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THE MEDICAL BRIEF

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[Written for the MEDICAL BRIEF.]

Adrenal Tumor of Vagina Secondary to Malignant Hypernephroma of the Kidney.

BY ALBAN DORAN, F. R., C. S.,

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Dwelling as much as possible on matters of clinical interest, and avoiding deep pathological subtleties, I will relate a remarkable case in my own practice where a malignant tumor developed in the vagina of a middle-aged woman, subject to enlarged kidney. I removed the kidney, and it was afterwards found that the

renal growth was a hypernephroma, a malignant tumor originating in adrenal tissue in that organ, while the vaginal growth was not a coincident primary sarcoma, but a secondary adrenal tumor. A very similar case, as I will explain, was under observation in London at the same time as my own.

My patient was a very sallow-complexioned married woman, aged forty, who called in her doctor on account of an attack of shivering, sweating and fever, early last autumn. A tumor was detected in the vagina, a racemose body attached by a well-defined pedicle to the lower part of the anterior vaginal wall. There were also three sessile growths in the posterior wall, one being jugulated. A small, movable tumor occupied the right iliac fossa. The lobules of the pedunculated growth were shed from time to time, and I sent them to Mr. Shattock, of the Royal College of Surgeons, and to my colleague, Dr. Cathbert Lockyer for examination. In November, 1906, I removed the abdominal tumor. It was a typical malignant adrenal growth in the lower part of the right kidney, which had become twisted in its pedicle so that the tumor lay uppermost, touching the liver, whilst the upper pole of the kidney lay downwards, rotated on the lower part of the lumbar spine. As there was considerable shock, I postponed the removal of the original growths. The patient survived the nephrectomy three months, after declining to allow a second operation for the removal of the polypus and the sessile tumors in the vagina. Until her death, lobules continued to come away from the vagina, and symptoms of pulmonary complication were observed. At the *post-mortem* secondary deposits were found in the liver, lungs and intestine. Under the microscope it was found that the vaginal polypus and the omental and visceral deposits were histologically identical with the renal tumor, a malignant adrenal growth, which was declared by the pathologists above mentioned to be an adrenal carcinoma, and not sarcomatous.

Just before I brought forward my case at a meeting of the Obstetrical Society of London, I mentioned it to Dr. Beckett-Avery, who, to my surprise, informed me that he had recently been in-

vestigating another, most striking for its similarity with my own, excepting that one clinical feature, sloughing and general septic infection, was absent. Beckett-Avery's patient was fifty-five years of age, alarmed on account of vaginal hemorrhage. A polypoid mass was found attached to the anterior vaginal wall. It was removed, and appeared, on microscopic examination, to be a very vascular sarcoma. A large tumor, occupying the right side of the abdomen, was detected when the patient was in the hospital. The vaginal growth recurred in its former site, and was removed within two months of the first operation. The patient died a month later. The tumor in the abdomen was a hypernephroma of the right kidney; the right suprarenal capsule was normal, but numerous secondary growths, some of large size, were found in the liver and lungs, and on comparing sections of these growths with sections from the vaginal tumors, there could be no doubt that they were all of the adrenal type, secondary to the renal growth.

Dr. Beckett-Avery read brief notes of the above case when my own was brought forward at the Obstetrical Society. In the discussion Dr. Cathbert-Lockyer related how he had watched for nearly ten years a woman subject to uterine fibroid; during the last six months a renal tumor had developed. He had operated on the patient, fifty-seven years of age, a few hours before the discussion was held, removing the diseased kidney, the uterus and also a parovarian cyst. Frozen sections showed the renal tumor to be a benign hypernephroma, an adenoma derived from adrenal "rests" in the kidney. Since this discussion Dr. Lockyer informs me the uterine tumor has been examined, and was found to be a fibro-myoma, including a sarcomatous patch quite free from any adrenal elements, benign or malignant. The third tumor with which this patient was afflicted, the parovarian cyst showed no evidence of malignancy of any type.

