

Carcinoma of the breast occurring during pregnancy*

by

Ettore De Girolami** and Federico Faerron

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The rapid development of cancer of the breast during pregnancy has been studied by several authors. The number of cases studied by each was small; the incidence of cancer of the breast in relation to that in non-pregnant women was consistently low. Also the prognosis was in each instance reserved in spite of certain optimism in a few authors. We may consider some bibliographical data on the incidence and evolution of carcinoma of the breast occurring during pregnancy.

AHUMADA and NOGUES (2) have one single case in 350 operations, a 24 year old woman five months pregnant, with anaplastic carcinoma grade III which evolved rapidly; death occurred seven months later (incidence 0.28%).

ZUKERMANN (10) states that out of 2806 cases of mammary cancer operated on through 25 years of practice, only 4 were associated with pregnancy; the proportion here is 1:701 (0.14%) to the incidence of breast cancer in non pregnant women.

MACLELLAN (6) observed 12 deaths in 14 cases of cancer of the breast occurring during pregnancy.

ADAIR (1) divided the patients with carcinoma of the breast occurring during pregnancy into three classes, namely:

- 1) Patients who had previously been operated on for cancer of the breast and who subsequently became pregnant.

* From Tumors Clinic of the Hospital "San Juan de Dios" San José, Costa Rica.

** Department of Histology of the University of Costa Rica.

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- 2) Patients whose breast cancer was discovered during the lactation period.
- 3) Patients whose breast cancer was discovered during the nine months of pregnancy.

Out of 59 patients with operable breast cancer who developed the disease during the nine months of pregnancy, or who having previously been operated on for breast cancer, subsequently became pregnant, 34 (57.6%) survived a five year period following mastectomy. Of 23 in this group who were *aborted*, 16 or 69.6 per cent survived five years; while of 26 who were *not* aborted, 11, or 44 per cent, survived the five years.

CHEEK's (5) survey of current opinions concerning carcinoma of the breast occurring during pregnancy is very interesting. A total of 151 cases occurring during pregnancy had been seen by a group of 43 competent physicians. After five years, only 8 cases (5.3 per cent) had survived. According to CHEEK, this suggests that mammary cancer in pregnant women is an uncommon disease and that prognosis in this class of patients is rather poor.

Having some interest in this problem, we have considered the 74 cases of mammary cancer which have been observed to date in the Tumor Clinic of the Hospital San Juan de Dios, San José, Costa Rica, which was opened for public service just three years ago. Within that group of 74 cases we found two patients who developed breast cancer during pregnancy. We had knowledge of a third, but were unable to follow it as it was a private case. Thus we can report first of all a statistical incidence of 3 cases of mammary cancer during pregnancy out of 74 cases of breast cancer, incidence 4.05 per cent during three years of practice.

CASE REPORTS

CASE 1 — C. A. — A 32-year-old woman, of Desamparados, married; was admitted to the hospital on May 13, 1952.

Family history:

parents healthy, no history of cancer in family.

Developmental history:

normal birth, psycho-somatic development normal. Teeth normal.

Gynecological history:

menarche at age 14, menstrual cycle normal. Deliveries 9, normal.

Past medical history:

suffered from measles, whooping cough, amoebic dysentery, ascariasis.

Social history:

does not smoke or drink liquor.

Present illness:

patient states that about five months ago tumor appeared in the right breast, very hard and painful at times. At the time patient consulted tumor clinic, she was six months pregnant.

suffered from measles, whooping cough, amoebic dysentery, ascariasis.

Physical examination of patient:

general condition	—	good
temperature	—	no fever, pulse 90 per minute, respirations 22 per minute, blood pressure 120/60
head and neck	—	nothing of importance
respiratory	—	nothing abnormal
cardiovascular system	—	cardiac sounds well defined and of normal rhythm
digestive system	—	distended abdomen and uterine development compatible with six months pregnancy
genito-urinary system	—	no menstruation for 6 months.

Laboratory examination:

May 14, 1952 stool examination: *Ascaris lumbricoides*.

May 14, 1952 coagulation time 5 min. 30 sec; bleeding time 1 min. 30 sec. Rh positive.

May 15, 1952 hemoglobin 90%; red cells 3,660,000; white cells 6,840; formula N. 57% E. 5% Stab. 5% L. 30% M. 3%.

May 26, 1952 total urea 15 mg./100.

June 5, 1952 blood group O (international IV).

June 24, 1952 hemoglobin 8.5 gm. erythrocytes 2,520,000.

