A Clinical Lecture

ON

THE EARLY DIAGNOSIS OF CARCINOMA OF THE PROSTATE.

DELIVERED AT THE LONDON HOSPITAL.

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ONE of the unexpected consequences of the work that has recently been done in connexion with the treatment of enlargement of the prostate is the discovery that malignant disease of the prostate is very much more common than was formerly believed. In the English textbooks of ten years ago cancer of the prostate is described as being of rare occurrence, and the chief symptoms noted are intense pain and profuse haemorrhage. As a matter of fact, it is unhappily very common, and in many instances there is neither a severe degree of pain nor profuse haemorrhage until the disease is far advanced. Of the last fifty cases of enlargement of the prostate in which I have been consulted, no less than ten were certainly malignant, and I am afraid two more will prove to be so, though I cannot say definitely yet. My experience may be exceptional, I admit. I do not mean that 25 per cent. of all cases of enlargement of the prostate are due to malignant disease, but only 25 per cent. of those which were brought under my notice. The majority of patients with enlargement of the prostate never consult any one at all, and probably most of the cases that were sent to me came because it was thought there was something unusual about them. Both considerations, of course, reduce the proportion; but, after making full allowance, cancer of the prostate cannot possibly be described as very rare. Others, too, have found the same. According to Young, cancer of the prostate is present in one-seventh of the cases of enlargement in men over 50 years of age. Lewissohn of Heidelberg found 18 cases of malignant disease out of 143, while Albarran and Hallé calculate that it is present in approximately 14 per cent. I have only met with one case of sarcoma growing in the prostate itself, and that was in a boy ten years old, so that the following remarks apply solely to primary carcinoma. Secondary cancer, which is also not uncommon, introduces so many complications that I shall leave it upon one side for the present.

Cancer of the prostate is always of the glandular type. It may be either hard or soft. The former is much the more common. In fact, I have only met with three instances of the latter, and Young, in his monograph on Cancer of the Prostate, in the *Johns Hopkins Hospital Reports*, does not appear to have met with any. The growth may originate either in a normal gland or in one that has already been the seat of enlargement for years past. In either case, it rapidly infiltrates the tissue around, flattening the outlying parts to some extent against the inner surface of the capsule, and only penetrates the capsule itself at a comparatively late period. The direction of the growth is almost always upwards, along the course of the ejaculatory ducts—which may be found plugged with columns of cancer cells—filling up the intervesicular space, and spreading from there along the lymphatics into the trigone of the bladder. From thence it grows outwards towards the walls of the pelvis on either side. The urethra may be compressed at an early date, or not, according to the position and direction of the growth, but it rarely becomes actually involved until late. The soft variety is an exception, as this very soon spreads into the neck of the bladder, sprouting out as a fungating, more or less villous mass. Two of the three cases under my care proved fatal from the bleeding that arose from this.

The internal iliac and then the other pelvic glands are the first to become infected. As these can hardly be felt, even when they are considerably enlarged, and not at all when the infection is only recent, it is very difficult to ascertain when this takes place. In many instances there is reason to believe that it is not till very late. Metastatic deposits, on the other hand, are sometimes

found exceedingly early, while the original growth is still quite minute, and are especially common in the long bones and ribs. An excellent instance of this, not by any means unique, is recorded in the *Archives of the London Hospital Pathological Institute*, vol. ii, p. 175. Deposits of carcinoma were found in the lumbar, iliac, and bronchial glands, pleural lymphatics, marrow of right femur and lumbar vertebrae, secondary to a growth in the prostate, which was only discovered by making a microscopic examination. The gland was in no degree enlarged, and exhibited absolutely no naked-eye change on section. Further, no signs of infiltration could be detected in the surrounding tissues. The patient, who had been admitted into hospital for excruciating pains in the chest and limbs—so severe as to prevent him from standing—never complained of any urinary trouble until ten weeks before death, when retention suddenly occurred, followed by incontinence of urine and faeces.