Adrenal Tumors—Much has been written during the past twenty years, both in Europe and America, about "hypernephroma" and "adrenal" tumors. The literature of the subject is now very voluminous and hard to study. We must be

careful to avoid confusing these new growths with malignant tumors of the suprarenal capsule itself, usually associated with abnormal growths of hair, and sometimes with insanity (Knowsley Thornton). In "hypernephroma," tissue resembling that which makes up part of the suprarenal capsule takes on more or less malignant action. This tissue forms the so-called adrenal "rests" in the substance of the kidney. Hypernephroma has been found in patients of almost every age. Dr. William S. Cheesman, of Auburn, N. Y., reported in the "Annals of Surgery," for January, 1907, a case where he removed a hypernephroma weighing four and a quarter pounds from an infant twenty months of age. This disease of the kidney seems very malignant; secondary deposits in the lungs and liver developing early. The suprarenal capsules themselves do not appear to be involved.

In the cases which I have related there can be no doubt that the vaginal growths were secondary to the renal tumors, unless we accept a theory suggested to me by Mr. Bland-Sutton that the disease in my patient's case was a general "lighting up" of malignant change in "rests" already present in the vagina as well as in the kidney; he even expressed an opinion that the vaginal growth might have been congenital, and also the primary seat of that change. We will assume, however, that in the cases under consideration the vaginal tumor was secondary.

The existence of new growths of the same type higher up the genital tract, has been recognized for some time. Dr. Eastwood's important monograph on the occurrence in the pelvis of malignant tumors originating from adrenal remnants, published five years ago in the fifty-third volume of the "Transactions of the Pathological Society of London," remains the best summary of the subject. Excluding instances of adrenal tumors in the male genital tract, we may note Marchand's case of adenoma of an accessory adrenal in the forward ligament of a woman aged fifty. Eastwood himself furnishes medical literature with the original report of an adrenal tumor connected with the uterus. The patient was a sterile woman, aged forty-eight, who had married when

thirty-eight years of age, the menopause occurring at as early an age as forty. For fifteen months the patient had been troubled with sacral and hypogastric pains, associated with irregular, dark-brown, and sometimes offensive, vaginal discharge. A solid tumor, movable and dull on percussion, reached midway to the umbilicus. Hysterectomy was performed. At the operation the presenting part of the tumor was found to be cystic, and two pints of yellowish fluid had to be drained off before the solid part of the new growth could be delivered through the abdominal wound. The tumor appeared to spring from the uterus, which was amputated through the top of the cervix, where the tissues appeared perfectly healthy. Both ovaries were removed at the same time, and found to be natural. No other abnormalities were detected. When examined one year later there was no evidence of recurrence, and no other sign of disease. Such was the original report, and it seems clear that neither kidney was the seat of a new growth. Dr. Eastwood has recently informed me that the patient, shortly after the above-noted examination, began to ail again, and clear evidence of general dissemination was detected. At the time of her death she was not under Dr. Eastwood's observation, and it appears that, unfortunately, there was no *post-mortem* examination.

Two cases of alleged adrenal tumor of the ovaries are included in Dr. Eastwood's monograph. The first was recorded by Neham. A suprarenal "rest" developed in the neighborhood of a cystic ovary, and invaded the cyst wall. The second, originally described by Weiss, occurred in a girl aged seventeen. A tumor developed in a suprarenal "rest," situated between the layers of the broad ligament. It first invaded the hilum of the ovary, and ultimately came to lie upon the fundus uteri. The enlarged and partially infiltrated ovary formed an excrescence on its upper aspect. Such was Weiss' interpretation of the pathology of his case, but he himself admits that the histological characters of the tumor differed much from those of a pure adrenal "rest." Eastwood, therefore, "can not think that Weiss has successfully excluded the possibility of his case being

really an angiosarcoma commencing about the hilum of the ovary, and subsequently invading the broad ligament."