Description of the lesion:

May 7, 1952. Situated in the upper internal quadrant of right breast, there was a tumor mass measuring 6 by 4 centimeters of semi-hard consistency, not adherent to the skin, but partially adherent to the underlying tissue. The nipple was retracted but no secretion of any kind could be obtained on pressure. Orange-peel surface phenomenon noticeable. The examination of axilla showed a small lymph node in its apex which was hard in consistency and which probably represented neoplastic invasion. Left breast and axilla completely normal.

Tentative diagnosis:

possible carcinoma of the right breast, with axillary metastasis, operable and complicating pregnancy. In view of clinical diagnosis an aspiration biopsy was made, which has been reported upon by the Department of Pathology (Biopsy N° 28. 345) on May 14, 1952, as follows: "Frotis as well as section are suspected of malignancy, but there is not enough cytological material for a diagnosis. Suggest repetition".

On May 23, 1952 a radiographic examination of lung and thorax was reported as without evidence of metastatic lesion in either lungs or ribs.

Disposition:

upon study of the case it was decided to proceed with a radical mastectomy, followed by interruption of pregnancy.

Treatment completed:

June 4, 1952. Patient submitted to a radical mastectomy. The pathological report of the specimen (Biopsy N° 28. 681) on June 11, 1952 was as follows: "Large, diffused carcinoma of 10 by 10 centimeters in diameter, infiltrating the adipose tissue. Only one small hyperplastic nodule was found in the axillar region. Microscopically carcinoma very anaplastic and active. Histologically grade IV" (Fig. 1).

ed by interruption of pregnancy.

Post-operative recovery was perfectly normal and on June 21, 1952 patient was sent to the maternity service. On July 15, 1952 patient was subjected to a Caesarean section with good post-operative result and a perfectly healthy baby. A bilateral oophorectomy was performed as a prophylactic measure. Patient left hospital on July 23, 1952 in good general health.

Follow-up of case:

this patient was under the subsequent care of the tumor out-patient department of the hospital.

Follow-up notes:

August 28, 1952. No evidence of disease.

Sept. 20, 1952. No evidence of disease.

October 18, 1952. Mass over the right clavicle covered by reddened infiltrated skin undoubtedly representing recurrence of carcinoma. The patient also complains of sharp pains in the lumbar region suggesting metastasis. Patient reentered hospital on October 28, 1952 in rather precarious general health. An X-ray of thorax and lungs was ordered on October 29 which showed no signs of metastasis to the lung parenchyma. X-ray therapy of the metastatic area over the right clavicle was started on October 30. Ten applications of 200 rads were administered over a field of 8 x 10 cm. of 250 K V. 1.5 Cu, 50 cm. T. S. D.

Patient was seen again on November 10, 1952, and she showed a recurrent area adjacent to the one previously noted over the sternoclavicular articulation. The new mass extended toward the left breast. Ten X-ray applications were ordered in that area, with the same above mentioned factors.

November 20, 1952: X-ray plate of the pelvis was ordered which showed: "Multiple metastatic lesions of the entire pelvis" (Fig. 2).

General health declined rapidly and the patient left the hospital for her home with only palliative treatment. Patient died in February 1953, 10 months after she was first seen in the clinic.

CASE 2—I. A. J.—A 30-year-old woman, of Puriscal, married; was admitted to the hospital on June 3, 1953.

Family history:

parents healthy. History of T B. in family but none of cancer.

Developmental history:

normal birth, psycho-somatic development normal. Teeth normal.

Gynecological history:

menarche at age 14, menstrual cycle normal. Deliveries 2, normal.

Past medical history:

suffered from measles, mumps, acute articular rheumatism. In August 1945 patient was hospitalized in San Juan de Dios in the department of ophthalmology for iridocyclitis. At this time the analysis of the stool was positive for: *Ancylostoma duodenale*, *Trichuris trichiura*, *Strongyloides stercoralis*. Wasserman and Kahn test negative.

Social history:

does not smoke or drink liquor.

