

# INTRACRANIAL CARCINOMATOUS METASTASES

WITH NOTE ON RELATION OF CARCINOMA AND TUBERCLE

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IN ANY large series of intracranial tumors there is certain to be found a definite percentage of metastatic carcinomas. Many of these are readily predictable following careful examination of the breast, and of late years the more routine use of chest plates has shown the true place of the lung as an unsuspected and often otherwise undemonstrable source of primary cancer. The infrequency of coexisting multiple primary intracranial tumors of different types, there being only four such examples observed in our series, makes the appearance of bilateral or combined cerebral and cerebellar signs of great diagnostic significance. The occasional systemic manifestations, the rapid onset of intracranial signs, and the speedy downward course which many of these patients pursue frequently offer a clue to a presumptive diagnosis in spite of inability to demonstrate a primary site of malignancy. There remain, however, a certain number in which the pre-operative diagnosis is missed, and it is in the hope of further correlating our known observations that the following statistics are offered.

In a series of 1,850 verified intracranial tumors to May 10, 1930, fifty-seven are metastatic, representing 3 per cent. of the total. Of these forty-four are carcinomas, four are hypernephromas, and nine are sarcomas. This does not, of course, represent the true relation of metastatic tumors to tumors as a whole, because the prognosis of these patients, generally speaking, is so unfavorable that they are rarely deemed fit subjects for operation, and consequently many of them remain in the unverified group.

Grant,<sup>1</sup> in a previous report from this clinic, summarized the records of the various intracranial metastases to March, 1926. In the present study particular attention will be given to the carcinomas.

The primary site of the forty examples of carcinoma in the Brigham Hospital series is shown in the following table:

Primary focus	No. of cases	Per cent.
Breast .....	10	25.0
Lung .....	14	35.0
Mouth and sinuses .....	2	5.0
Liver and intestines .....	2	5.0
Generative organs .....	1	2.5
Kidney .....	1	2.5
Primary focus unknown .....	10	25.0

As may be seen from the above, lung and breast comprise 60 per cent. of the series, and are the only tumors in sufficient numbers to make general

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estimations of value. Fried and Buckley<sup>2</sup> have stressed the insidious course of primary lung cancers with suddenly developing intracranial signs, and it is impossible to judge the time of onset of the primary malignancy.

Breast carcinomas, however, since they are so frequently operated upon, lend themselves to more detailed records, and in the following table a summary of the ten cases of intracranial metastases in which the primary focus occurred in the breast is given.

Case	Age	Period from breast operation to onset of intracranial symptoms	Period from presence of lump to onset of intracranial symptoms	Survival period after intracranial operation	Survival period after onset of intracranial symptoms
1	61	6 yrs. 4 mos.	7 yrs. 10 mos.	(No operation)	8½ mos.
2	42	6 mos.	.....	(No operation)	4 mos.
3	65	11 yrs. 9 mos.	.....	(No operation)	3½ mos.
4	50	3 mos.	.....	3 mos.	8 mos.
5	53	2 yrs. 6 mos.	.....	1 day	6 mos.
6	49	.....	1 yr. 10 mos.	2 weeks	3½ mos.
7	59	6 yrs. 2 mos.	.....	3 weeks	9 mos.
8	30	3 yrs. 4 mos.	3 yrs. 11 mos.	5 mos.	9 mos.
9	50	.....	(Duration not noted)	1 mo.	7 mos.
10	52	1 yr. 1 mo.	.....	Living	Living
Average	51	3 yrs. 10 mos.	.....	6 weeks	6 months

In this group, the ages vary from thirty to sixty-five years, the average being fifty-one years. The longest survival period after operation is five months, the average being six weeks, while the longest survival period after the onset of intracranial symptoms is nine months. The time interval between the breast operation and the appearance of the intracranial symptoms varies widely, the shortest period being three months, and the longest nearly twelve years, an average of over three and a half years. Since tissue from the primary tumor is usually unavailable, it is impossible to hazard more than a guess as to the rôle the type or extent of the tumor plays in determining the probability of intracranial metastasis. From the diagnostic point of view no positive stand can be taken on mere time interval alone even after considering the age of the patient and histological grade of malignancy of the primary lesion. Moreover the so-called typical clinical history of very rapid progress of an intracranial lesion, often with an accompanying psychosis, cannot always be relied upon, even in cases of established breast cancer. As an example of this the following case is cited.

CASE I.—P. B. B. H. Surg. No. 35806. Admitted January 9, 1930. Woman, L. M. N., forty-eight years of age, complaining of severe headache of three months' duration. *Family history* unremarkable.

