ON THE
STRUCTURE AND NATURE OF THE SO-CALLED
COLLOID CANCER.

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Received March 15th.—Read April 22d, 1856.

ALTHOUGH the subject of colloid cancer has attracted considerable attention from pathologists, many points in regard to the structure and nature of the disease remain in obscurity. The following account will be found to differ in several particulars from the descriptions usually given, which do not, I think, convey a perfectly satisfactory idea of the peculiarities of the disease. The fact of the association of a membrane in and with the stroma of colloid has been indicated by several authors; but I am not aware of any account of the disease, in which the characters and development of this membranous stroma have been fully described. The description, too, of the contents of the stroma will be found to differ somewhat from that which has hitherto been given.

The names colloid, and colloid cancer have been applied to a great variety of pathological conditions; and it is probable

that many diseases having no relation to one another have been thus classed together. Some writers, and especially those of Germany, apply the term colloid to almost any thick fluid, the name alveolar cancer being given by them to those diseases which we commonly call colloid cancer. It is well known that almost every grade of transitional formation is met with, from the colloid cancer, as seen in the stomach, to the thick adhesive serum of some cysts, and it may sometimes be difficult to state with certainty to which class a particular case belongs. In the following communication it is therefore proposed to restrict the descriptions to unequivocal examples of colloid or alveolar cancer. I have observed nine examples of this disease, and, in addition to these, specimens have been examined from other cases furnished me by friends, besides a considerable number of those colloid diseases which are generally considered not to be cancerous; such as occur in the thyroid and in other parts of the body.

Although the microscopical appearances of colloid may vary in different cases, almost as much as the naked eye characters, yet as a general type of structure is found to prevail, this type will be first described, and then the various aberrations from it.

Colloid cancer, as seen by the unassisted eye, is obviously composed of a fibrous looking stroma supporting a quantity of gum-like material (fig. 1). The proportion in which these elements are combined varies extremely; indeed, it appears that in some cases the stroma may be nearly absent, and then the disease assumes the form of an ill-made jelly; on the other hand, it may be so abundant that the mass is as firm as a cartilaginous tumour.

Colloid is essentially an infiltrating disease, i. e., its elements are produced amongst a pre-existing tissue; and so in a section of colloid, portions of the structure which had become the seat of the disease are generally detected. Good examples of this condition are frequently seen in the stomach, where muscular fibre and areolar tissue may be observed mixed up with the morbid product (fig. 8).

It is probable that all the fibrous structure, which is similar to normal areolar tissue, belongs to the organ or part infiltrated, and not to the new growth. This view is chiefly borne out by the fact that areolar tissue is completely absent in the looser and possibly purer portions of colloid, and that it is most abundant where there is to the eye the greatest amount of the original tissue remaining.

The stroma of colloid, in its most characteristic form, assumes the shape of a convoluted membrane. In many places it is entirely composed of this tissue, when it then appears like the lining membrane of a multilocular cyst, such as occur in the kidney or ovary. The membrane is simple, thin, finely granular, with occasional markings, chiefly in straight lines, upon it (figs. 2, 7). In places it is so thin and transparent that its presence may be overlooked. The markings or lines upon this membrane are wanting on the smooth portions; but are extremely abundant where it is folded or creased. In such parts the lines correspond to the folds of the membrane, and spread out in a fan-shaped form from the twisted portion. In places the stroma has a fibrous appearance, which in some instances is obviously owing to the folding and stretching of the membrane; in others this structure is probably due to the membrane having split up into fibres in a direction corresponding to the folds.

In many places, however, well-defined fibres, presenting peculiar characters, are seen; they are more or less flat or ribbon-shaped, extremely thin and transparent, generally faintly, but sometimes coarsely, granular. No nuclei can be discovered among them. Here and there they expand out and are continuous with the membranous stroma already described. In some places they are thin and filamentous; but in others they resemble the yellow fibres of areolar tissue. The above similarity in texture, and the frequent junctions of these fibres with the membrane (fig. 4), indicates that they are parts of the same tissue.

Although the stroma of colloid is generally described as being entirely fibrous, some authors have recognised the presence of a membrane associated with these fibres.