In dismissing the subject of adrenal tumors in the upper part of the female genital tract, let us bear in mind this uncertainty about angiosarcoma and adrenal tumor. The tissues of the latter type of new growth are often extremely vascular. Such was the case both in my own specimen and in Dr. Beckett-Avery's, where the vagina was the seat of the secondary growth, but I shall presently refer to Klien's case of vaginal sarcoma, which was described as an angio-endothelioma. If Weiss took a malignant angioma for an adrenal tumor, Klien may have made the reverse error. Perhaps both these writers were correct; yet, if so, it does not follow that others may have not fallen into an error of the kind above suggested. In other words, adrenal tumors of the vagina may have been misinterpreted and recorded under wrong titles.

Hitherto, however, whilst we see that adrenal tumors of the upper portion of the genital tract have been already reported, the two cases which I relate are the first in which that class of new growth has been recognized in the vagina.

Solid Vaginal Tumors—As in my case and Dr. Beckett-Avery's, the principal vaginal tumor was pedunculated. Theirs simulated a connective tissue tumor of the vagina which, whether innocent or malignant, is frequently attached to the vaginal mucous membrane by a more or less distinct stalk. Primary cancer of the vagina usually appears as a deep ulcer with a hard base, or before ulcerating it may spread superficially over the surface of the vagina, converting it into a rigid tube. Pedunculation seemed practically unknown in this class of new growth until Macnaughton Jones and Lockyer reported, at a meeting of the British Gynecological Society in March, 1907, an instance of primary carcinoma of the vagina, where the new growth was botryoidal in character, and the deeper part was pedunculated." The patient was a widow, aged sixty-five. This case was exceptional, and therefore we may dismiss carcinoma altogether.

We are bound, on the other hand, to devote some attention to fibroma of the vagina on account of its clinical resemblance to primary sarcoma of the vagina in the adult, and to the secondary adrenal tumor, the subject of this communication. This type of new growth is practically inseparable from myoma.

The best monograph on fibro-myomatous tumors of the vagina is that prepared by Dr. Richard R. Smith, of Grand Rapids, Mich., and published in the forty-fifth volume of the *American Journal of Obstetrics*. He collected one hundred and one cases. In only two was the new growth multiple, a feature of importance, for in sarcoma, as in my adrenal tumor, multiplicity is rare. In twenty-seven cases the tumor was designated as sessile, and in thirty-nine as pedunculated, and although there remain thirty-five cases where no statement is made as to this point, it remains clear that pedunculation is very common.

We must bear in mind Dr. R. H. Smith's important statement that his statistics prove how there is a marked tendency in fibro-myoma of the vagina to undergo necrosis. The same change, as has long been known, is frequent in primary sarcoma of the vagina, and in my own case it gave rise to constitutional symptoms which led to the detection of a tumor. Dr. R. H. Smith's evidence shows that sloughing is not in itself a proof of malignancy.

There remains the type of primary tumors of the vagina which the adrenal new growth in my own case most resembled. That type is specifically known as "primary sarcoma of the vagina in the adult," so as to distinguish it from a yet more malignant type which appears in infancy and childhood. By "primary sarcoma," I understand the adult type. Many authors, such as Veit and Gow, have written on primary sarcoma. Perhaps the best monograph on the subject is that prepared by Jellett and Earl, of Dublin, and published in the fifth volume of the *Journal of Obstetrics and Gynecology of the British Empire*. They tabulated thirty-nine cases where malignancy was undoubted, but the histology of many of these cases remains open to doubt. Thus, seventeen were reported as "spindle-