*Past history.*—Twelve years ago she began to have fainting spells which lasted from a few minutes to almost an hour and were unaccompanied by convulsions. Her second attack came on one year after the first, and over a period of four years she had irregularly recurrent seizures with no increase in frequency or severity. At this time she was subjected to an appendicectomy, the uterus was suspended and a small ovarian cyst was

removed. Within a year of this operation her attacks ceased save for a single lapse of consciousness five years ago. She had no further complaints and believed herself in excellent health.

Two years ago, in January, 1928, she noted a hard painless lump in the upper inner quadrant of the left breast. This gave her no concern but its persistence caused her to seek examination a little more than a year later and the mass was noted as being 4 centimetres in diameter, slightly adherent to the skin and with no evidence of axillary or supraclavicular involvement. The opposite breast was normal. On June 6, 1929, eight months prior to entry, a radical amputation was performed and although grossly no axillary extension was demonstrable, section showed a carcinoma simplex of scirrhous type, Grade II, with metastases to lymph-node. Healing was good and recovery rapid.

*Present illness.*—Four and a half months before entry (two and a half months after her radical breast operation), she began suddenly to have severe occipital and vertical headaches. Patient immediately thought of her eyes, but altered lenses gave no relief. The headaches continued with frequent remissions up to the time of admission and the last two months were definitely milder until one week before entry, at which time she had a very severe headache with nausea and vomiting. She had had no peripheral motor or sensory symptoms and no visual disturbances.

*Neurological examination* showed a very slight secondary atrophy of left nerve head without choking and no further signs whatsoever.

*X-ray findings.*—Skull plates disclosed a mass 9 by 9 by 7 centimetres in the right temporal region which was of markedly increased density. There were mild skull changes of increased pressure. The röntgenologist's impression was that it was a meningioma. The lungs were noted as clear.

*Operation.*—In view of the positive X-ray findings, operation was performed in two stages on January 31, 1930, and February 1, 1930, with removal of a meningioma rich in calcium. As removal progressed, the last remaining attachment of the mass contained the main branch of the middle cerebral artery, injury of which caused a fatal hæmorrhage. Subsequent section of the brain failed to reveal any sign of metastatic carcinoma.

*Comment.*—The history of sudden onset of terrific headaches, nausea and vomiting in a woman of forty-eight, who seven months before entry had a radical breast amputation for a scirrhous carcinoma of rather high malignancy with axillary metastases, strongly suggested intracranial metastasis until the routine X-ray examination disclosed a partially calcified meningioma. The case well illustrates the difficulty that may confront the surgeon in making up his mind from the clinical history alone as to the nature of the lesion he expects to find.

If this difficulty exists in the case of patients with obvious breast tumor or with the scar of a breast amputation to suggest the probability of the nature of the intracranial growth, the diagnosis of a primary carcinoma of the lung is still more obscure, the primary lesion having been recognized in only four of the fourteen cases, in contrast to 90 per cent. of correct pre-operative diagnoses of metastases from the breast.

It is the usual clinical practice to consider a syndrome of a single etiology, and when two supposedly antagonistic lesions, both capable of producing the same intracranial signs, are found in the same individual, one is faced with a diagnostic problem in which the opinion of various observers must be evaluated. Just such a situation existed in the following case.

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CASE II.—P. B. H. Surg. No. 35063. Admitted October 18, 1929, woman, M. G., aged thirty, with complaint of occipital headaches, failing vision, nausea and vomiting of four months' duration.

*Family history.*—Direct and prolonged exposure to active tuberculosis among members of her immediate family, four of whom succumbed to pulmonary tuberculosis and with whom she was associated intimately from childhood.

*Past history.*—In 1903, at the age of four years, she had tuberculosis of the right

