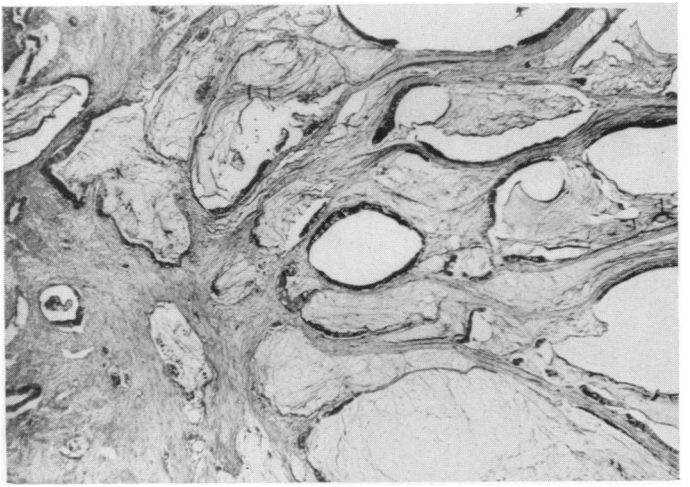

Fig. 9. Photomicrograph showing the typical histology of a colloid carcinoma (Case 4). × 40.

Two years later a bilateral block dissection of the groins was carried out, and a metastasis was found on the right side. After a further two years, a perineal recurrence was treated by deep X-ray therapy. Further secondary deposits developed in the groins and on the penis, and he died from intestinal obstruction due to multiple peritoneal metastases, five years and eight months after his first operation.

Case 5. Mr. B. Z., aged 84 years, first seen 12th January, 1942, complaining of multiple boils around the anus and perineal pain of eight years' duration.

Examination showed extensive induration with multiple fistulous openings in both ischio-rectal areas and posteriorly *per rectum,* submucous induration could be felt. The fistulae and abscesses were laid open. Subsequent biopsies revealed colloid carcinoma and Mr. W. B. Gabriel carried out a radical perineo-abdominal excision with a wide sweep of skin and perirectal tissues.

When the operation specimen was examined no tumour was found in the rectum but the openings of two fistulae were seen in the lower third of the rectum and another in the anal canal (Fig. 10). Extensive perianal thickening was

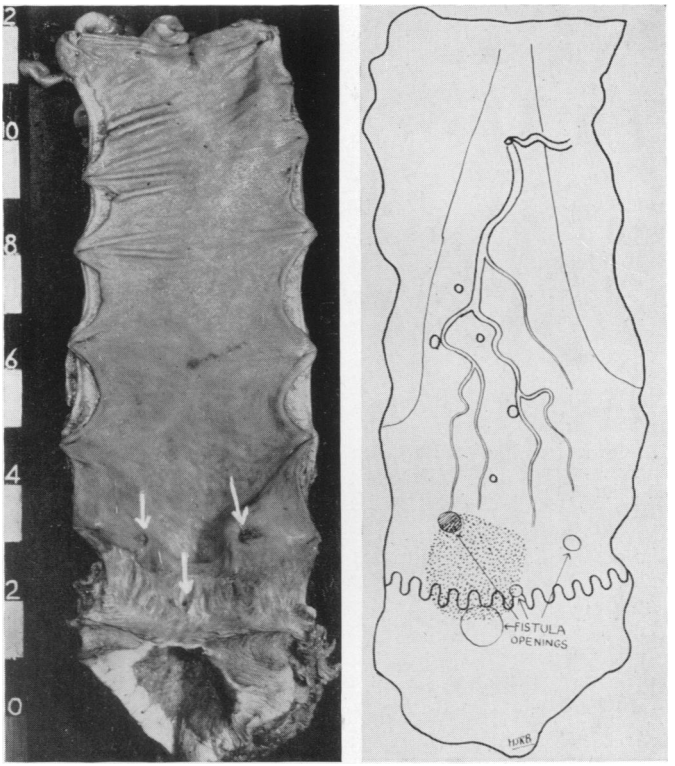

Fig. 10. Rectum removed by perineo-abdominal excision from Case 5. No tumours or ulcer was found in the rectum or anal canal but fistulous openings were noticed, three of which are marked by arrows. In the photograph of the gland dissection the region containing malignant growth is indicated by stippled area.

noticed, and sections revealed colloid carcinoma which had spread widely along fistulous tracks and into ischio-rectal fat and ano-rectal muscles. No growth was found in the mucous membrane of the anal canal or rectum. Five lymphatic glands examined were free from metastases.