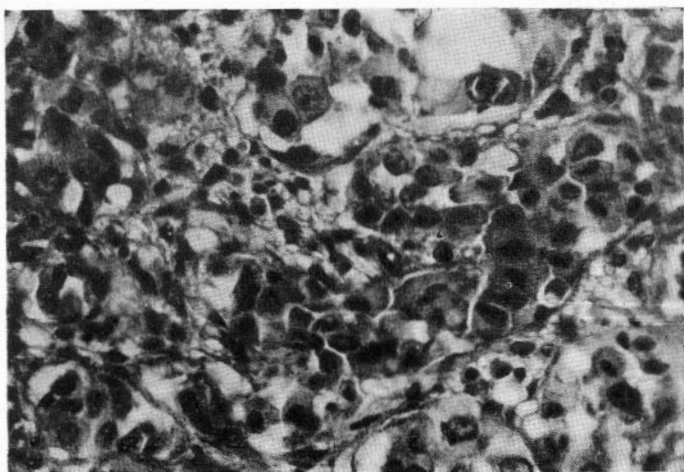


Fig. 1: Histological picture of the carcinoma of Case I \times 450

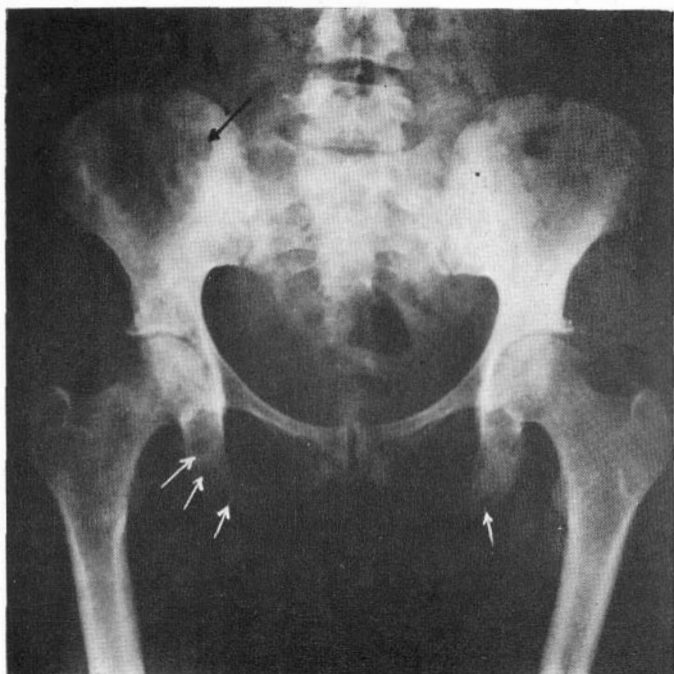


Fig. 2: Radiography of pelvis, Case I. The arrows indicate metastatic lesions.

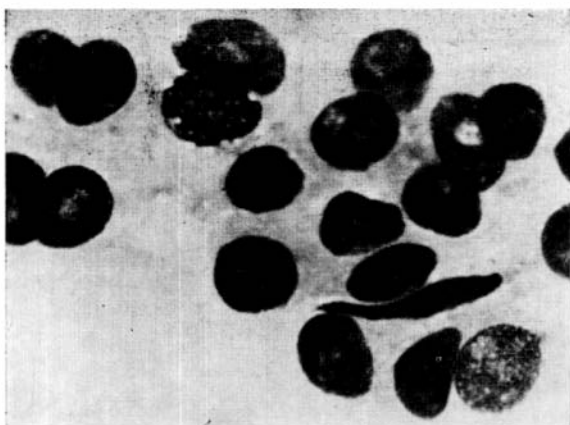


Fig. 3: Aspiration biopsy. Case II. Note polymorphism variation in size and increase in granularity of the nuclei; and increase in size and number of nucleoli. All cells lack cytoplasm. $\times 900$.



Fig. 4: Case II, the day before delivery (*left*).

Fig. 5: Detail of Fig. 4. Note slight, physiologic, hypertrophy of the right breast in contrast with pathologic enlargement of left breast (*right*).

Present illness:

three months ago the patient had noticed a very rapid increase in size of the left breast, it had become hard and had assumed a dark reddish color, becoming finally somewhat painful. In the left axilla the patient had noticed a small tumor. At the time of consultation to the tumor clinic she was pregnant, delivery due in about 15 days.

Physical examination of the patient:

general condition	— good
temperature	— during the period of hospitalization, irregular pyretic curve, pulse 80 per minute, respiration 20 per minute, blood pressure 120/90
head and neck	— nothing of importance
respiratory	— nothing of importance
cardiovascular system	— cardiac sounds well defined and of normal rhythm
digestive system	— distended abdomen of nine months of pregnancy
liver and spleen	— not palpable
genito-urinary system	— no menstruation for nine months.