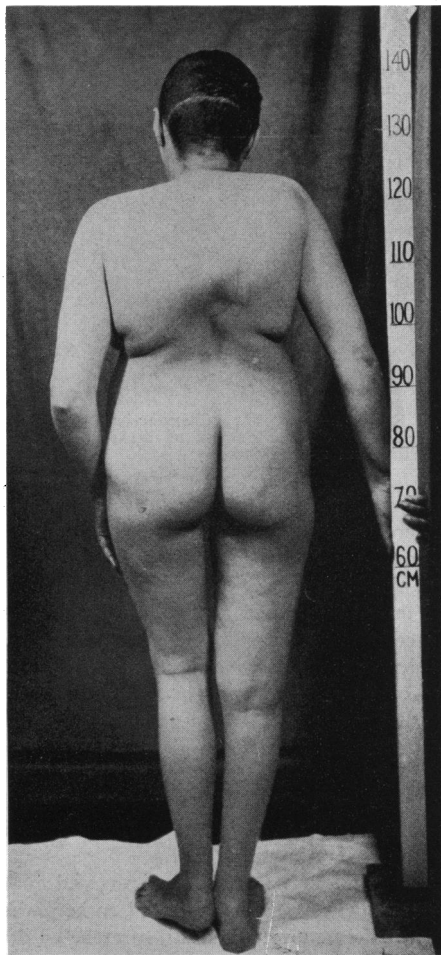
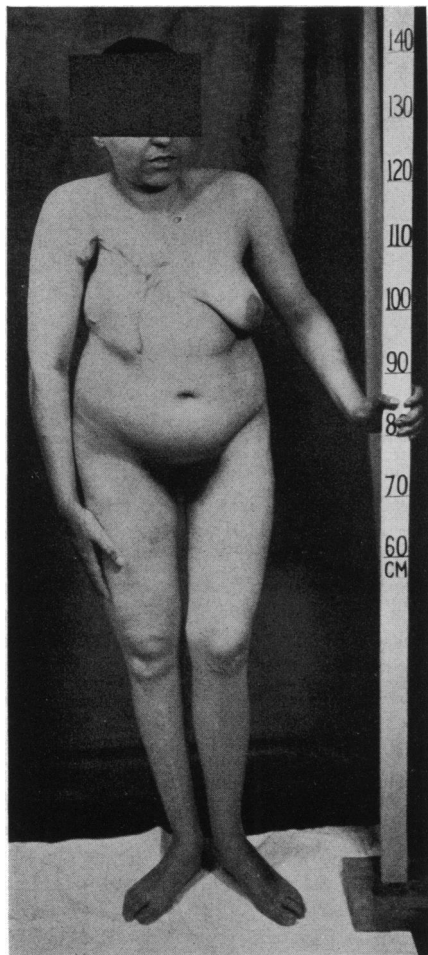


FIG. 1.—Case II. Showing scar of radical breast amputation and deformity of hip.

FIG. 2.—Case II. Showing marked spinal deformity. Note scars of suboccipital exploration and spinal fusion operation.

ankle with discharging sinuses, which after treatment for three years at the Children's Hospital finally healed satisfactorily.

In 1905 she began having symptoms associated with the left hip-joint, and a year later was admitted to the wards of the Children's Hospital for treatment of tuberculosis of this joint. She did fairly well under observation for the next two years until a tuberculous abscess developed at the end of that period.

In 1913, at the age of fourteen, she was admitted to the Carney Hospital with tuber-

culosis of the spine. An Albee spine operation was performed with fusion of the fourth to tenth dorsal processes.

Except for a story of "influenzal pneumonia" in 1919, the history during the next thirteen years was quite uneventful.

In 1926, at the age of twenty-seven, the patient was again admitted to the Carney Hospital, with complaint of a lump in the right breast of seven months' duration. February 18, 1926, a radical amputation of the breast was performed, with removal of a

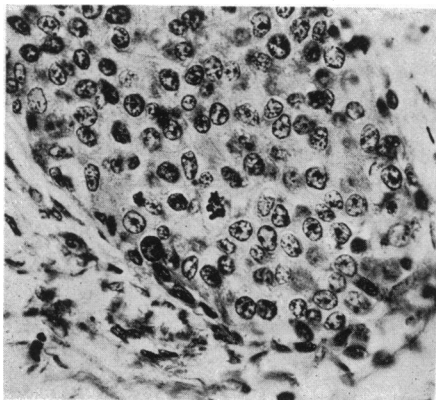


FIG. 3.—Case II. Characteristic field of scirrhous carcinoma simplex of breast. (Hema-toxylin eosin stain x 600.)

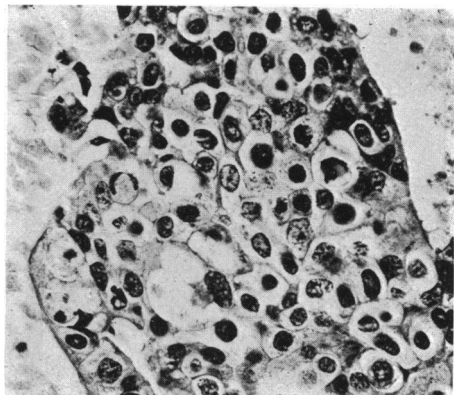


FIG. 4.—Case II. Intracerebellar metastasis of the same tumor shown in Fig. 3. The cells are much larger and there are numerous mitoses. (Hema-toxylin eosin stain x 600.)

very hard nodular carcinoma in the left upper quadrant, which was adherent to the skin. There were no masses in either axilla except for one small gland in which no evidence of malignancy was found.

*Present illness.*—For four months severe occipital headaches associated with stiffness of the neck, nausea and vomiting; diminution in vision; irregularity of menses. For three months diplopia, persistent until two weeks before entry. Four weeks ago the patient suffered two seizures in which she lost consciousness and bit her tongue, though no clonic movements were observed. On both occasions she complained of transitory numbness of the left hand preceding the attack.

