

Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

Carcinoma
of the Vulva

STAFF MEETING BULLETIN
HOSPITALS OF THE . . .
UNIVERSITY OF MINNESOTA

Volume X

Friday, January 20, 1939

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Published for the General Staff Meeting each week
during the school year, October to May, inclusive.

Financed by the Citizens Aid Society.

William A. O'Brien, M.D.

I. LAST WEEK

Date: January 13, 1939

Place: Recreation Room
Powell Hall

Time: 12:15 to 1:30 P.M.

Program: Movie: "Catalysis"

Announcements

Thrombophlebitis and
Pulmonary Embolism

Charles B. Craft

Discussion

J. S. McCartney
John R. Paine

Gertrude Gunn
Record Librarian

II. MOVIE

Title: "Ski Flight"

Released by: Warner Brothers

III. ANNOUNCEMENTS

1. LEONARD A. LANG, M.D.

Announces the Opening of His
Office

Suite 431
Medical Arts Building

Practice limited to
Obstetrics and Gynecology

Office Hours: Phone: Office: GE4221
1 P.M.-4 P.M. Daily Res: BR7942
and by appointment.

2. NEXT WEEK

We will have as our
guests at staff meeting the Hospital
Administrators in attendance at the
Institute in Hospital Administration.
There will be approximately 65 or 70
persons in the group, and it is sug-
gested that those who can do so should
eat early, so as to leave room for the
visitors.

In addition to this demonstration
there will be a program of nursing
procedures, Monday, January 23 from
1:30 to 3:30 p.m., demonstration of
operating room nursing techniques
Tuesday, January 24, from 8:00 to 9:00
p.m. in the operating room, and a demon-
stration of medical and surgical hospi-
tal procedures on Friday afternoon
from 1:30 to 3:30.

IV. CARCINOMA OF THE VULVA

John McKelvey
Chas. E. McLennan

Carcinoma of the vulva has been chosen as the subject for presentation by the Department of Gynecology and Obstetrics for certain well defined reasons. The department is engaged at the present moment in clarifying and standardizing the handling of its malignant tumor problems. The clinical material of the department has been peculiarly rich in this disease as will be shown in a presentation of the material which is reported herewith. The outlook for the patient suffering from a vulvar carcinoma has materially improved in recent years, perhaps due to the improvement of the technique of treatment. There is reason to hope that it may eventually be possible here to approximate the results at present obtained with adenocarcinoma of the body of the uterus. That this is an essential improvement is shown by the fact that the older literature reports an average 10% five year cure rate, while Taussig in this country has recently reported six times that for his adequately treated material. It is only fair to say that this figure has not been approached by any other clinic and Taussig himself doubts the general validity of his results.

With your permission it has been thought wise to present this report in three parts. A general consideration of the place of carcinoma of the vulva in the tumor group and some of the problems concerned with the peculiarities of the disease will be followed by a presentation by Dr. C. E. McLennan of the findings, treatment and results in the last 40 cases handled by the department. Then consideration will be given to the method presently used by the department in treating the condition.

It is probably true that the problems of treatment of the more rarely occurring tumors have neither been given adequate attention nor progressed to even approach the ultimate possible from the methods available. Attention has been focused upon the tumors commonly seen. Carcinoma of the vulva is a relatively rare disease.

Statistics from various sources show the relative incidence of malignant tumors in the male and female to vary, of course, with age groups, but a fair average of the reports available would show a relation of approximately 40:60. Of this 60% occurring in the female, 27% occur in the genitalia and, of these, 3.2% are carcinomas of the vulva. Thus a little less than 1% of the female malignant tumors and a little more than 0.5% of the total malignant disease material is vulvar carcinoma.

Vulva tumors are not a homogeneous group. It should be stated at once that the site of origin produces tumors of different morphology, different site, and so, direction of metastasis. In this large group the most common tumor is that arising from the surface skin of the labia and surrounding tissue. This is three times as frequent as the next most common site, the glans clitoris. Tumors arising from the vestibule and periurethral region, and from Bartholin's glands, are rare.