Laboratory analysis:

- June 5, 1953 Vdrl negative; urine: a few white cells, many epithelial cells
 June 8, 1953 stool analysis: *Trichuris trichiura*, *Enteromonas*.
 June 22, 1953 blood group A (International II)
 June 23, 1953 coagulation time 5 minutes
 June 24, 1953 urine: no albumen, sugar, nor cylinders; few white cells
 June 24, 1953 blood examination: hemoglobin 12 gm. per cent, red cells 3,510,000
 white cells 7,040 formula N. 71% Stab. 2% E. 10% L. 16%
 M. 1%
 July 3, 1953 Vdrl and Kahn negative.

Description of lesion:

June 6, 1953. In the left breast occupying the entire upper and lower external quadrants, there was a hard tumor, increasing the size of the breast to about twice its normal size. The skin covering this mass was thickened and of orange peel appearance. There was no retraction of the nipple but because of the tumor it had become erased. The entire skin which covered the breast showed distended veins. The left axilla showed a hard fixed node probably of metastatic origin. The right breast and the right axilla were negative.

Tentative diagnosis:

carcinoma of left breast, advanced, with axillary metastasis and complicating a nine month pregnancy. An aspiration biopsy was made of the tumor mass which was reported upon by the Department of pathology (Biopsy N° 33.067) as "carcinoma" (Fig. 3).

Disposition:

delivery to be induced as soon as possible in order to decide how to proceed in this case afterwards. (Figs. 4 and 5).

Development of case:

On June 12, 1953 delivery was induced by means of 1 liter of glucose serum and two ampules of Pitocin. Normal delivery of a healthy girl.

On June 16, patient left the Obstetrical Service and was referred to the Surgical Service.

It was decided to give the woman the benefit of a radical mastectomy. An X-ray picture of the lungs was ordered, which was reported upon on June 16, 1953 as follows: "Accentuation of cardiac pulmonary arc, image of lung stasis". On July 6, 1953 the patient was brought to the operating room for the indicated intervention.

At the time of the operation the surgeons noticed that the scene of the lesion was enormously accentuated, describing it as an immense cancer of the left breast of the inflammatory type with axillar metastasis and great infectious dilatation of vessels of the chest wall and evidence of mediastinal pressure. In view of this, it was decided not to carry out a radical mastectomy and only a bilateral oophorectomy was performed.

The patient was brought to the Tumor Clinic on July 21, 1953 where X-ray therapy of the lesion was ordered. She received palliative therapy on various fields up until the month of September. In September the patient had temperature up to 39°C and complained of pain in the right leg especially upon palpation. The doctor of the service made a possible diagnosis of thrombophlebitis. The process stopped rapidly with antibiotic and local treatment. Patient left hospital in September 6 in better condition and was ordered to return to the Tumor Clinic within 15 days. This order was not followed by the patient and on October 20, 1953 we were notified of her death, her husband reporting that in her last days she had complained of severe bone pains. The survival of this case was of four months after the patient was first seen at the Tumor Clinic.

DISCUSSION

OBSERVATIONS ON THE CASES

Both patients were married, young—from 30 to 32 years of age—without family history of cancer. In both the menarche occurred at 14 years of age, menstrual cycle was normal, both were multiparae. No remote pathological history was found having relation to the present illness. The general condition of the patients was good and physical examination brought out no remarkable features. Patient C. A. (Case N° 1) noted an increase in the size of the right breast from the first month of pregnancy. Patient I. A. J. (Case N° 2) reported not noticing the growth of the left breast until the sixth month of pregnancy. Both patients came under observation at the Tumor Clinic three to five months after noting the first manifestations. These facts support AHUMADA and NOGUES's (2) remarks as to early diagnosis of carcinoma of the mammary gland in pregnant women, which becomes very difficult because it is masked from the beginning by the normal turgidity of the gland, and which is recognized only later when axillary metastasis appear.

Probably these patients relate the increase in size of their breasts with their pregnancy and such increase does not alarm them on time. CHEEK after noting the first manifestations. These facts support AHUMADA and

(5) also agreed that the increase in fullness and size of the breast during pregnancy makes the detection of the mass, either by the patient or by the physician, much more difficult, so that in general the tumor at the time of its discovery is already in an advanced state.