Rokitansky¹ has described a membranous form of stroma in cancer, which he says is strongly marked in the colloid variety; the arrangement he compares to a trellis-work intervening the colloid material. Mr. Paget, in his lectures, speaks of the stroma of colloid as formed by "fibres or fibred membranes," elongated nuclei being frequently seen among them.

It is thus seen that the stroma divides the colloid substance into loculi. These may be sub-divided again and again into still smaller spaces by similar but more delicate stromal tissue.

The size of the loculi thus formed is extremely variable, the smallest being little larger than a blood-corpuscle, the largest the size of a hen's egg. Between these extremes every possible variety in size may occur, and this fact constitutes one of the most remarkable features of the disease.

The spaces enclosed by this membranous stroma are filled with the essential element of the disease, that is with colloid material. This is arranged in more or less globular masses, or in a cluster of such masses (fig. 5). They may easily be separated from the stroma either by pressure or by scraping the surface of a section. The bodies which are thus separated are similar in shape and size to the loculi from which they have been withdrawn. The fact of their becoming displaced so readily appears to indicate the existence of a complete partition between many loculi where no line of separation can be detected by the eye.

These rounded masses of gelatiniform substance, which are termed colloid bodies or corpuscles, may be composed of a central body or kernel surrounded by gelatinous substance, or may be wholly made up of the latter material.

The central portion or kernel may be nearly spherical or ovoid, or it may appear as if splitting up into several parts (fig. 11). It is often composed of a large number of simple spherical cells closely packed together, each of which, in many cases, appears to contain a large spherical nucleus;

¹ Rokitansky, 'Path. Anat.,' vol. i; and his *Essays on 'Cancer stromata' and 'Colloid Cancer,'* quoted in the above, Syd. Soc. Edit.

in some instances indications of a cell-wall surrounding these may be seen. In other examples the cells composing the kernel are less definite in form, and may be represented only by an aggregation of granules, probably phosphate or carbonate of lime.

The jelly-like substance surrounds the central kernel with a certain degree of uniformity in all directions, like the soft part around the stone of a fruit. It is elastic, and on being indented, readily regains its former shape. Occasionally, concentric lines may be detected. If, however, the concentric arrangement is not obvious in the natural condition of the structure, slight pressure, or the addition of a little iodine or acetic acid will render it apparent. Granules, and, occasionally, cells, will also be seen arranged in these concentric lines. A little examination will soon prove that the lines are not fibres, but that the appearance is due to the substance of which the "colloid body" is composed, having a concentric arrangement, similar to the coats of an onion. This may be conclusively demonstrated by placing one of the colloid bodies beneath a dissecting microscope, and turning it over with a needle, whilst still in view.

In many specimens, it appears as if some of the granules lying between these concentric laminae, had become the nucleus or kernel of a new colloid body (fig. 6), thus forming a compound colloid corpuscle (figs. 9, 12).

Moreover, fresh corpuscles may arise in the interior of younger ones, and in this manner, endogenous growth may take place to almost any extent (fig. 6).

Frequently, however, there is but little evidence of a central body or kernel to the colloid corpuscle. It then appears as a more or less spherical mass of gelatinous substance, having generally a laminated arrangement, granules and cells being scattered throughout its interior. The cells so placed are subject to irregularities both in form and size. Some are as small as blood-corpuscles, whilst others approach the magnitude of ordinary colloid bodies; suggesting to the observer that the smaller, supposing development to continue, would gradually attain the

dimensions of the larger bodies; in other words, that they would become ordinary colloid corpuscles.

Occasionally, the smaller cells of colloid are very numerous, and sometimes occur in great numbers near the surface of the colloid body, and thus appear to form an epithelial lining to the membranous stroma.

It is commonly stated that when acetic acid is added to a section, nuclei are seen in the stroma. On careful examination I have not been able to detect either cell or nuclei among the stromal tissue. I am inclined to believe that the structures which are rendered apparent in the gelatinous substance by the addition of acetic acid, have been mistaken for, and described as stroma containing nuclei. The effect, however, of the reagent is to obscure the stroma, and this result is produced not so much by any action on that tissue itself, as by the acid rendering strongly conspicuous the laminated arrangement of the transparent portion of the mass, which thus marks the intervening stroma. It is possible that many of those bodies resembling oat-shaped nuclei, which are seen in the gelatinous portion of the corpuscles, are only separations or spaces between the laminæ.