The microscopic appearances in cancer of the prostate may be characteristic, but in many instances they are so varied and so complicated by those due to pre-existing enlargement and chronic inflammation that a very exhaustive examination is required before a definite opinion can be formed. There may be a large amount of stroma, with only a few elongated slit-like alveoli between the bundles, so that the whole is as hard as scirrhus; or there may be very little, and that of the most delicate description. The alveoli may be of the most irregular shape and size, and filled with cells until the central cavity is obliterated; or they may be perfectly uniform, lined with a single layer of cells, and enclose a rounded space as regular in shape as if the section had been made through a normal tubular gland. The cells may be cylindrical with a nucleus of moderate size near the base, or cubical, or quite irregular with nuclei of all shapes and sizes. There may be great intra-alveolar growths, indistinguishable from the proliferating intracystic growths so common in the hypertrophied gland, and in the same specimen there may be every gradation between the two extremes. In short, while in some cases the diagnosis with the microscope is perfectly straightforward, in others it is almost impossible, certainly from a single section, to make sure whether the growth is carcinoma, or merely one of those rapidly growing adenomata that occur so frequently in an enlarged prostate. A very good example of this difficulty is recorded by Young.¹ He describes how, in a case in which the cancerous process had grown down into the prostate, probably from one of the vesiculae seminales, it was only after a second series of sections and repeated examination that it became evident that what had been taken to be adeno-carcinoma of the prostate was in reality alveoli, packed with epithelial and polynuclear cells, a process of inflammation, and not carcinoma. In several instances under my own care I have found the same difficulty. In many parts the growth appeared to consist almost entirely of tubules, perfectly uniform in shape and size, with no appreciable difference from the normal ones, yet spreading into and under the trigone of the bladder, and even between the muscular bundles. Nor could I find any evidence of infiltration of the stroma by epithelial cells. Albarran and Hallé have applied the term "epithelioma adenoid" to some of these appearances which suggest the beginning of malignant formation in lobules apparently purely adenomatous. Whether such a borderland as diffuse adenoma is advisable or not, it is quite evident that at present a considerable number of cases occur which are very doubtful in character; and some, of which the one described in the *Archives of the London Hospital Pathological Institute* is an instance, in which a positive opinion is impossible without a prolonged investigation. Unfortunately this detracts considerably from the value of Young's proposal, that in doubtful cases a section should be made and examined on the spot, while the operation for removal is proceeding; for it is in just those cases in which the clinical diagnosis is most difficult that the microscope is most likely to fail.

The age of my patients ranged from 45 to 79 years, the majority being between 58 and 65. The duration of the symptoms before they came to see me varied from less than a month to over twenty years. This, of course, depended on whether the cancerous growth originated in a gland otherwise normal, or, as more frequently happens,

in one that was already the seat of some degree of enlargement. Whether the growth was hard or soft, the symptoms were the same in character as those present in the ordinary non-malignant form of enlargement—increased frequency of micturition; delay at the beginning, dribbling at the end; a certain degree of urgency; pain, which in the later stages sometimes became very severe, and haemorrhage. The distinctive feature was the rapidity with which these symptoms progressed when once they had set in, and the degree of severity to which they attained in a very short time, without there being cystitis or any similar cause to account for it.

Increased frequency of micturition was present in them all. In some it had been present for years, in others it had begun quite recently; but there was this feature about it—a feature the development of which one of my patients who had already suffered from increased frequency for some time himself noted to me—that the disproportion between the frequency during the day and during the night was not nearly so great as it usually is in cases of simple enlargement, and that the act of micturition did not give the customary degree of relief. As a rule, if there is no cystitis or calculus in a case of enlargement of the prostate, the act of micturition is followed by a period of comfort, which lasts for a longer or shorter time. In carcinoma it is not; relief is not complete. The desire is always there, though it may be less immediately after the completion of the act, and this naturally leads to a very rapid increase in the number of times. A patient with non-malignant enlargement of the prostate has often risen once or twice every night for many years before the frequency becomes so great as to suggest the propriety of seeking advice. In malignant disease, whether it originates *de novo* or is consecutive to enlargement, the frequency often becomes as great in as many months.