Both cases have evident clinical signs of mammary carcinoma with homolateral axillary metastasis. In the first case, the tumor occupied the upper internal quadrant of the right breast; in the second, the tumor occupied the whole upper and lower external quadrants of the left breast. In our department, aspiration biopsy of mammary tumors is customary on the day before operation, as a means of diagnostic certainty. However, patient C. A. was operated on for radical mastectomy 15 days after having obtained the cyto-pathological results of the aspiration biopsy of the lesion, and 40 days later she underwent a Caesarean operation when pregnancy was $8\frac{1}{2}$ months old, thus respecting foetal viability. Prophylactic bilateral oophorectomy was carried out concurrently. Patient I. A. J., on the other hand, in spite of the recommendation from the Tumor Clinic, underwent only aspiration biopsy with the purpose of diagnostic certainty. In the operating room surgical intervention was thought inconvenient, and only a prophylactic bilateral oophorectomy was performed.

We do not think that, in Case N° 1, the time lapse between the cyto-pathological diagnosis and radical mastectomy had any relation to the prognosis of the disease. In the second case, it is interesting to note that, in the period between June 16 and July 6, the clinical aspect of the lesion showed a remarkable change, to the point of changing definitively the surgeons' opinion as to operating.

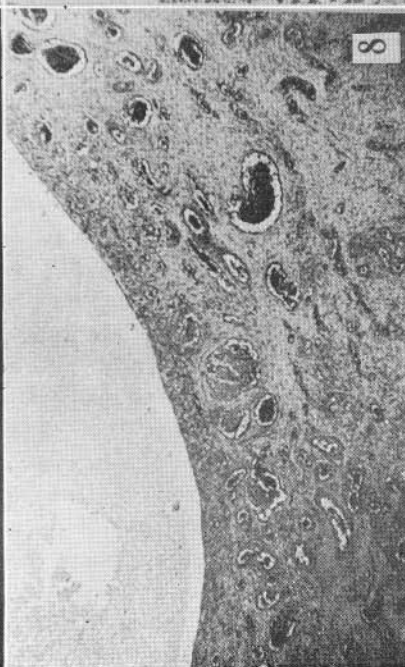
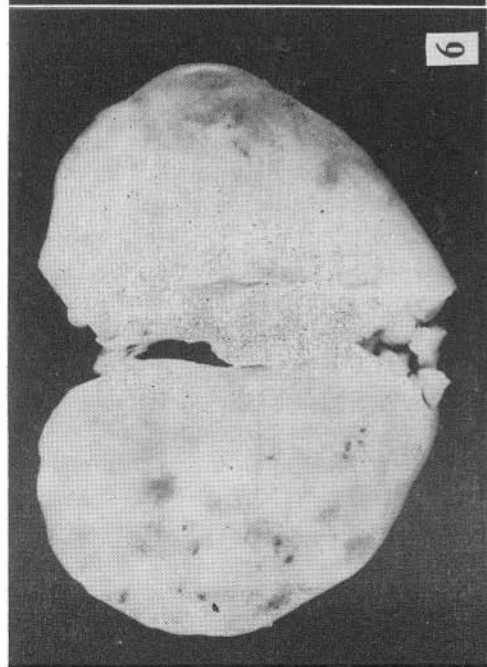
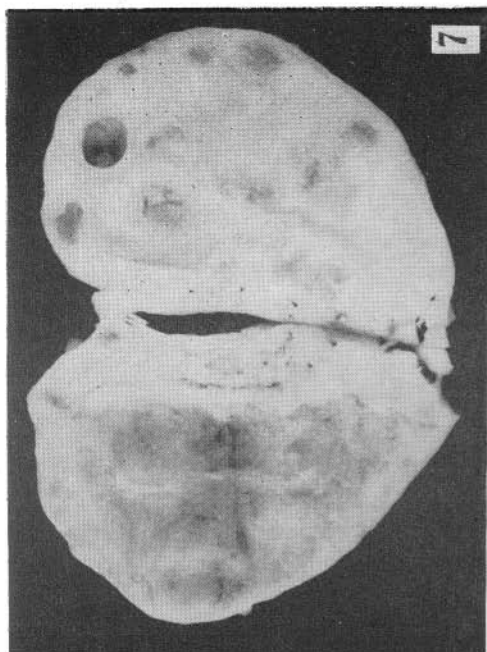
Evidently, the name of carcinomatous mastitis, given by some authors to mammary cancer evolving during pregnancy, is justified to a certain point, considering the inflammatory phenomena which usually accompany the carcinoma. In fact, there is present only a carcinoma of remarkable malignancy with a marked inflammatory reaction.

Macroscopic examination of the patient's ovaries in the second case showed haemorrhagic petechiae and multiple cysts (Figs. 6 and 7) which histological examination showed to be follicular cysts (Figs. 8 and 9).