The patient died four years and 11 months later.

Case 6. Mr. E. T., aged 50 years, first seen 4th July, 1938, complaining of anal swelling and rectal bleeding of seven months' duration. Eleven years previously he had had anal symptoms which resulted in an operation two years later for alleged tuberculous fistula.

Examination now showed multiple external fistulous opening filled with colloid material. *Per rectum* a polypoid mass projected into the anal canal. A biopsy was taken and reported as colloid carcinoma. A left iliac colostomy was first done by Mr. W. B. Gabriel and this was followed later by a perineal excision with a wide sweep of skin and perianal tissues.

Examination of the operation specimen showed that in the region of the anal canal there were several fistulous openings which discharged mucus (Fig. 11).

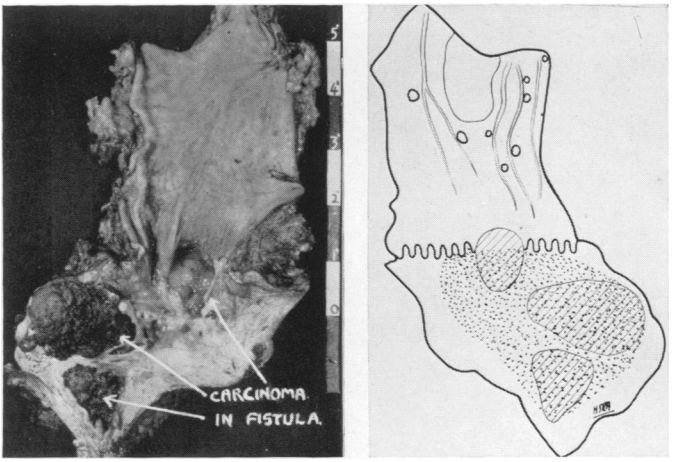

Fig. 11. Operation specimen removed by perineal excision from Case 6. A fungating mass protruded from the fistulous openings in the anal canal and perianal skin. The extent of spread of the carcinoma is indicated by the stippled area in the photograph of the gland dissection.

The tracks extended into the muscles of the anal canal, the ischio-rectal fossa, and subcutaneous tissues. They were lined by mucus secreting carcinomatous cells—a colloid carcinoma of low grade malignancy which was spreading into the anal canal from without. No lymphatic metastases found.

A perineal recurrence two years later was treated by diathermy. He died from this recurrence five years after his first operation.

Case 7. Mr. P. S., aged 66 years, first seen 10th June, 1936, complaining of occasional perianal swelling, bleeding and rectal discharge of one year's duration.

Examination showed two large perianal swellings one mainly at the left anterior quadrant, and the other right lateral. A biopsy reported colloid carcinoma invading the anal canal. A laparotomy and left iliac colostomy was performed by Mr. O. V. Lloyd-Davies followed two weeks later by a perineal excision taking a wide area of skin and deeper tissues to the ischial tuberosities. A perineal fistula developed postoperatively and persisted for two years.

The operation specimen showed an oval ulcer, about one inch in length, situated on the posterior quadrant of the anal canal (Fig. 12). A small papilloma was noticed on the right lateral wall of the rectum three inches above the ano-rectal line, and the internal openings of three fistulae were present just above this. On section masses of colloid growth were found in the subcutaneous tissues and the muscles of the anal canal. No lymphatic metastases found.

He was kept under close observation for three years and then was not seen again until he returned with large malignant inguinal glands and a recurrence at the base of the scrotum. He died five years and five months after the first operation.