Another point of some value in connexion with this is the effect produced by passing a catheter. The passage of a catheter for the first time in a case of enlargement of the prostate is always a serious matter, but unless there is some exceptional feature present, such as unusual difficulty causing haemorrhage from laceration of the mucous membrane, it is not followed by any local irritation. The patient has not to pass water more frequently. On the contrary, perhaps because the bladder has been emptied more thoroughly than usual, he can often wait a longer time. This is not the case when carcinoma is present. Nearly always it will be found that in these circumstances there is a definite increase in frequency afterwards which only subsides at the end of twenty-four hours; and if an attempt is made to treat such a case by the habitual passage of a catheter the last thing at night, it will very often be found that the symptoms are aggravated rather than relieved. Much, of course, depends upon the exact position of the growth, but in no case is it very long before the hyperaemia that surrounds a growing focus of carcinoma succeeds in reaching the urethra, and making its lining membrane more sensitive.

Pain, when it occurs in association with enlargement of the prostate, is always serious. In the ordinary form of enlargement there is no pain. When it does set in, it is due to the presence of some complication, such as cystitis or calculus. Sometimes under these conditions pain may be very severe, but whatever the degree it is always associated with the act of micturition, and almost invariably is described as shooting down the urethra to the end of the penis. When the enlargement is due to chronic inflammation, whether tuberculous or gonorrhoeal, pain is not uncommon, but this too is associated with micturition, and is only severe when there is ulceration at the neck of the bladder. In these cases, however, there is often besides this a sense of uneasiness and fullness in the perineum. The patient will volunteer the statement that he often has a certain amount of discomfort there, and that this is relieved by firm continued pressure, but it is rarely spoken of as actual pain. In cancer, so long as the growth is small and placed so that there is some thickness of normal prostatic tissue around it, there may be no pain. As, however, the growth enlarges and begins to stretch, or still more to involve the capsule, pain seldom fails to make itself felt. But this pain differs in many respects from that which is present in cases of cystitis or calculus. It is constant day and night, and is referred to something deep in the perineum, almost in the rectum, so that the patient

imagines there is something pressing forcibly against the wall of the bowel. It bears no relation to micturition, and though it may spread down the urethra even to the glans, it is not confined to that region, nor felt most severely in it. Later still, when the malignant growth has spread beyond the capsule, and has begun to involve the structures around, the pain may become agonizing, radiating down all the branches of the sciatic plexus. One patient came to consult me because of sciatica, which nothing seemed able to cure, and which was growing worse every day. It was bilateral, but worse upon the right side, and was continuous night and day. The prostatic symptoms from which he suffered he regarded as of no importance, but on examining him per rectum, the cause was only too plain. There was an extensive growth of stony hardness spreading up from the prostate, and firmly fixed to the wall of the pelvis on either side. Pain such as this is characteristic, but unfortunately when it occurs the diagnosis is usually already obvious, and the only treatment possible is palliative.

Haemorrhage is not an early symptom of carcinoma of the prostate, and it is such a common occurrence in connexion with the simple form of enlargement, that it is only under special circumstances that it can be considered a symptom at all. In the hard variety of carcinoma, which is the most common, there may never be any haemorrhage. It is usually present when the growth has ulcerated, but the quantity is rarely large. As usual when the source of the bleeding is at or near the neck of the bladder, the blood precedes, or more often follows, the stream of urine. It is not mixed with the urine, but this is equally true of many other lesions in the same locality. Haemorrhage is only characteristic when it is causeless, frequent, and profuse, like that which occurs in villous tumour of the bladder. The soft form of carcinoma, when the growth has spread into the bladder, resembles this in many ways. It is quite as vascular, and the walls of the vessels are equally delicate. The least injury, even the contraction of the bladder wall around it, is sufficient to make it bleed. When the bleeding once begins, it is almost impossible to check it, for everything that is done only injures another portion of the growth, and makes that bleed. In two out of the three cases of soft carcinoma under my care, the haemorrhage proved fatal, in one directly, in the other from loss of strength entailed by the continued drain of blood.