In both cases the evolution was exceedingly malignant. Three months after delivery, patient C. A. showed diffuse infiltration and reddening of the zone above the homolateral sterno-clavicular articulation (note that the primary lesion affected the upper internal quadrant of the right breast) and a month later the infiltration had spread towards the left breast with multiple bone metastases throughout the pelvis (Fig. 2). She died 7 months after delivery.

Patient I. A. J. had practically no benefit from oophorectomy, and only temporary relief with Roentgen therapy. She died 3 months after delivery. It is evident that the patient who underwent operation lived 4 months longer than the one who didn't; but the fact remains that the latter arrived at the Clinic with a more advanced clinical picture.

- Le Fig. 6: Case II. Left ovary, surface view. Note hemorrhagic
dir petechiae particularly on the left, and small dark areas
corresponding to follicular cysts.
- a Fig. 7: The same as in Fig. 6; sagittal section. Note dark areas
dir corresponding to follicular cysts, one of which is clearly
se shown in section (upper right).
- cal Fig. 8: Histological section of the wall of the follicular cyst
n shown in Fig. 7. $\times 40$.
- F Fig. 9: Detail of Fig. 8. Cyst wall is formed by elements of
rn theca interna. Note conspicuous vessels dilated and ab-
ab normally abundant. $\times 100$.



THE MALIGNANCY OF THE ILLNESS

Having observed the evolution of the two cases under consideration, we may now discuss the probable causes which may influence the unfavorable prognosis of cancer of the breast developing during pregnancy.

1.—During pregnancy, the mammary gland undergoes extensive modifications, and its microscopic structure differs greatly from the inactive gland's. Connective tissue, previously abundant, is reduced to thin zones which enclose voluminous lobes formed by ducts and alveoli in the process of secretion. It is equally noteworthy that estrogens in post-menopausal cases and androgens in pre-menopausal cases of mammary carcinoma determine the histologic modification of the neoplastic mammary tissue, favoring proliferation of the connective tissue component which presses upon the malignant cell clusters and retards karyokinesis in them (8).

In the case of mammary carcinoma during pregnancy we find a completely different histologic picture. After an early period during which ovarian hormonal influences predominated, a second stage ensues during which the placenta contributes considerable quantities of estrogenic and luteinizing hormones. BECH (3) also affirms that estrin and progesterone are secreted by the placenta and easily enter the blood stream. It is known that estrogens stimulate the development of mammary ducts during pregnancy and that progesterone reactivates the formation of glandular acini.

We have no knowledge of the etiology of such new growth, but we can understand the high malignancy of mammary carcinoma developed during pregnancy. Malignant cells develop in an environment poor in connective tissue, which favors their proliferation, and are under the hormonal stimuli which affect them also as well as the benign cells. According to RONDONI (9) estrogens are not true cancerogenous substances comparable to polycyclic aromatic hydrocarbons, but they act as activating substances in the growth and development of the tissues of the genitalia and breasts. Our assumption is confirmed by the beneficial results obtained by ADAIR (1) after 5 years of treatment in a group of 23 patients in whom abortion had been established.

On the other hand, we don't think that oophorectomy is advisable in cases like ours, when pregnancy is allowed to continue to full term in order to save the life of the foetus. In such cases, placental hormones are so important, that those of the ovary are secondary. BECK (3) mentions that bilateral oophorectomy may not be followed by abortion if the operation is carried out after the first trimester of pregnancy. This fact confirms the enormous importance of placental hormones. Besides, after the oophorectomy, there is a modification in the cytological picture of the hypophyseal elements and a relative modification within the framework of the endocrine correlation.

BURT and CASTLEMAN (4) give the following results in relation to some histological effects of estrogens and castration on the anterior pituitary in women with carcinoma of the breast (Table 1).

TABLE 1

Differential counts on anterior pituitary

Type of patients	NB	SGB	Ac	Chr	HA
PM	10.5	5.5	33.4	49.7	0.9
CB	15.3	6.2	37.1	36.6	4.8
E	21.0	4.9	38.7	33.8	1.6
C	14.1	4.8	29.2	46.8	5.1
CE	4.7	1.8	56.1	35.9	1.5

NB: normal basophils

SGB: sparsely granulated basophils

Ac: acidophils

Chr: chromophobes

HA: hypertrophic amphophils

PM: postmenopausal women who had died rapidly and who had no history of cancer or endocrine disorder.

CB: women with a history of carcinoma of the breast.