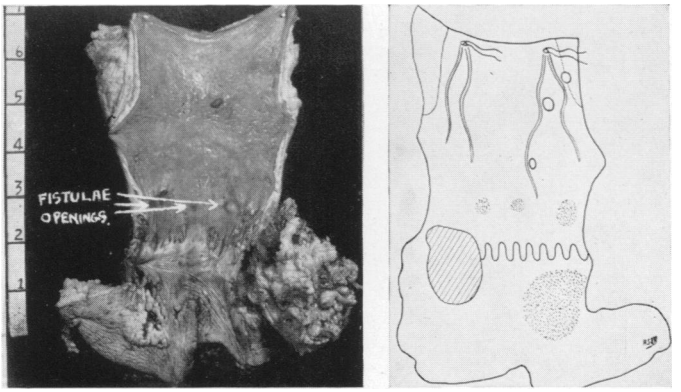

Fig. 12. Operation specimen removed by perineal excision from Case 7. The openings of fistulae are marked by arrows in the photograph of the operation specimen, and the position of deposits of mucoid material is indicated by stippling in the photograph of the gland dissection.

Case 8. Mr. D. H., aged 71 years, first seen 26th February, 1936, complaining of diarrhoea of eight weeks' duration, with bleeding, pain and perianal swelling.

Examination showed an anal stricture, and abscesses and fistulae connected with a huge mass in the right posterior quadrant. The fistulae were filled with colloid material, and a polypoid mass was palpable at the ano-rectal ring, which on section appeared to be a well differentiated adenomatous tumour with changes suggestive of malignancy in one area only.

Mr. O. V. Lloyd-Davies carried out a left iliac colostomy and took a further biopsy, which revealed the presence in the subcutaneous tissues of clumps of mucus secreting columnar epithelium apparently derived from a colloid carcinoma arising in a fistulous track. Other tracks were lined with what seemed to be normal mucus secreting columnar epithelium.

A month later the liver was found to be enlarged and tender and the patient developed jaundice. He died two years and one month after his first operation.

In the preceding eight cases a diagnosis of cancer within fistulous tracks was definitely established by microscopic examination. We shall now give details of two other cases of similar character except for the fact that there was no clinical, or histological evidence of malignancy. We included them because we think that they have a closely related pathology and we consider that they provide a clue to the puzzling problem we are attempting to elucidate.

Case 9. Mr. W. H., aged 71 years, first seen at St. Mark's Hospital 10th September, 1950. Thirty-two years previously he had been treated for a stricture of the rectum first by dilatation and then two years later by colostomy. For more than thirty years he suffered from multiple perianal abscesses and fistulae. A Frei test was found to be negative in 1938 and again in 1944. Gross scarring of perineum and skin overlaying the sacrum was noted in 1950 accompanied by multiple fistulous openings and an ano-rectal stricture which would not admit a finger. A synchronous combined excision was performed by Mr. H. R. Thompson with a wide excision of skin and perianal tissues.

Examination of the operation specimen showed that the lower third of the rectum was surrounded by a dense fibrous ring, above and below which were numerous fistulous openings. Dissection revealed that the perianal tissues were riddled with fistulous tracks filled with what seemed to be granulation tissue, together with collections of cysts filled with mucus. When sections were examined microscopically clumps of mucus secreting columnar epithelium were found both in the fistulous tracks and lining the cysts, but this epithelium was well differentiated and did not appear to be malignant (Fig. 13). Though the

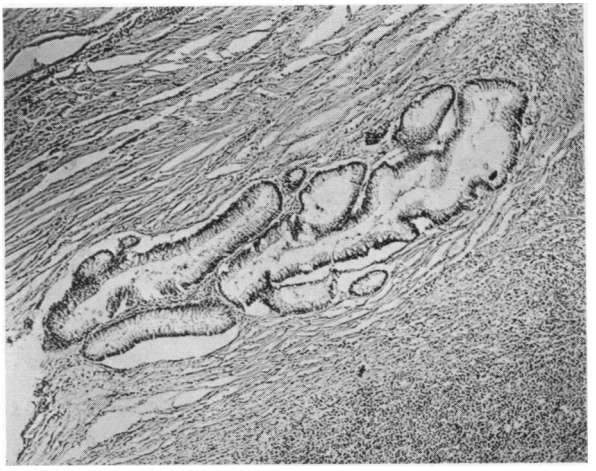

Fig. 13. Photomicrograph showing well-differentiated mucus secreting glandular epithelium lying in anal muscles (Case 9). × 45.

operation of excision of the rectum led to some improvement in his health it was followed by a troublesome perineal urinary fistula. An attempt was made to repair this when the patient was 73 years of age, but he died from cardiac failure two days later.