celled," but the authors suspect that at least six out of the seventeen were probably endotheliomata. Veit, himself the author of an earlier work on primary sarcoma, warns us therein not to be too hasty in defining the histology of malignant growths in the vagina, or in concluding that they are primary. Klien's case, of which I have already made some mention, is doubtful. Veit suspects that it was a carcinoma. Klien himself classifies it as a lymphangio-endothelioma cavernosum hæmorrhagicum. The new growth appeared as two friable, pedunculated, tuberculous, elastic tumors. It was found, under the microscope, to be reticular in structure, with its meshes filled with blood. Now, when we turn to Neusser's treatise on diseases of the suprarenal capsules in Nothnagel's encyclopedia, we find that pathologists have noted how adrenal "rests" in the kidney and elsewhere tend to become malignant. One prominent feature of this degeneration is extreme vascularity, so that the tumor appears almost telangiectatic. Klien's patient suffered from recurrence, but, though watched for a time, she seems to have passed away from his observation, after refusing to return to the hospital. There is, moreover, no mention of any examination of the abdomen during the time that she was being watched. Hence I can not help suspecting that Klien's tumors might have been of adrenal origin, and if not, I must repeat that in other reported cases the adrenal nature of the "primary sarcoma" might have been overlooked, for adrenal tissue is unfamiliar to the gynecologist.

In comparing primary sarcoma with my case of vaginal tumor three other features deserve consideration, namely: Pedunculation, pigmentation and sloughing. Pedunculation is very frequent in primary sarcoma, but it represents a later stage of the sessile tumor, both stages being observed in my adrenal tumor where the growths, as is often the case in primary sarcoma, were multiple. Multiplicity almost proves malignancy, for, as we have seen, Richard H. Smith has shown that not two per cent of fibro-myomas of the vagina are otherwise than single.

Pigmentation is a most interesting feature in primary sarcoma of the vagina, and one of the sessile growths in my own case was pigmented. Boldt, of New York, reported a case before the New York Obstetrical Society last year. The patient was a multipara aged thirty-seven; the tumor, figured in the *American Journal of Obstetrics*, October, 1906, was made up of small, round cells, the deeper being laden with dark pigment. Horn and Moreston, on the Continent of Europe, have both reported instances of pigmentation, but both trace the pigment in the cells to the blood, so that the tumor was only "pseudo-melanotic." Such appeared to be the case in the sessile adrenal growth which I have described above.

Sloughing is very frequently observed in cases of primary sarcoma; indeed, it is probably constant in the later stages. Howard Kelly dwells on this complication which, as he observes, may be the direct cause of death. My experience shows that an adrenal tumor of the vagina tends to slough. When decomposition began in the case which I have related, rigors and fever set in, and not till then was the vaginal tumor discovered. Before death all the vaginal growths had undergone very extensive sloughing.

In two authentic cases of primary sarcoma of the vagina secondary deposits developed in the lungs. During convalescence from the nephrectomy, as I have above stated, symptoms of that complication developed in my own patient. Bearing in mind the two cases, I was therefore led to suspect that the primary seat of the pulmonary deposits was the vaginal growth, but the microscope showed that both were secondary to the renal tumor.

Conclusion—These cases teach us the great importance of careful microscopic research, especially in respect to prognosis, in all cases of connective tissue tumors of the vagina. The fact that a vaginal tumor is histologically of the adrenal type is, as we see from the above cases, highly unfavorable. Its association with a primary hypernephroma of the kidney is particularly grave, as secondary deposits in the viscera, often impossible to diagnose, are usually present at the same time. In my case the torsion

and consequent inversion of the affected kidney was a feature of interest to the general surgeon. Nephrectomy for hypernephroma is fairly satisfactory as to ultimate results, provided that no secondary deposits are present. Unfortunately, that was not the case with my patient.

[Written for the MEDICAL BRIEF.]

An Investigation into the Modes of Action of the Group of Antiseptics.

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No. II.

In continuation of this subject I may point out that De la Croix, Miguel and others have followed the line of observation laid down by Koch, and, as they have experimented with the same chemicals, but with a different micro-organism (viz., the non-specific bacterium *termo* cultivated in meat infusion), a comparison of the results thus gained is interesting:

TABLE II.