In a case of gelatiniform cancer of bone, Wedl¹ has observed the laminated arrangement of the colloid substance around the central mass. The same author noticed that, on the addition of acetic acid, both in this case and in one of colloid of the breast, bodies like elongated nuclei were seen arranged in concentric lines. He considers that this appearance was caused by the action of the acetic acid, and that the elongated bodies were 'coagulating mucin.' The stroma in these cases is described as fibrous.

The description that has been given applies to all the more dense forms of colloid cancer, but where the disease assumes the appearance of a simple jelly, many of these characters are lost. As Dr. Jenner has very accurately described the structure of this substance in a case he brought

¹ 'Path. Histology.'

before the Pathological Society¹ I need only very shortly recite its characters.

The transparent jelly-like substance from Case 5, when examined under the microscope, is composed of an homogeneous material, in which some cells and a few granules are embedded. Of these cells, a few are transparent, spherical, and about the size of pus-globules, whilst others are larger, and filled with granules like compound granular corpusclés.

By the addition of acetic acid, it becomes opaque, and extremely tough. If now placed under the microscope, it exhibits a somewhat indistinct appearance of parallel striæ, the granules and cells before mentioned being arranged with their long diameters in the direction of these streaks. It is evident that this structure does not indicate the existence of fibres, but resembles the streaking which may be seen in mucus after the addition of acetic acid.

The opaque blanc-mange-like substance, from the same case, appears to be almost entirely formed of dark, spherical granules, and some larger angular bodies, embedded in a transparent matrix. As was originally described by Dr. Jenner, these granules very closely resemble those of fat; both these and the larger bodies are dissolved by hydrochloric acid, the latter leaving an animal basis without change of form. Some are dissolved without obvious action, but in the majority, a brisk effervescence may be noticed. The acid which was added is now found to have become impregnated with phosphoric acid.

An unusual and very remarkable structure was observed in one of the cysts from the same case (No. 5). It was about the size of a hazel nut, and did not present any external characters by which it could be distinguished from its neighbours. When cut into, a transparent jelly-like substance protruded, in which an immense number of little sacs were embedded. The small sacs or cysts were mostly spherical, and rather more opaque than the surrounding material; in size they varied from that of a blood-corpuscle

¹ 'Trans. of the Path. Soc.,' vol. v.

up to that of a hempseed. They were composed of a membrane enclosing a globular mass of jelly-like substance (fig. 9). The membrane was coarsely granular, easily torn, and of some thickness. Smaller cysts were often enclosed in the large ones. Large numbers of granules and cells (fig. 11), such as are usually met with in colloid were seen in all parts of the jelly-like substance. Cholesterine, which is seldom absent in colloid, was very abundant in this example.

Although at first sight the structure of this particular cyst appears distinct from that of the firmer forms of colloid, the difference is only in the degree of consistence of the various portions of the disease. As a general rule in firm colloid, the density of the stroma is not greatly different from that of the contained substance. If, however, we imagine a compound colloid body, in which the membrane both of the parent and of the enclosed corpuscles were thick and tough, whilst the contents were somewhat looser than usual, the structure would be precisely that of the cyst described. This cyst may, therefore, be regarded as a compound colloid body.

The free jelly-like substance may be explained as the result of an extreme development of colloid substance, with scarcely any stroma. It is not improbable that the comparative absence of stroma may be occasioned by the rupture of some of the cysts, and the continued secretion of colloid material from their walls.

Development.—The mode of origin of colloid is far less easy to trace than its manner of increase. The disease, in its most elementary form, probably exists as a simple cell. The colloid cell appears to be developed around certain granules or nuclei, which are found in an otherwise healthy tissue near the disease, and may or may not be previously aggregated into a mass.