From a morphological point of view, the skin tumors are relatively well differentiated, at least in their early stages, and approach the slow growth and metastasis of the tumors of the skin elsewhere. Carcinoma of the glans clitoris is similar to carcinoma of the glans penis, producing most often an undifferentiated tumor which is made up of small round cells which in their appearance, invasion and metastasis may resemble in varying degrees the sarcoma. Tumors of Bartholin's gland produce adenocarcinomas of a relatively undifferentiated form. Thus, the primary site of the tumor carries a certain prognostic importance.

Related to this is the prognostic and clinical importance of the site as related to the lymphatic drainage distribution. The upper two-thirds of the vulva and perineal skin drain to the superficial and deep inguinal glands. Here the differentiated tumors tend to remain localized for relatively long periods of time. The common extension from here is along the femoral canal and vessels to the glands of the external iliac vessels and so on up the aortic

chain. What must be remembered in any form of therapy is that there is a rich connection of the lymphatic vessels over the pubic region with the glands of the opposite side. Unilateral gland excision or radiation is not justified by the anatomy.

One must also remember that the lymphatic distribution from the vulva to the glands does not follow the vulva to spread laterally from a mid-point over the pubis, but fans out to take a more or less direct course to the gland in question. The further posteriorly the tumor lies, the wider the excision or other form of therapy must extend.

The posterior third of the vulva drains to the perirectal glands. This is often overlooked and is not stated in most texts. This is well demonstrated by the common extension of lymphogranuloma inguinale to the peri-rectal region with the production of local paradenitis and the fusiform rectal stricture. A vulvar carcinoma recently treated in this hospital showed involvement by metastatic tumor of a peri-rectal gland. This has, of course, an obvious clinical significance.

The tumor takes various forms. The usual history is of a small, itching nodule which ultimately breaks down, to later heal again. Gradually there is developed an ulcer, extending nodules, a papillary tumor or a diffuse, hard, infiltrating mass. These types may be mixed. The various forms carry little demonstrable significance. What is of importance is an etiological relationship which may be demonstrated in about half of the tumors. The majority of those which have such an association develop in vulvae which are the seat of leukoplakic changes or of a related condition, kraurosis vulvae. This is not to say that leukoplakia is a real precancerous lesion as it is in the tongue. There is rather a suggestion that the forces which set up these conditions are the same as those active in the production of malignant disease. Not all leukoplakia or kraurosis vulvae becomes malignant. Histological differentiation is, however, required.

Carcinoma of the vulva also arises in direct association with papillomas, from

the margins of syphilitic ulcers, from condylomata and apparently as a result of preputial concretions. All of these conditions should be held suspicious of malignant change when they have persisted for long periods and should be treated, partly, at least, with the object of removing this danger.

The greatest incidence of carcinoma of the vulva falls in the 7th decade of life and this is a factor which must be given consideration in choice of treatment. The majority of the patients suffering from this disease are poor surgical risks. This has led to the use of unsatisfactory or incomplete techniques in treatment and perhaps accounts in part for the poor results obtained. Prolonged surgical procedures with prolonged general anesthesia and the almost universal presence of pathogenic microorganisms have tended to limit the treatment given.

One other factor which bears upon the choice of treatment, but particularly upon prognosis, should be mentioned. Patients suffering from vulvar carcinoma tend to bring their complaint to the physician at a relatively late stage. The reason for this is not clear. They routinely state that they expected the lesion to cure itself. This is unusual in chronic ulcerative superficial lesion and particularly in those types which produce symptoms. The problem of improving the cure rate is largely the problem of the control of the stage of the disease which is presented for therapy. Early lesions give an excellent prognosis.

Analysis of Cases of Carcinoma of the Vulva Treated at University of Minnesota Hospitals During 11 Years, 1928-1938.

The following analysis includes all cases of primary carcinoma of the vulva treated during the past 11 years, 1928-1938, inclusive, with the addition of one case first seen in 1927 which was added in order to round out an even-numbered total of 40 cases. Inasmuch as the hospital's cross-index of diagnoses is incomplete for the years 1925-1927,

it is not possible to trace the old cases back beyond 1928. The one case from 1927 turned up accidentally, having been indexed a second time during a readmission in 1931.