Case 10. Mrs. T. H., aged 44 years, first seen 25th May, 1951, complaining of a discharging sinus subsequent to an operation for an ischio-rectal abscess eight years previously.

Examination showed three fistulous openings anteriorly and to the right of the anus, but no palpable tumour in the rectum. Sigmoidoscopy negative. Exploratory operation by Mr. L. Norbury revealed several tracks, one passing upwards and forwards between the rectum and the vagina. These tracks were excised with the skin around the external openings. Her postoperative course was uneventful and the wound healed completely.

The operation specimen showed several large fistulous tracks surrounded by fibrous tissue (Fig. 14). Microscopically, these tracks were lined by mucus secreting glandular epithelium resembling that found in normal rectum. In many places the glandular epithelium was folded to form crypts exactly resembling crypts of Lieberkuehn (Fig. 15). The tracks led in all directions and some showed a well defined muscularis mucosa. Although the epithelium lining these tracks was certainly extra-rectal, there was no histological evidence of malignancy.

When seen in November, 1955, four-and-a-half years later, the patient was well and had no recurrence of her rectal condition.

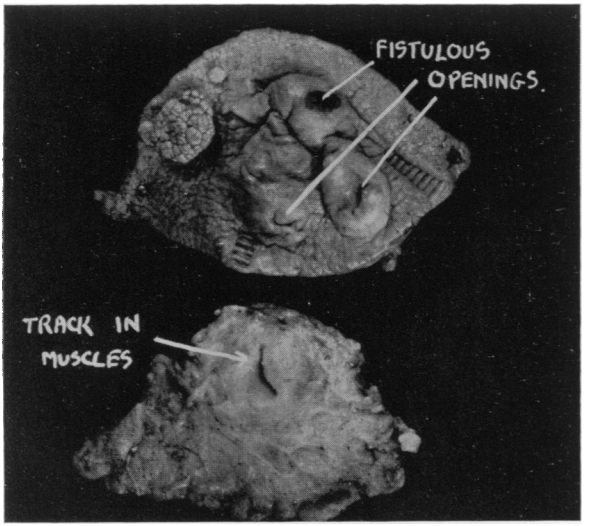

Fig. 14. Photograph of excised fistulous track showing external openings on the anal skin and track lined by columnar epithelium running upward through ano-rectal muscles (Case 10). Natural size.

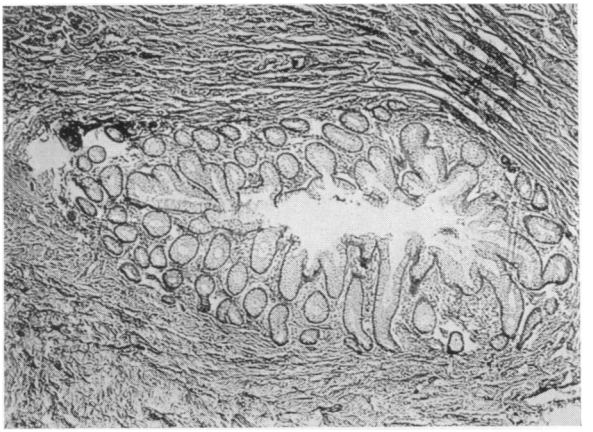

Fig. 15. Photomicrograph showing apparently normal mucus secreting epithelium lining the fistulous track passing upwards in the recto-vaginal septum (Case 10). × 28.