	Koch.	De la Croix.	Miguel.
Sublimate Solution.....	1:300,000	1:30,208	1:14,300
Oil of Mustard.....	1: 33,000	1: 3,353
Iodine.....	1: 5,020	1: 4,000
Salicylic Acid.....	1: 1,500	1: 1,003	1: 1,000
Boric Acid.....	1: 800	1: —	1: 130
Carbolic Acid.....	1: 800	1: 669	1: 313
Alcohol.....	1: 12.5	1: 21	1: 105

Klein, in an elaborate and exhaustive inquiry into the antiseptic properties of phenylpropionic and phenylacetic acid, has, in a yet more striking manner, shown that any generalization from results of the germicide action of one chemical agent on one form of micro-organism to its action upon another is not admissible.

For instance, he finds that a non-specific micrococcus and bacterium *termo* requires one to two hundred phenylpropionic acid to destroy its vitality, whereas *bacillus anthracis* requires a solution of one to eight hundred only, both being exposed for the same length of time, and under similar conditions; and, again, the virus of tubercular matter requires to be exposed to a solution of one to two hundred

for ninety-six hours before it loses its activity, whereas that of swine plague is destroyed by being exposed to one to eight hundred for twenty minutes.

Marteris, Weeks, Yerson, and others have compiled long series of tables as to the results gained by exposing various micro-organisms to the action of different antiseptics for variable lengths of time, but our ignorance of many of the fundamental laws which govern the growth and development of these germs, and their adaptability to altered conditions, must make us very cautious in accepting observations which differ so widely from each other, though performed apparently under similar conditions.

In such experiments the chief sources of possible inaccuracy appear to be due to:

1. The fact that some forms of micro-organisms appear to be more virulent than others, though both are of the same species. As an illustration of this may be quoted the fact, that if a healthy mouse be inoculated with the blood of a sheep suffering from anthrax, death results in the course of twenty-four to thirty-six hours, but the converse proposition does not hold good; to a healthy sheep, which is inoculated with the blood of a mouse affected by anthrax, the disease is not communicated from the mouse.

2. The spores of those organisms which produce them are much less vulnerable than the bacilli; and

3. The bacillus of cultivation is not so well calculated to resist the action of the antiseptic, though equally well able to reproduce the disease. For this reason, therefore, it is most desirable that the micro-organisms thus experimented with, if of a specific character, should be passed from time to time through an animal that is capable of inoculation by the disease, in order to increase and refresh their power and virulence.

Much valuable knowledge may be gained from perusing these results, which distinctly indicate the great service germicides are able to render when direct application is possible to those sites where the septic or zymogen processes are taking place; through their deterrent effect the process may be checked or entirely arrested, either by placing the organisms

under such untoward circumstances as to render their further life impossible, or by poisoning the nourishing media, so as to kill the microbes completely.

But these are not the only factors to be taken into consideration, even in regard to the external application of antiseptics, and highly important is the following problem, viz.:

4. What is known regarding the action of germicides on the tissues of the body?

The local action of many of the antiseptics is that of an irritant, even of an escharotic, if used in a sufficiently concentrated form, and there seems but little doubt that a germicide may not only prevent the activity of the microbes present, but, by its stimulating nature, may also act upon the cells of the tissues, and thus produce a more healthy and vigorous condition, which renders them better able to disintegrate the enfeebled germs by which they are infested.

Many of the antiseptics already tabulated are so destructive in their action to living tissues (when sufficiently concentrated to show a germicide action) that they have to be abandoned for all practical purposes, and it does not, with our present knowledge, seem possible to recognize to which reagents the cells of the tissue or the micro-organisms themselves are the first to yield, although it is a most important point to appreciate.

Difficult as the subject is in relation to the external application of antiseptics, the difficulty is tenfold increased when we come to consider the value of antiseptics administered internally, whether when given by the mouth and absorbed from the alimentary canal or exhibited by subcutaneous methods.

Under these circumstances the problem of the reaction between the cells of the tissues and the antiseptic is of vital importance, and still it is one of which little practically is known. In considering the internal administration of antiseptics it will be necessary to approach the subject under three heads:

1. Do the antiseptics, when administered internally, produce an antiseptic condition of the blood, and the tissues of sufficient concentration to check or arrest the growth of micro-organisms?