

CARCINOMATOUS CHANGES IN AN AREA OF CHRONIC ULCERATION, OR MARJOLIN'S ULCER.¹

BY JOHN CHALMERS DA COSTA, M.D.,

OF PHILADELPHIA,

Professor of Principles of Surgery and of Clinical Surgery in the Jefferson Medical College.

DURING the past year I have seen two cases of this rare condition. The first case was a woman sixty-eight years of age, who was a patient in the Surgical Ward of the Philadelphia Hospital. For many years she had suffered from what was regarded as a varicose ulcer of the leg. During the last six months the discharge had become very foul; the edges of the ulcer had become thick, everted, hard, and rose-colored; and a section of the margin of the ulcer shows that it was epitheliomatous. The patient declined amputation.

The second patient was a woman fifty years of age, and was seen in the Jefferson College Hospital. Her father died at the age of 105; her mother, at eighty-seven years. While pregnant with the last child, fifteen years ago, she developed varicose veins of both legs; from the left leg, in the region which now is the seat of the ulcer, there was a considerable hæmorrhage, and a sore. The latter healed after her delivery, and remained well until two years ago, when it again broke out. It healed up in a few weeks, remained well for a month or so, and then broke out again; since that time it has remained open. On two occasions she went to hospitals and had it burned with caustic. Eighteen months ago it was the size of a ten-cent piece; now it is seven inches in width and six inches in length. She has considerable pain in the bone of the leg, which is much worse at night. The ulcer at some spots has undermined edges, and is elevated at certain places on the margin; its border is hard and dense, and sections which have been removed for examination show it to be an epithelioma. The patient declined to submit to amputation.

¹ Read before the Philadelphia Academy of Surgery, November 3, 1902.

The two cases cited above are instances of chronic ulcers of the cutaneous surface which became carcinomatous. The characterization of this condition as Marjolin's ulcer I think to be proper, because it was first carefully studied and accurately described by Professor Marjolin, of Paris, over fifty years ago.

It is a very ancient and well-demonstrated belief that cancer may arise, and, in fact, is rather apt to arise, in an area of chronic inflammation; for instance, on the lip of a pipe-smoker, on the tongue of a lather or carpet-layer—who holds nails or tacks in his mouth—on the scrotum of chimney-sweeps and paraffin-workers, in a gall-bladder containing gall-stones, on the skin of the nose where the bridge of an eye-glass or of a pair of spectacles has rested, on the tongue where the sharp edge of a tooth has been in contact, and in numberless other locations. It has been demonstrated that a laceration of the cervix uteri or an ulcer of the tongue is likely to become cancerous, and that an ulcer of the stomach occasionally becomes so.

The question of the relationship between gastric ulcer and gastric cancer is very much disputed. Strümpell and others are positive that there is a causal relation between them; and Schmidt has pointed out that a cell-degeneration, identical or of similar character, is to be found about each of these lesions.

On the cutaneous surface of the body, it is a rare occurrence for an innocent lesion to become cancerous, although occasionally this does take place. There is, of course, a certain relation between innocent and malignant epithelial growths, in the fact that in both there is an excessive growth of epithelium. We find this excessive epithelial proliferation in warts, in *Molluscum contagiosum*, and in some syphilitic and tubercular lesions; but, although in innocent conditions there is epithelial overgrowth, there is never unlimited and unrestrained growth, and the multiplying cells grow outward, as a rule; and even if they grow inward, they do not infiltrate tissues, and do not abolish the normally clear division which exists between derm and epiderm.

We have seen an area of chronic eczema on the left hand

of a locomotive engineer become cancerous. It is this hand that habitually rests upon the throttle-valve; and the throttle-valve is often warm, or even hot. We have seen cancer arise from a wart, from the scar of a burn, from the margins of an anal fistula. Nevi and moles occasionally become cancerous; but, as a rule, the malignant growth which springs from either one of these is sarcoma rather than carcinoma. We have never seen a carcinoma arise from a corn, although it has been alleged that it sometimes does so. That it occasionally arises from an old area of lupus, a syphilitic ulcer, or an ordinary chronic ulcer of the leg is undoubted.

When a cancer arises from an ulcer, it is not to be supposed that the connective tissue of the ulcer has been converted into epithelium. The proliferating epithelium of a cancer must spring from pre-existing epithelium; hence, it sometimes comes from epithelial elements, such as sweat-glands or hair-follicles, that lie undestroyed among the granulations of the ulcer, or, what is more common, from the edges of the ulcer itself. In the vast majority of instances, a malignant growth that arises in an area of ulceration on the cutaneous surface begins at some point on the margin of the ulcer.

The fact that malignant growth can follow chronic irritation is not proof positive that the irritation is its direct cause. A great many hold that in such a case the ulcer is not directly converted into a cancer, but that the chronic irritation in the ulcerated area simply allows of the admission and favors the destructive action of some cancer germ.

It is certainly not proved, at the present time, that cancer is due to a germ, although many of the ablest students and observers are of the opinion that it is. There is no theory as to the cause that is really capable of explaining all the phenomena of cancer. Beside the fact that regions that are irritated or injured are particularly prone to develop cancer, the parasitic theory has gained support from the observation that metastases take place; and that it may be possible to inoculate the growth into the lower animals, or that an accidental inoculation may take place at another part of the body of the indi-

vidual who is suffering from the disease. But there is considerable doubt as to the real cancerous nature of many of the tumors that have been transplanted from one animal to another; and, further, a great many different parasites have been alleged to cause cancer. Many supposed parasites are, however, really cell-degenerations; and, whereas yeasts and blastomycetes may exist in a carcinoma, it is very doubtful whether they are causative.