DISCUSSION

We have given details of ten patients with chronic multiple ano-rectal fistulae containing much mucoid secretion such as is usually found in a so-called colloid carcinoma of the rectum, but in none of these cases was there any primary tumour within the rectum or anal canal. Yet in eight of these ten cases a malignant growth with the typical histological picture of a colloid carcinoma of the rectum was found to be extending

along extra-rectal fistulous tracks, and in three of these cases other tracks lined by apparently normal mucus secreting epithelium were also present. In the remaining two of these ten cases multiple fistulous tracks lined by normal mucus secreting epithelium were found but there was no clinical or histological evidence of malignancy.

Since in most of these cases the presence of carcinoma within the fistulous tracks was diagnosed by microscopic examination of biopsy material, the most probable explanation was thought at first to be an extension from an undiscovered primary tumour in the bowel. This possibility was of course always considered, but eventually excluded because, in each case after the operation of excision of the rectum, the operation specimen was most carefully examined. In no case in this series was there any primary carcinoma of the rectum or anal canal, though, in one case (Case 8) an anal stricture was present, in two other cases (Cases 7 and 3) a flat ulcer was found and in a further two cases (Cases 8 and 6) a polypoid mass projected into the anal canal. These lesions, however, were all secondary consequences of the growth of an extra-rectal tumour. We are satisfied that in the eight cases in which malignancy was found this began outside, and not inside, the bowel.

Another possibility which we considered was that the carcinoma might have been deposited in a pre-existing fistula having been derived by implantation from a carcinoma at a higher level in the bowel beyond the reach of the sigmoidoscope. It is well known that carcinoma cells can become implanted on granulation tissue (Goligher, Dukes and Bussey, 1951 ; Cole, 1952 ; Beahrs, Phillips and Dockerty, 1955). We have studied two cases of implantation in a fistula at St. Mark's and in each there was a longstanding fistula containing much granulation tissue. The essential point of difference between those two implantation cases and those now being reported was that in the implantation cases the remainder of the fistulous track was lined with granulation tissue and not with columnar mucus secreting epithelium and in each there was a definite carcinoma higher in the bowel. Moreover clinically in these implantation cases the secondary growth in the buttocks was of a very septic character producing pus in large quantities but no colloid. For these reasons therefore we have excluded implantation cases from our present series.

Another possible explanation we considered was that these extra-rectal tumours and fistulous tracks were in some way related to the so-called intramuscular glands, which are known at times to cause abscesses and fistulae (Lockhart-Mummery, 1928 ; Tucker and Hellwig, 1934). These glands open into the rectum and anal canal just above or below the dentate line, and the ducts pass outwards and downwards through the internal sphincter to end in bulbous expansions. The ducts are lined with stratified squamous or transitional epithelium and the bulbous extremities with columnar epithelium often arranged in two

layers (Fig. 16). In the inner layer a few mucus secreting cells may be found, but the outer layer is composed of columnar epithelium with basally placed nuclei. The epithelium lining intramuscular glands bears little resemblance to the columnar mucus secreting intestinal epithelium with characteristic goblet cells which are found in the fistulous tracks in the cases we are now describing.

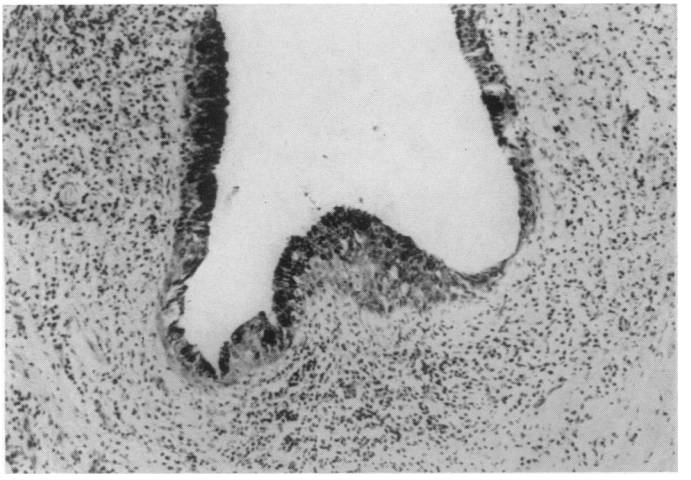

Fig. 16. Showing the typical epithelial lining of an intramuscular gland. × 130.