The endogenous mode of growth of these colloid bodies is as follows; the kernel frequently exhibits a tendency to split up into a number of separate masses (fig. 10), each of

which may become the kernel of a fresh colloid body. In some instances a few nuclei or even granules become detached from the surface of the kernel (fig. 6), and form a fresh one. In this manner, a compound colloid corpuscle is produced; the process may, moreover, be repeated again and again.

The fact that the kernels of many if not of the majority of the colloid corpuscles are composed of granules, tends to disprove the hypothesis which suggests itself, viz., that these granules are simply degenerated nuclei.

A number of colloid bodies arising and increasing in the manner indicated, become blended together into a mass, and the cell-walls of the colloid bodies become partially absorbed. This process is traced with greater or less distinctness in different cases, but was extremely obvious in a case of colloid of the peritoneum (fig. 9).

The stroma of the disease is thus formed by the coalescence of the walls of the colloid bodies, and hence its close similarity to the lining membrane of a multilocular cyst. The peculiar ribbon-shaped fibres which are seen spreading out into portions of membrane, are no doubt the remaining portions of the same tissue, the rest having been absorbed (fig. 4).

The character of the fibres of the stroma, as well as the complete absence of nuclei among them, indicates a different nature and mode of growth from that of ordinary areolar tissue. Most of these fibres are produced by the splitting up of the membrane, perhaps some may be formed by the coagulation of a fibrinous blastema.

It is difficult to account for the peculiar lamination of the colloid material. The nearest analogy in structure is probably that which is described to exist in the vitreous humour. It is possible that the endosmosis by which the colloid cells become distended goes on at irregular rates, or perhaps with intermissions, so that one lamina becomes as it were consolidated before the next one is formed over it. Another hypothesis which suggests itself is, that the arrangement is produced by a process similar to that by which

fibrinous concretions are formed in the peritoneal cavity,¹ i. e., by the deposition of the material, lamina after lamina, on a central body or kernel.

Relation to cancer and other diseases.—The want of uniformity of opinion as regards the relationship of cancer and colloid, to a certain extent depends on the variety of diseases that have been included under the name colloid. Formerly colloid, in all its forms, was classified with malignant diseases, but it is now more generally taught that it may assume a non-malignant or a malignant character; and it is the latter class only which is under consideration.

In order to determine the claim of the so-called colloid or alveolar cancer to be placed among the cancerous diseases, it will be well to bear in mind what are usually admitted to be the essential characters of the latter disease, viz. :

1. Its structure and chemical nature.
2. Its infiltration among the natural tissues of the body.
3. Its invasion of the lymphatic vessels and glands.
4. Its tendency to destruction by ulceration and sloughing.
5. The occurrence of secondary growths, particularly in the lungs and liver.
6. Its tendency to recurrence after removal by operation.
7. The presence of a peculiar cachectic condition of the system.

Although one or two of these conditions may be absent in individual examples of the disease, still a group of cases in which the same character or characters are uniformly absent cannot with propriety be called cancer.

As to structure, the arrangement of colloid that has been described is altogether dissimilar from the ordinary forms of

¹ 'Path. Trans.,' vol. vi.

scirrhus, medullary, or epithelial cancer. Bodies resembling cancer-cells, are, it is true, not infrequently met with in colloid, but careful examination will generally prove them to be growing colloid-cells. So also chemical analysis of colloid shows it to be a substance perfectly *sui generis*.

With regard to the affection of the lymphatic glands, the only way in which they appear to become involved is by the extension of the disease to them, and thereby enclosing them in the tumour. There does not appear to be any evidence of their proneness to become affected with the disease rather than the other tissues.

As to secondary growths, it will be seen that, although in several cases there was more than one example of colloid disease in the same body, in none were these tumours in the substance of the liver, or in that of the lungs. Moreover, I cannot refer to any completely recorded example in which growths were discovered in the substance of those organs,¹ still there are several well authenticated cases, in addition to those appended, in which more than one colloid tumour was present in the same individual.

In those cases in which several organs were involved, it is obvious that this peculiarity arose from the extension of the original disease, its almost complete continuity having been traced.