E: women with a history of carcinoma of the breast treated with estrogens.

C: women with a history of carcinoma of the breast treated by castration; no hormone therapy.

CE: women with a history of carcinoma of the breast who received estrogens following castration.

According to BURT and CASTLEMAN, in postmenopausal women with carcinoma of the breast who were not subjected to hormonal manipulation, the normally granulated basophils and the hypertrophic amphophils in the anterior pituitary are significantly increased as compared with women with no history of carcinoma. This type of abnormality is not pathognomonic of carcinoma of the breast but does suggest some type of adrenal overactivity. Also, as may be seen in Table I, the number of hypertrophic amphophils in the anterior pituitary is significantly increased in women with a history of mammary carcinoma treated by castration without hormone therapy as compared to women with no history of carcinoma.

Hypertrophic amphophils are regarded by MELLGREN (7) as pathognomonic of adrenal activity.

Therefore, and because of a law of endocrine compensation in the human organism, oophorectomy in a latter period would not have the desired results

because of the increase in steroid production in the suprarenals. On the other hand, we consider castration justified in relatively young women who are operated on for breast cancer and who might become pregnant a second time. In this case, to the estrogen stimulus provided by the ovary is added the risk of the eventual placental endocrine stimulus, which we think should be avoided.

2.—During pregnancy, blood supply increases in the mammary glands. It is known that blood supply varies with activity, being much greater in an active gland than in an inactive or involuted one. Besides, estrogens have a vaso-dilatory effect. In ordinary mammary carcinoma, metastasis usually take place along lymphatic vessels to homolateral axillary ganglia, and bone metastasis are usually late. In breast carcinoma during pregnancy, on the contrary, metastasis along blood vessels are facilitated by the obvious increase of vascularization. With regard to our patients, in the first case, three months after delivery there were diffuse reddening and infiltration of the zone above the homolateral sterno-clavicular articulation, and one month later there were already multiple bone metastasis throughout the pelvis (Fig. 2) In Case N^o 2 (Figs. 4 and 5) the increase in vascularization was the cause for the change of the clinical picture in a relatively short time, forcing the surgeons to discard definitively the possibility of operating. Radiological control was impossible in this case, as the patient did not return to the Tumor Clinic for treatment; but her husband reported that in her last days she had complained of severe pains in her bones (probable bone metastasis?).

3.—The cause for the presence of haemorrhagic petechiae and multiple follicular cysts in the ovaries of patient I. A. J. was not determined. It would be interesting to note if other authors with access to a greater number of cases should study this anomaly and decide whether this is to be considered as an isolated occurrence or whether this is the usual picture in such patients. We could not find the histological specimen of the ovary of the patient C. A.; we were forced, therefore, to leave the point *sub judice*.

4.—The problem remains that of early diagnosis of the tumor, which, as already pointed out, is masked by the clinical picture of mammary gravidic hypertrophy and may go unnoticed by the patient and the physician.

SUMMARY

1.—Seventy-four cases of breast cancer have been observed in the Tumor Clinic of Hospital San Juan de Dios, in San José, Costa Rica. Two of these were cases of mammary carcinoma occurring during pregnancy. Including one other private case, such cases form only 4.05 per cent of the total incidence of breast carcinoma.

The authors present the clinical history of two patients, and offer some considerations on the development of the clinical picture and the palliative treatment given.

2.—The malignancy of gestational mammary carcinoma is considered by the authors as due in part to:

- a) the normal histological modification of the mammary glands during pregnancy, favoring karyokinesis of neoplastic elements;
- b) the effect of the hormonal component formed by ovarian and placental hormones, the latter being especially important. The fact that patients are usually relatively young, in full hormonal activity, is also significant in this respect;
- c) the increase in blood supply of the breast during pregnancy, increasing the possibility of circulatory metastasis as is shown by the frequency of bone metastasis at an early date. The increased blood supply, besides, constitutes a greater *pabulum vitæ* for malignant cells;
- d) the difficulty of early diagnosis of the tumor, the latter being masked by the natural increase in the turgidity of the breast and to the disregard of the observed changes by the patient, who relates them to her pregnant condition.

3.—In the light of BURT and CASTLEMAN's report of pituitary cytological modifications in breast cancer patients, the authors consider oophorectomy of little value as a palliative treatment in cases of mammary carcinoma occurring during pregnancy, because of the increased production of estrogens by the suprarenals caused by a corticohypophysiary compensatory stimulus. On the other hand, oophorectomy is considered advisable in cases of mammary carcinoma occurring in young premenopausal women, in order to eliminate the danger of placental endocrine stimulation in the event of pregnancy after mastectomy.