Cancer may certainly arise in intramuscular glands, but in those cases in the literature which have been recorded with sufficient detail to be accepted as of intramuscular gland origin (Scarborough, 1941 ; Kay, 1954 ; Close and Schwab, 1955) the microscopic appearance has been predominantly of a squamous or transitional cell type with little or no adenomatous elements. Even these latter in no way resemble the columnar epithelium with goblet or signet ring cells, producing large quantities of mucus as found in our extra-rectal colloid carcinomata.

We are convinced then that the ectopic tracks which were present in the five cases described in this paper are of congenital origin. These structures were lined by normal mucus secreting columnar epithelium folded to form crypts of Lieberkuehn resembling in every way the epithelial lining of the adjacent rectum. Moreover, in two cases (Cases 1 and 10) a well marked muscularis mucosa was found, in one of which (Case 1) the whole track was surrounded by a well defined smooth muscle coat continuous with that of the rectum. We conclude, therefore, that these were small duplications of the bowel at this point (Gross, 1953). The ano-rectal region is an area of complex embryological change, and it is probable that such duplications arise at a very early stage in the development of the embryo either by sequestration of a growth of cells from

the primordial intestinal tube (Lewis and Thyng, 1907) or alternatively by fusion of the adjacent longitudinal folds of the rectal lining with subsequent ingrowth of the outer coats (Keibel and Mall, 1912).

Since duplications such as these are lined by epithelium identical with that of the mucous membrane of the rectum they are liable to be the site of origin of similar neoplasms. We consider that the cases we have described are instances of primary carcinoma arising in unsuspected reduplications of the intestinal tract. The fact that in three of our malignant cases we were able to find other fistulous tracks lined by " normal " mucus secreting epithelium, seems to us to be a convincing proof that the fistulous tracks were congenital malformations whose existence was revealed by the subsequent development of cancer within one of them.

TREATMENT

The first essential in the treatment of such fistulae, whether or not associated with carcinoma, is of course accurate diagnosis. This usually can be achieved by taking a biopsy from the deeper portions of the tumour or fistula, an operation which is best carried out under anaesthesia. At the same time an assessment of the extent and mobility of the local lesion should be made, and the rectum examined by sigmoidoscopy.

If biopsy reveals the presence of malignant disease in the fistulous tracks and surrounding tissues then the most radical excision possible must be performed. Two of our cases were treated by a synchronous combined excision of the rectum, four by a perineal excision in two stages, one by the perineo-abdominal method, and one patient had a colostomy only as the growth was locally inoperable. We consider that in most cases a combined excision is the procedure of choice, because by this method the most radical excision of the growth and the related lymphatic fields can be achieved. However, four of the eight patients with carcinoma in our series were in such a poor state of health that a two stage perineal excision was adopted as a safer procedure. Although on general principles it seems advisable to recommend the widest possible surgical removal yet it must be admitted that local recurrence or recurrence in the inguinal glands is almost inevitable sooner or later. The only patients who have a chance of being cured by surgery are those who are diagnosed and treated whilst the malignant growth is still at an early stage of development.

For cases in which there is no clinical or histological evidence of malignancy the only treatment called for is the laying open and excision of all fistulous tracks and leaving a large wound to heal slowly by granulation.

SUMMARY

This paper discusses the pathology and treatment of cases in which colloid carcinoma is found within fistulae of the ano-rectal region, though no primary tumour can be discovered in the rectum or anal canal.

The explanation suggested is that the carcinoma has arisen in a malformation such as a reduplication of the intestinal track. Support for this hypothesis is provided by the fact that in some of the cases now reported fistulous tracks lined by normal rectal mucosa were found in association with other fistulous tracks containing colloid carcinoma. The clinical and pathological findings in ten cases are reported. In eight of these colloid carcinoma was found in fistulous tracks, but in two others the tracks were lined by apparently normal mucosa. The results of surgical treatment are reported.

ACKNOWLEDGMENTS

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