It is also seen that in all the examples of multiple colloid tumours the disease was confined to the abdominal cavity, and not only to this but to two parts of it, the peritoneum and the intestinal canal. The manner in which the intestines were affected is strikingly peculiar; colloid growth taking place at isolated portions of the muscular coat of the

¹ The condition of the lungs in the very interesting case given by Dr. Warren ('Med.-Chir. Trans.,' vol. xxvii), may appear an exception to this rule. The loss of transparency which occurred in these tumours on being kept in spirit, renders their colloid nature very doubtful; so that in the absence of microscopical description it cannot be considered as perfectly proved that these were really examples of the so-called colloid cancer.

bowel, as in Case 4.¹ Of the manner in which the disease spreads over the surface of the peritoneum, Case 5 furnishes a good example.

This strict limitation of the disease contrasts strongly with the ubiquitous character of cancer, from the invasion of which no tissue and no part of the body is free.

Without entering into the question of the value of cachexia as a distinctive character of cancer, I believe there is no proof of the existence of any special cachexia in colloid, beyond that induced by the presence of serious and fatal disease.

May colloid be associated in the same growth with cancer? The appended cases do not furnish an example of the coincidence of colloid and cancer. There does not, however, appear, *à priori*, to be any reason for believing that the two might not sometimes be associated in the same way that cancer occurs with cystic disease.

Occasionally an apparent combination of colloid and encephaloid cancer is seen in the stomach; that is to say, there is a cancerous ulcer in some part of the stomach, with thickening near the pylorus, which somewhat resembles that produced by the so-termed alveolar cancer. I have carefully examined two examples in which these appearances were noticed; but in both the thickening near the pylorus depended solely on hypertrophy of the muscular coat.

Again, certain tumours of the firmer forms of medullary cancer sometimes exhibit an apparent combination of colloid and cancer; that is, portions of these tumours are singularly clear and translucent, closely resembling in this respect colloid cancer. In all such cases, however, that I have examined, the characteristic structure of colloid is wanting.

Relations of colloid to tubercle.—Whilst the indications of the association of colloid with cancer are so slight, the large proportion of cases in which it was associated with tubercle is striking. In some examples the tubercle appears not only of recent formation, but to have been in a state of

¹ See also 'Guy's Hospital Reports,' Series III, vol. i, where a somewhat similar case is recorded.

activity. When bringing forward an example of the concurrent development of cancer and tubercle,¹ these cases were not adduced, as they were not considered true examples of cancer.

The foregoing leads me to the conclusion that, as far as can be judged from the cases that have fallen under my observation, colloid is a disease perfectly *sui generis*, and is neither of a cancerous nature nor frequently associated with cancer. The cases, moreover, on which this conclusion is chiefly founded are examples of several of the most characteristic forms of the first-mentioned disease.

Little can be said regarding the treatment of colloid. When within reach of the knife there can scarcely be a doubt as to the propriety of removing the tumour, for although the cases of external colloid before the profession are not sufficiently numerous to decide the question, they show that the disease, if not radically cured, is at least slow in returning.

In concluding this paper, I have to thank my friend, Mr. Flower, for the accompanying drawings, which very faithfully represent the microscopical appearances of the disease.

APPENDIX.

The following is an abstract of the cases mentioned in the foregoing paper. With the exception of Case 2, they were all patients of the Middlesex Hospital :

CASE 1.—A female servant, unmarried, æt. 21,² was

¹ 'Med. Times and Gazette,' 1853.

² The ages given are those of the patients at the time of attack, or when the disease was first discovered.

admitted, August, 1852. She had suffered from pain and difficulty of defecation for twelve months. A stricture of the rectum was discovered, which resisted the usual treatment. She died somewhat suddenly, from a perforating ulcer of the colon, after the disease had existed for fourteen months.

Post-mortem.—The rectum, from ten inches above the anus to the sigmoid flexure, was converted into firm “colloid cancer,” which, in many places, was two inches in thickness. The other viscera were healthy. (See Museum of Middlesex Hospital).

CASE 2.—A tumour formed in the breast of a lady, æt. 45. It increased gradually and without pain, till it attained the size of a walnut, and was then (November, 1851) excised by Mr. O. Clayton. The tumour, on section, presented the ordinary appearance of firm colloid cancer. The wound healed rapidly after the operation. The patient remains perfectly well at the present time (March, 1856). The scar is healthy.