Gaylord and others strongly maintain that protozoa are the cause, but their experiments seem to have failed to demonstrate absolutely that epithelial cells were not transferred. There is no doubt that epithelial cells can be transplanted. We carry this process out deliberately in skin-grafting; and yet we do not assume that a parasite exists because the transplanted cells grow. It is equally possible to transplant the embryonal cells of cancer; and if they take root and grow, this is no proof that parasites are present.

The existence of metastases seems, at first glance, to be strongly suggestive of a parasitic influence. These secondary tumors are, however, not due to the proliferation of lymphatic structure in that region, as would be the case in an ordinary infection; but they are the result of the transfer of epithelial cells from the primary focus, the deposition of these cells in the lymphatic tissue, and their multiplication in this tissue. As Nicholas Senn says, a parasitic origin is improbable from histology and histogenesis; and the secondary tumors are not due to the growth of pre-existing lymphatic structures.

In view of the possibility that an ulcer of the cutaneous surface may become malignant, it becomes highly important that every chronic ulcer should be subjected to a thorough study for the purpose of making a careful diagnosis. As previously stated, in any chronic ulcer malignant change is most apt to appear at the edges, and persistent and increasing induration should excite suspicion. Of course, in the ordinary indolent ulcer there is a great mass of scar tissue, which often fastens the ulcer to the bone; but this mass of tissue does not have a local beginning, as it seems to appear and advance equally at

all parts of the edges, and also at the base of the ulcer. Then, again, the edges, though thick, are often smooth and are usually free from tenderness. The most chronic form of indolent ulcer is known as the callous ulcer; and this ulcer, unlike a malignant growth, is distinctly sunk below the cutaneous level. Its entire border is hard and knobby. It is not tender, and the appearance of the ulcer varies scarcely at all from week to week or from month to month.

When a carcinomatous change takes place in a chronic ulcer, induration usually begins at a portion of the margin and spreads slowly, progressively, and inexorably; although, even after it has existed for a considerable time, we may find but one-third or one-half of the margin of the ulcer to be malignant, the balance of its edge being non-malignant. In fact, it is extremely rarely that the entire margin of a large ulcer is converted into malignant disease; it requires a long time to effect this.

An important fact to remember is that, whereas very chronic, simple ulcers are rarely tender or painful, in malignant disease there is both induration and pain. This pain, as Paget long ago pointed out, is of a hot, scalding, or darting character.

The discharge of a chronic ulcer which becomes cancerous is increased in amount and becomes ichorous, and marked bleeding may occur. A foul, and even stinking, discharge, containing visible masses of destroyed tissue, is a usual feature.

Again, as Paget has likewise shown us, we find, here and there, on the margins of such a malignant growth, spots where apparent healing has occurred; but this is not due to the healing of actual cancerous tissue, but to the fact that non-cancerous regions have healed or that portions of the malignant growth have sloughed out, leaving a non-cancerous bed which will heal.

When the growth has attained a considerable size, we shall find that its base and margins are densely indurated; that the patient suffers from shooting or burning pain in the ulcerated area; that the floor is uneven, and frequently of a warty appearance or like a cauliflower; and that there is a profuse, stinking, and bloody discharge.

At some time or other the anatomically related lymph glands are bound to enlarge; although this seems, as a rule, to be late, probably because the previous induration has blocked up the lymph channels.

The most difficult case in which to make a diagnosis is one in which there has been great pre-existing induration of a chronic ulcer, and the knobby induration of the cancerous change is not appreciated and differentiated for a considerable time. In every doubtful case of chronic ulcer, portions should be removed from the margins and be studied by a skilled pathologist.

And right here a caution should be put forth. In two cases a pathologist reported carcinoma of the tongue, but recovery followed the administration of antisyphilitic treatment. In one case of ulcer of the leg a pathologist declared the condition to be cancerous, but Dr. Hearn and I were doubtful, and specific treatment effected a cure. Such mistakes sometimes arise because of the common belief that embryonal or atypical epithelial cells justify always a diagnosis of cancer, and yet healing sometimes occurs even when such a finding has been made.

What really does justify a declaration that carcinoma is present is the unrestrained multiplication of epithelium as shown by the infiltration of the apparently sound tissue at the margin of the growth. The finding of the pathologist is of the greatest value if proper material is sent to him to study. When the surgeon removes a bit of a growth for microscopic investigation, it should be large enough to make many sections, and should include not only a portion of the obvious growth, but also a portion of the adjacent and apparently healthy tissue.

If a carefully made clinical diagnosis is not in accord with the microscopist's diagnosis of carcinoma, no such radical operation as amputation should be performed until the situation has become clear and the diagnosis positive.

When a positive diagnosis of cancer arising in an ulcer of an extremity is made, there is only one proper operative

treatment; *i. e.*, amputation well above it, and the removal of anatomically related glands, even if another incision has to be made to accomplish this. For instance, if dealing with an ulcer in the middle of the leg, we should amputate well above the knee, and should then make an incision into the groin that will permit us to remove the inguinal and femoral glands. That a condition such as this is very rare is shown by the fact that the elder Gross, in more than a half-century of surgical experience, saw only three cases of ulcer of the leg that required amputation.

Marjolin's ulcer may be greatly benefited by the X-ray; hence, before considering amputation try this agent, if glands are not obviously enlarged. The late period at which glandular enlargement is apt to occur makes this plan hopeful.

In an advanced case in which operation is refused, the X-ray may still be of service in lessening the rapidity of the growth, checking discharge and hæmorrhage, and subduing pain.