4.—The presence of multiple follicular cysts in the ovaries of one patient suggests the need of further investigation of this condition, its occurrence and significance in cases of mammary carcinoma in general and particularly in gestational cases.

RESUMEN

1.—En la Clínica de Tumores del Hospital San Juan de Dios de Costa Rica se han presentado 74 casos de carcinoma mamario de los cuales dos se desarrollaron durante el embarazo. Considerando también un caso privado, la frecuencia del carcinoma de la mama durante el embarazo, en el presente estudio es del 4,05 por ciento.

Los AA. presentan la historia clínica de dos pacientes y hacen algunas consideraciones sobre el desarrollo de la enfermedad y su tratamiento.

2.—*La malignidad del carcinoma de la mama que se presenta durante el embarazo según los AA. parece ser debida a los siguientes factores:*

- a) durante el embarazo las glándulas mamarias sufren una modificación histológica del parénquima que favorece las carioquinesis de las células malignas.
- b) las hormonas producidas por los ovarios y la placenta tienen una especial importancia, por sus estímulos sobre la proliferación celular, en la malignidad del cuadro clínico. Si además se considera que se trata de pacientes jóvenes en el máximo de su actividad hormonal, este factor es todavía más significativo.
- c) el aumento de la vascularización en la mama de una embarazada puede facilitar las metástasis por vía sanguínea, razón esta de la gran frecuencia de metástasis óseas en período temprano. Además es probable que el aumento de la circulación favorezca la alimentación de las células malignas.
- d) *la dificultad de un diagnóstico precoz, enmascarado por la turgidez fisiológica de la mama en el período de embarazo, es un factor importante postergando la paciente su primera consulta médica.*

3.—Los AA. consideran la ooforectomía un tratamiento apenas paliativo en los casos de carcinoma de la mama que se presenta durante el embarazo, porque, en esas condiciones, la hipófisis estimula las suprarrenales a una producción supletoria de estrógenos. Al contrario es aconsejable la ooforectomía cuando el carcinoma mamario se presenta en mujeres jóvenes para eliminar el peligro de un estímulo endocrino ovárico y placentar debido a un eventual embarazo posterior.

4.—Se aconseja hacer una investigación de los ovarios de pacientes portadoras de carcinoma mamario en embarazo, habiéndose encontrado en un caso presencia de múltiples quistes foliculínicos.

RIASSUNTO

Gli AA. considerano due casi di carcinoma della mammella che si svilupparono durante la gravidanza. Aggiungendo un terzo caso privato non studiato la frequenza é del 4.05 per cento su un totale di 74 casi di carcinoma del seno trattati nella "Clínica Tumores del Hospital San Juan de Dios" di San José (Costa Rica).

Gli AA. credono che la causa della altissima malignità del carcinoma del seno durante la gravidanza sia dovuta ai seguenti fattori:

Gli AA. considerano due casi di carcinoma della mammella che si svi-

- a) Durante la gravidanza aumenta il parenchima delle ghiandole mammarie, diminuisce lo stroma e si favorisce la cariocinesi delle cellule maligne.
- b) Lo stimolo cellulare dovuto agli ormoni prodotti dalle ovaie e dalla placenta é già noto, a questo si aggiunge il fatto che si tratta di donne quasi sempre giovani nel massimo della loro attività ormonale.
- c) L'aumento della vascolarizzazione nel seno gravidico sembra poter facilitare le metastasi per via sanguinea e spiegarci la frequenza delle metastasi ossee anzitempo, inoltre l'aumento della vascolarizzazione potrebbe essere un miglior *pabulum* per le cellule maligne.
- d) La diagnosi precoce, mascherata dal turgore fisiologico del seno gravidico, é quasi sempre impossibile e la paziente consulta il medico quando già la malattia ha progredito.

Si considera la ooferectomia un trattamento paliativo nei casi dichiarati di carcinoma del seno in gravidanza, mentre invece si consiglia in pazienti giovani mastectomizzate per carcinoma del seno con il fine di impedire una futura gravidanza e di conseguenza futuri stimoli ormonali ovarici e placentari.

La presenza di cisti follicoliniche nelle ovaie di uno dei casi considerati apre la possibilità di un ulteriore studio delle ovaie di pazienti portatrici di carcinoma della mammella durante la gravidanza.

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