It is interesting to note that in 1938 more than twice as many cases as in any other single year presented themselves for treatment. This marked increase in incidence may be due partly to the fact that accurate departmental records of all cancer cases, both hospital patients and out-patients, have recently been developed by the gynecology service. This corrects what appears to be a major defect in the present hospital record system which makes no provision for indexing diagnoses on out-patients. Obviously, a certain number of cancer patients who present themselves are never admitted because of the hopelessness of their conditions or possibly on account of other factors -- yet these patients are chargeable to our clinic and must be reckoned with in any compilation of cure rates.

The distribution of the cases by years was as follows:

1938	9 (includes 2 out-patients)	1932	4
1937	2	1931	3
1936	4	1930	2
1935	2	1929	3
1934	2	1928	4
1933	4	1927	1

The following table shows the age distribution of these patients by decades:

30-39	2	5.0%
40-49	6	15.0
50-59	13	32.5
60-69	12	30.0
70-79	4	10.0
80-89	3	7.5

The previously recognized tardiness of these women in seeking treatment is demonstrated in 33 of the 40 cases in which there is fairly accurate information on this point. An average of 8.9 months elapsed between recognition of the lesion by the patient and the institution of therapy. The individual time intervals

range from 3 to 24 months. Considering only the 14 patients who had some form of treatment prior to coming to this clinic, we find that an average of 31 months elapsed between the first treatment and subsequent admission here. For certain of these, of course, this might well represent total duration of the tumor when one considers the hopeless inadequacy of the initial therapy. The time interval range for this latter group was 3 months to 7 years.

The records are deficient in regard to evidence of so-called precancerous lesions (leukoplakic vulvitis). Only 15 contain actual observations (gross or microscopic) or strongly suggestive histories of previous pathologic changes in the vulvar skin. Two cases were negative to both observation and questioning, while in 23 the evidence recorded was insufficient for drawing conclusions.

There is recorded evidence that 33 (82.5%) of the 40 cases had microscopic confirmation of the diagnosis. It is possible, of course, that a few pathologic reports never reached the records because of errors in unit numbers and spelling of names, and 4 of the omissions may conceivably be excused on the ground that the patients were considered too far advanced for treatment. It is obvious that biopsy confirmation is essential in carcinoma of the vulva because of the not infrequent difficulties in differential diagnosis.

Preliminary treatment elsewhere:

14 of the 40 cases had some form of treatment prior to coming to this hospital. 11 different combinations of therapy were used, with the distribution amongst the cases as follows:

Vulvectomy, bilateral gland excision and deep x-ray to groins	1
Vulvectomy and bilateral gland excision	2
Vulvectomy and x-ray to inguinal glands	2
Vulvectomy alone	1

Local excision of lesion and unilateral gland excision . . .	1
Local excision, radium and x-ray to vulva	1
Local excision and radium to vulva .	1
Electrocauterization and radium to vulva	1
Radium alone	1
Local excision alone	2
Electrocauterization of local tumor.	<u>1</u>

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Treatment of new (untreated) cases:

14 different combinations of therapy were applied to the 26 cases which received their initial treatment at this hospital. Grouping them as nearly as possible in decreasing order of completeness, they appear as follows:

Radical vulvectomy, bilateral gland excision, interstitial radon to vulva	1
Vulvectomy, bilateral gland excision, x-ray to vulva and groins	1
Vulvectomy, gland excision, x-ray to groins	2
Vulvectomy, unilateral gland excision, x-ray to groins	1
Vulvectomy, x-ray to vulva and groins, radon to groins . . .	1
Vulvectomy, x-ray to vulva and groins	3
Vulvectomy, x-ray to groins	2
Vulvectomy alone (x-ray planned, pt. expired - embolus . .	1
Radium and x-ray to vulva, x-ray to groins	4
Radium to vulva, x-ray to groins. .	2

Local excision, x-ray to vulva and groins	2
X-ray to vulva and groins	2
X-ray to vulva, unilateral gland excision	1
Local excision (x-ray planned, pt. expired - embolus)	1
No treatment (far advanced lesions)	2

26

Treatment of cases with therapy elsewhere:

Radical vulvectomy, bilateral gland excision, interstitial radon to vulva	1
Vulvectomy, radon to vulva, x-ray to groins	1
Local excision, bilateral gland excision, x-ray to groins	1
Local excision, radon to vulva, x-ray to vulva and groins	1
X-ray to vulva and groins, radon to vulva and groins	1
Local excision, x-ray to vulva and groins	1
X-ray to vulva and groins	3
Radon to vulva	1
No treatment	4

14

Treatment of Recurrent Lesions:

A. After primary treatment here:

Local excision, radon to vulva, x-ray to vulva and groins	1
Local excision, x-ray to vulva and groins	1
Radon to vulva, x-ray to vulva and groins	3
Radon to vulva	<u>2</u>
	7

B. After secondary treatment here:

Local excision, radon to vulva, x-ray to vulva and groins	1
Radon to vulva and electrocauterization	1
Local excision of lesion	<u>1</u>
	3

Clinical Classification of lesions according to Taussig's five stages:

Stage I (tumor 1-3 cm. average diameter, no palpable metastases)	8
Stage II (tumor 4-7 cm. diameter, no metastases)	7
Stage III (ulcer over 7 cm. diameter, or deeper infiltration, or palpable gland metastases)	11
Stage IV (large ulcer with vaginal involvement or large cancerous lymph glands	10
Stage V (far advanced, with broken down glands and cachexia)	<u>4</u>
	40

Classification according to the site of origin was somewhat difficult because of the meagre information on many of the older records. Judging from the available information, however, it would appear that 36 of the 40 cases were primarily epidermal, 3 possibly originated in the clitoris, 1 in a Bartholin gland, and none was vestibular.

Summary of results:

Total number examined with view to treatment	40
Not treated (considered unsuitable)	6
Treated	34
Alive without recurrence	11
Alive with recurrence	1
Lost sight of	2
Died of intercurrent disease	3
Died of cancer	23

Absolute five-year cure rate (on basis of 13 cases receiving initial treatment here; 2 living without recurrence) 15.38%

Relative five-year cure rate (excluding patients not treated - 2 out of 13) 18.18%

Living without recurrence less than five years:

4.5 years	1 case
3 "	1
2.5 "	1
2 "	1
Less than 1 year	5

Treatment

The striking feature of the study of the department's material is the unusual variety of the methods of treatment employed. The question arises at once as to whether or not such individualization of therapy should be continued. By and large, an investigative approach to such a problem as this requires a

considerable degree of standardization to produce a homogeneous material for critical study. Is such standardization possible and is it in the best interests of the patient? I believe that both can be answered in the affirmative.

Let us consider for a moment the problems which must be given consideration in determining the type of procedure to be applied. The bilateral inguinal metastasis already pointed out will require that whatever form of therapy be chosen, both inguinal regions be treated. The possible spread of the tumor into the inguinal and femoral canals must also be considered and the lymphatic drainage removed as high as can be justified by the primary mortality involved and the possibilities of cure which may be offered. The peri-rectal metastasis must be recognized and treated where possible, although anything approaching a satisfactory therapy here has not been demonstrated. Fortunately this form of metastasis is rare, since the tumor usually occurs in the anterior portion of the vulva.

It is true that the majority of patients who appear for therapy are old. The disease reaches the height of its incidence in the 7th decade of life, ten years older than our average patient. They also present variously advanced degrees of the effects of chronic infection and tumor intoxication. This should not be accepted as an indication for lesser procedures than the ideal, but rather one should search for ways and means of avoiding complications arising from these difficulties. Cleansing procedures, food, rest and blood transfusions are of the greatest value in this regard. The replacement of general by local anesthesia has allowed the operative procedures to be lengthened safely and the side effects of the various inhalation anesthetics to be avoided.

No satisfactory method has been evolved for the adequate control of bacterial infection in the tumor mass. The majority of the advanced tumors harbor pathogenic streptococci. Chemotherapy may be of value here. The greatest single source of primary mortality lies in the

spread of infection. This, however, is not great since the tissues laid open in any operative undertaking less than the wide radical operation are relatively efficient in localizing the infection.