CASE 3.—A swelling made its appearance in the right parotid region of a woman, æt. 61. This slowly increased for six years, till, in February, 1853, it was excised by Mr. Shaw. The tumour was then as large as a goose’s egg, and exhibited the usual appearance of colloid cancer. The wound healed, and she was perfectly well when seen last, about the end of 1855.

CASE 4.—A man, æt. 40, had suffered for six months before his death with pain after food, constipation, and vomiting. He died, May, 1854, with symptoms of obstruction of the bowels.

Post-mortem.—The pyloric end of the stomach was converted into firm “colloid cancer” half an inch in thickness. There was similar disease at the lower end of the ileum, and also in the colon. There were numerous crude tubercles in the lungs, on the pleura, and on the peritoneum.

CASE 5.—A man, æt. 43, died, in January, 1854. He had suffered from “coldness” in the stomach, vomiting, and swelling of the abdomen, for six months.

Post-mortem.—The whole of the abdominal viscera were completely bound together by colloid cysts and colloid material. There was also about a pint and a half of free colloid, resembling ill-made jelly. A portion of the disease was as firm as enchondroma. The various viscera were surrounded, but not invaded by the growth. (See Museum of Middlesex Hospital.) The lungs were infiltrated throughout with miliary tubercle, which presented the usual structure under the microscope.

CASE 6.—A man, æt. 40, was attacked with dyspepsia, particularly after taking animal food. Soon after this he suffered from pyrosis, and died, May, 1855, six months after the first symptoms of disease.

Post-mortem.—The stomach retained its natural form ; but was converted into a hard unyielding sac. The walls being infiltrated with “colloid cancer” and being nearly five eighths of an inch in thickness. There were some old and recent tubercles in both lungs.

CASE 7.—A man, æt. 40, discovered a tumour, about the size of a walnut, in his right iliac region. This slowly increased till he died, December, 1854, five years afterwards. He had suffered principally from irritability of the bowels and the frequent passage of blood.

Post-mortem.—A “colloid” constriction of the ascending colon, with infiltration of the neighbouring bowel.

CASE 8.—A man, æt. 63, suffered from diarrhœa and occasionally from vomiting, for seven months, and died, May, 1855.

Post-mortem.—A tight constriction of the transverse colon was discovered, with deposit of colloid material in the walls of the bowel, and principally in the muscular coat. The colon a short distance below, was affected with similar disease.

CASE 9.—A tumour formed in the right breast of a female mulatto, æt. about 35. This slowly increased for twelve months, when the breast was excised by Mr. Moore, December, 1855. The tumour was then about the size of a hen's egg, and was composed of hard, translucent colloid. The wound healed rapidly, and she left the hospital apparently well.

DESCRIPTION OF THE PLATES.

PLATE I.

Fig.

1. Section of colloid of the breast (Case 8).
2. Section of colloid of the stomach (Case 6).
3. Section of colloid of the rectum (Case 1).
4. Fibrils and stroma of colloid of the breast (Case 8).
5. Stroma of colloid of the peritoneum (Case 5).
6. Section of colloid of the breast, to which acetic acid has been added (Case 8).

PLATE II.

7. The membranous stroma from colloid of the breast.
8. The muscular coat of the stomach invaded with colloid.
9. Development and fusion of the colloid cysts from the peritoneum (Case 5).
10. Simple colloid bodies.
 - a. In the natural condition.
 - b. After the addition of iodine.
 - c. After the addition of acetic acid.
11. Kernels of the colloid bodies (Case 8).
12. Compound colloid body (Case 1).

Fig. 1

Fig. 2

120 diam.³

Fig. 3

Fig. 4

200 diam.³

Fig. 5

120 diam.³

Fig. 6

Fig. 7.
200 diam.^s

Fig. 12.
300 diam.^s

Fig. 8.
200 diam.^s

Fig. 10.

a.

b.

Fig. 9.
200 diam.^s

Fig. 11.
400 diam.^s