The physical signs in the early stages of carcinoma of the prostate are vague and ill-defined. If the growth originates deep in the substance of a gland that is enlarged already, they may be altogether wanting for a time. As in the case I mentioned before, it sometimes happens that they remain latent throughout. As a rule, however, by the time the symptoms have become sufficiently severe to induce the patient to seek advice, the physical signs are plain and well marked. The stony hardness of the prostate, when examined from the rectum, is the most striking feature of the ordinary variety of carcinoma. In the early days this may be limited to one or more areas, the intervals between which are still soft and elastic. Later, these areas fuse together, and the whole gland becomes intensely hard, inelastic, and unyielding. In chronic prostatitis, and in that form of fibroid enlargement which resembles it so closely, the gland is often harder than natural, but it very rarely attains the peculiar stony feel which characterizes the common form of carcinoma. The finger can make no impression upon it. The soft variety of cancer is entirely different. I have not met with any instance in which the growth was still limited to one portion of the gland. In none of the cases under my care was there any material increase in size on rectal examination. The surface was uniformly soft and pulpy, not elastic or fluctuating; and the margins were ill-defined, so that the upper border of the gland could not well be distinguished from the adjacent portion of the trigone. The gland was flatter than normal. It had quite lost its natural rounded contour, and instead of meeting the finger at once, as it entered the rectum, the prostate had, as it were, to be felt for. This, of course, is what might be expected from the growth of a soft carcinoma enclosed on all sides, except towards the bladder, in an unyielding fibrous capsule. The firm normal tissue of the prostate is replaced by a much softer substance, which spreads in the direction of least resistance, and leaves the capsule unsupported.

The shape of the prostate when it is the seat of malignant disease may be as characteristic as the consistence, but here again the same reservation must be made. The alteration may make its appearance early and be well marked, or there may be no alteration at all, even to the end. In the simple form of enlargement the gland, as it increases in size, pushes all the surrounding structures to one side. It swells out towards the rectum as an elastic rounded mass, very variable in shape, perhaps studded on the surface with bossy elevations, differing from the rest in consistence, but the contour remains well defined, even in the small fibroid variety. The upper border is convex from side to side, or, if concave from the extreme upward growth of the two lateral lobes, it is steeply cut and rounded off. At the sides the margins of the gland are clear and distinct. The trigone beyond is free, or if there is a growth spreading into it, it forms a defined invading mass, not a general infiltration. Malignant disease, on the other hand, infiltrates everything. Almost always the first part to become affected is the tissue surrounding the ejaculatory ducts, so that what feels to the finger like a horn of growth spreads upwards on either side towards the vesiculæ seminales, and at last spreads into them. Then the intervesicular space becomes thickened—this is much better appreciated when there is an instrument in the bladder at the same time. In a little while the change involves the tissues on either side and around the base of the prostate. The margins of the gland can no longer be defined. Hard cords can be felt running up towards the walls of the pelvis, and very soon the prostate becomes fixed and immovable. In the later stages of the disease, when it is advanced, the diagnosis is easy. In the earlier ones the difficulty may be very great; and, as it is imperative to make certain whether cancer is or is not present, it is always advisable to examine the patient under an anaesthetic in the lithotomy position, while firm pressure is being made over the pubes, so as to force the prostate down into the perineum.

The cystoscope is, unfortunately, not of much service in the early diagnosis, though it gives valuable information later. Much more can be learnt from the passage of a catheter, especially if a rectal examination is made at the same time, so as to form some conception of the condition of the intervesicular space.

It is always a matter for grave suspicion if the characteristic symptoms of prostatic enlargement have made their appearance suddenly—within a twelvemonth, for example—and if on passing a catheter in expectation of finding a large amount of residual urine, an ordinary olive-pointed instrument slips in easily and only a few drops come away. It means that all the ordinary symptoms of prostatic enlargement are present without any overgrowth of the median portion or of the lateral lobes to account for them. Perhaps this—the disproportion between the symptoms of which the patient complains and the physical signs that are found on examination—is the most significant point of all in the early diagnosis of cancer. From what the patient says about himself, a well-marked case of prostatic enlargement with residual urine is expected. What is found is a very slight degree of enlargement with nothing that will explain the frequency of micturition. If in such a case the patient complains of a constant pain in the perineum; or if there is a nodule of stony hardness in the prostate, or an extension of the growth towards one of the vesiculæ seminales; or if when a sound is introduced into the bladder and the beak is reversed, there is definite thickening of the intervesicular space, the diagnosis hardly admits of doubt.