The characteristics of the area in which carcinoma of the vulva occurs limit the possibilities of the application of adequate depth doses of radiation energy. For practical purposes it is impossible to cross-fire the inguinal region. Tumor metastasis may lie 5-6 cm. from the surface. The moist skin of the vulva will take only two-thirds of the radiation tolerated by the skin on most other body surfaces. The surfaces are grossly irregular so that radiation is technically difficult to accurately apply. The field for therapy is so large that interstitial radiation in adequate amounts is excluded. Attempts at treatment with radiation have consistently produced unsatisfactory results. One is left, then, with the surgical approach, with perhaps radiation as supporting treatment.

There are certain advantages in the site and natural history of the tumor which should be used to the full. The usual lymphatic drainage area is readily accessible for a relatively long distance and the majority of the tumors metastasize late and remain at the first lymphatic gland area for some time, before extending beyond this. Large amounts of tissue may be removed from this region without the production of serious deformities. Perhaps the greatest advantage of this tumor is that only very late in the course of the disease does it break through by direct extension to involve the fascial planes beneath it and almost never does it involve the periosteum of the underlying bony structures. It is true that extension to the vagina and urethra are common, but these again allow of wide surgical removal without serious disturbances. Finally, the area is amenable to the use of local anesthesia.

Many types of treatment have been used here and elsewhere. Local excision has nothing whatever to support it.

Limited radical operations are also not justified. Radiation therapy alone is not desirable for the reasons stated, and the results obtained from its use have borne this out. Unsatisfactory forms of radiation therapy added to incomplete operations need no consideration. In this case, again, two halves do not make a whole.

We are brought then to a consideration of the use of forms of radical vulvectomy with gland excision and with or without the application of radiation for specific purposes. Extensive vulvectomy is associated with all of these. Some dispute has arisen as to the extent to which gland excision should be carried, and a definite answer to this is not yet available. Stoeckel of Berlin has been the leader in the use of very extensive intra-peritoneal gland excision. This carries in his hands a primary operative mortality, varying between 10 and 15 per cent. Obviously the opening of the peritoneum is dangerous in the presence of large, grossly infected tumors and the excessive mortality rate has been attributable almost entirely to infection. There is no evidence that this technique is acceptable.

A somewhat less radical operation, based upon that known as the Bassett operation, has found considerable support. This involves opening the inguinal and femoral canals, section of Poupart's ligament and stripping of the lymphatic supply to the lower part of the external iliac vessels. The peritoneum is not opened. Taussig, in this country, in particular has advocated this approach. It complicates the operation, adds somewhat to the dangers and has not been demonstrated to improve the end results. The impression seems to be borne out that once tumor has spread beyond the femoral and inguinal gland groups, recovery is not possible with any of the methods presently available. Taussig, himself, has, I understand, given it up.

The method which seems to most adequately satisfy the theoretical requirements and which is at present in routine use in the department may be briefly described. It is carried out in all cases, irrespective of the extent of the tumor

or the site of demonstrable metastasis. The whole of the lymphatic bearing fat of the inguinal and femoral regions, on both sides, is removed from the superficial fascial lamella, down to the fascia of the external oblique muscle and the fascia lata. This involves removal of the upper five or six centimeters of the saphenous veins. The femoral canals are cleaned of their lymphatic tissue up to the peritoneum and the inguinal canals are similarly treated. The lymphatic bearing fat is left attached at its medial aspects, and a wide radical vulvectomy down to the periosteum of pubis and ischium and to the obturator fascia, lateral to this, and up as far as necessary in the vagina, allows removal of the whole mass in one piece. Interstitial radiation by means of radon seeds is then applied to the margins of the vagina and perineal skin where that has been contiguous to the tumor. It is planned to supply tumor destructive quantities of radiation only to an area one centimeter wide at the areas described. Closure is then carried out where that is readily accomplished and the remainder left open to granulate. Much of the skin closure in the inguinal and pubic region are routinely grafted at a subsequent time.

The use of local anesthesia in patients adequately prepared has undoubtedly extended the surgical possibilities. Patients who would otherwise be severe surgical risks tolerate this procedure well.