With regard to the question of treatment there is very little to be said. Suprapubic enucleation should never be attempted for cancer. Except by accident the whole growth cannot be removed in this way. The operation is not one suited to cancer. Recurrence *in situ* is almost invariable, and from thence the growth spreads to the suprapubic wound, or involves the orifices of the ureters. The only method that holds out any hope of success is that devised by Young, in which the whole of the prostate with its capsule intact, the vesiculæ seminales, and the adjacent portion of the neck of the bladder are removed *en masse* through the perineum.

REFERENCE.

¹ Johns Hopkins Hospital Report, vol. xiv, p. 288.

An Address

ON

THE DIAGNOSIS AND TREATMENT OF SOME
COMMON INFLAMMATORY AFFECTIONS
OF THE EYE,FROM THE STANDPOINT OF THE GENERAL
PRACTITIONER.DELIVERED BEFORE THE STRATFORD DIVISION OF THE
BRITISH MEDICAL ASSOCIATION,

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IN discussing the differential diagnosis and treatment of the common inflammatory affections of the eye from the standpoint of the general practitioner, I propose to limit myself to three affections—namely, conjunctivitis, iritis, including cyclitis, and acute glaucoma.

All three are accompanied by at least two of the cardinal symptoms of inflammation—redness and pain—with the addition of one other, the peculiar property of the region affected, photophobia. This last symptom is probably somewhat inaccurately named, as the nerve affected is the fifth nerve, which is not sensitive to light. The shrinking from light displayed is due more to exposure to the air and variations of temperature than to any direct action of the light rays.

Well marked cases of these three affections should present little difficulty in diagnosis, but in the early stages, before some of the more characteristic symptoms have had time to make their appearance, a most careful examination of the affected organ may be necessary before arriving at a satisfactory conclusion, and it is to be remembered that any mistake in treatment may be followed by the most disastrous consequences.

Recognition of Ciliary Injection.

In the differential diagnosis between these three affections the presence or absence of ciliary injection plays a most important part, I therefore propose briefly to recapitulate the points that distinguish ciliary from conjunctival injection.

In conjunctival injection there is present a superficial network of larger and smaller vessels, readily movable with the conjunctiva. The colour of the injection is a vivid scarlet or brick red, and cannot, owing to the freedom of the collateral circulation, be made to fade on pressure with the finger. This form of injection is most intense on the lids, and diminishes towards the cornea.

Ciliary injection, on the other hand, occurs as a rose-red or pale-violet zone surrounding the cornea, in which it is impossible to recognize clearly the individual vessels, and which is not movable with the conjunctiva. In the more severe cases of ciliary injection a coarse network of vessels at a greater distance from the cornea is also visible; these may be distinguished from conjunctival vessels by their hazy appearance, violet colour, and immobility relative to the conjunctiva. Owing to the numerous anastomoses between both sets of vessels, severe inflammatory affections of the uveal tract are always accompanied by a certain amount of conjunctival injection, but the essential point is to recognize the existence of the ciliary injection, as this always indicates inflammation of some structure deeper than the conjunctiva.

Symptoms and Treatment of the Ordinary Forms of Conjunctivitis.

The subjective symptoms will naturally depend on the severity of the case, but it may be stated that severe pain is only met with as the result of some complication, such as ulceration of the cornea. Complaint will be made of discharge from the eyes, with itching and burning sensations, generally becoming worse towards night. Vision is interfered with by the passage of flakes of discharge in front of the cornea. The discharge tends to glue the lids together during sleep.

On examination the surgeon finds that conjunctival injection is present, confined at first to the palpebral surface, and most marked in the lower cul-de sac.