It has allowed us to avoid entirely the theoretically undesirable two-stage operations and has allowed extension of the operation to the desirable limit in all cases.

A short bibliography is attached. No attempt has been made to complete this, but important publications are included.

BIBLIOGRAPHY

1. Broders, A. C.
Epithelioma of the genito-urinary organs.
Ann. Surg., 75: 574-604 (1922).

V. GOSSIP

Extension leaders in agriculture resent the statement that the Center for Continuation Study is Minnesota's first attempt to meet the needs of mature men and women who have finished school. For many years they have carried on programs thruout the state and at the Agricultural Campus. The University is entertaining one of these groups this week, called the Farmers' and Homemakers' Short Course. An extensive and varied program covering every phase of education in agriculture is offered. A registration of over 2700 farmers and their wives is in attendance. They live in the farm school dormitories and take their meals on the Campus. In addition to the formal program, there is an elaborate schedule of entertainment features. The Center for Continuation Study is also a beehive of activity this week with 63 ophthalmologists in residence, taking a post-graduate course in ophthalmology, under the direction of Frank E. Burch. Eleven states and provinces are represented (Wisconsin, Minnesota, North Dakota, South Dakota, Montana, Washington, Kansas, Nebraska, Iowa, Manitoba, and Saskatchewan). Planned primarily for ophthalmologists, nearly half the registration is made up of Academy members or those who have been certified by the American Boards. The entire ophthalmology staff from the Mayo Foundation and the Medical School is being assisted by William Thornwall Davis, Washington, D.C.; Albert D. Ruedemann, Cleveland; Sanford Gifford, Harry S. Gradle, and Georgiana Dvorak Theobald, Chicago. The program which is patterned after the American Academy Meeting consists of illustrated lectures, demonstrations, and round table conferences. A mimeographed copy of each lecture is supplied, and, in addition, round table conferences are recorded on cylinders from microphones placed about the room. Copies of all questions and answers will be available to the registrants. This is the first time this type of recording device has been used in a Medical Post-graduate Course. The students are very enthusiastic about the Center and the program. Also in attendance are 18 graduate students from the Department of Ophthalmology. Next week the Institute in Hospital Administration will start

on January 23rd and close on Saturday, under the chairmanship of Ray Amberg, Superintendent of University of Minnesota Hospitals. The program will consist of lectures, field trips, (Miller, Ancker, Midway, and Bethesda Hospitals, St. Paul; Abbott, Etel, Swedish, and St. Mary's Hospitals, Minneapolis; University of Minnesota Hospitals, State Department of Health Laboratories, and Minneapolis Board of Education Special School for training Janitors and Engineers), round tables before dinner, and special moving pictures in the evening. Faculty visitors will be C. Rufus Rorem and Dr. Arthur C. Bachmeyer, Chicago; E. A. Van Steenwyk, Philadelphia; Ada Belle McCleery, Evanston; Dr. Melville H. Manson of the Commonwealth Fund, New York (Friday); Dr. Malcolm T. MacEachern, who will be here Saturday, January 28, will remain for the Institute for Record Librarians, which starts on January 30 for a three day program. The University faculty will include Director J. M. Nolte, Psychologist Howard P. Longstaff, Chief Anesthetist, Ralph T. Knight, Food Consultant Gustav A. Krueger, Cost Accountant Robert H. Tuttle, Nursing Educator Lucille Petry, Physiologist Ancel Keys, Gardener Robert A. Phillips, Professor of Law Wilbur H. Cherry, and Tuberculosis Sanatorium Administrator E. S. Mariette. Dr. A. F. Branton from Willmar will also take part, as well as Drs. McKelvey, Rigler, Stoesser, and Koucky. There will be a corps of University Hospital nurses and physicians who will give demonstrations. One of the unique features will be the demonstration of training janitors and engineers. Believe it or not, the Rockefeller Foundation reports that Minnesota's special training school is the only one of its kind in the United States. Scientific job analysis has determined the proper length of a broom handle, time necessary to lock and unlock doors, proper mixture of soap and water to clean floors, and how to eliminate fly ash in firing boilers.

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