*Physical examination.*—The signs of her healed tuberculosis were a partially ankylosed right ankle and left hip, and immobilization and deformity of the dorsal spines with marked kyphosis (Figs. 1 and 2). The chest was free of signs, but X-rays showed evidence of old healed pulmonary tuberculosis. There was no evidence of local recurrence in the skin of breast or axilla.

Neurological examination revealed bilateral choked discs  $4\frac{1}{2}$  D. right and 3 D. left. Deep reflexes were exaggerated on both sides.

*Pre-operative diagnosis.*—Cerebellar tumor. The localizing symptoms were insignificant except for the history of suboccipital headaches. Owing to rigidity of the leg and dorsal kyphosis, gait and station were difficult to test. Although a lesion of the posterior fossa was suspected, in view of the story of left-sided attacks a preliminary ventriculography was made, which disclosed an internal hydrocephalus.

*Operation.*—October 24, 1929. Suboccipital exploration with disclosure of what was regarded as a patch of tuberculous adhesive meningitis over left hemisphere, and a large subcortical tuberculoma associated with an abscess within the right hemisphere. Extirpation of tumor, which was nodular and adherent, and Zenker fixation of wall of abscess. Charring of surface involvement by coagulating current. Closure of wound in layers as usual.

*Pathological diagnosis.*—Metastatic carcinoma. (Figs. 3 and 4.)

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*Subsequent notes.*—Patient made a rapid recovery and was discharged free from symptoms on November 21, 1929. In January, 1930, she was admitted to the House of the Good Samaritan. At this time there was hemiplegia of the left side. There was gradual recurrence of intracranial symptoms, and death occurred March 12, 1930.

*Comment.*—The oft-recurrent tuberculosis which this girl had shown from early childhood with involvement of many sites weighed heavily in favor of a presumptive diagnosis of tuberculosis, particularly since the onset and course of her neurological symptoms so closely simulated that of the common cerebellar tuberculoma. In spite of the three-and-a-half-year interval since the breast was amputated, and the medium grade malignancy of her breast cancer, the course of such a tumor in a woman of twenty-six is ordinarily so rapidly fatal that we should doubtless have more seriously considered cancer in the differential diagnosis.

Although Van Wageningen<sup>3</sup> has shown the dangers of disseminating meningitis following operative removal of tuberculomas of the cerebellum, the electrosurgical method now at our disposal, by means of which dissection of tissue may be carried out without dissemination of inflammatory products and with simultaneous surface sterilization and sealing off of the structures traversed, offers the surgeon great opportunity in attempting a radical extirpation of such a lesion. It was for this reason that the extirpation of the supposed tubercle was undertaken in this patient rather than leaving the operation as a decompression.

*Cancer and tuberculosis.*—One cannot well report a case of coincidental carcinoma and tuberculosis without some reference to the recent revival of interest in the possibility that the two diseases are antagonistic.

The first observation of the infrequent coëxistence of cancer and tubercle is ascribed to Cruveilhier, who in 1828 concluded that the relative rarity of the double lesion was due to the widely different age-groups usually attacked by the two diseases. Rokitsky,<sup>4</sup> in 1846, as an outcome of his experience offered a theory heavily tinged with "humoral" concepts which postulated an antagonism between the tubercle "crasis" and the cancer "crasis." His astute observation that the primary site of cancer is rarely that of tuberculosis and that the converse is also true is unquestionably correct, but his assumption of the antagonism of the "crases" of the two diseases was immediately attacked, notably by Lebert<sup>5</sup> who in 1852 flatly stated that the idea was untenable because he had many times observed the coincidence of tubercle and cancer. Paget<sup>6</sup> in 1853 agreed with Rokitsky as to the antagonism of the cancerous and tuberculous "diatheses" and noted a case of a woman of twenty-five with a rapidly growing breast cancer which was surgically removed and in whom six months later both local and axillary metastases occurred with sloughing ulcerations. This situation obtained for one year and then quite suddenly healing took place, although the woman had gradually failed in strength and died two years post-operatively. At autopsy she presented extensive fulminating tuberculosis with cavitation in both apices and widespread smaller tubercles throughout the lungs in addition to fairly extensive

carcinomatous metastases in distant areas. He concluded that "the progress of the tuberculous process was commensurate with the remarkable regress of the carcinomatous extension."

The widespread influence of Rokitansky both here and abroad led to very frequent consideration of the above premise, and a precisely similar division of opinion exists today as to the frequency and infrequency of the coëxistence of the two processes, with corollary observations on the altered course of cancer when tuberculosis has been superimposed either naturally or artificially. Marked disparity in autopsy statistics on relative frequency of the diseases is explained by a failure to note the ages of the patients, the activity or extent of the tuberculosis and by failure to exhaustively search the material when once the main cause of death has been ascertained.

Bastedo<sup>7</sup> in 1904 summarized the then reported cases, and showed the following distribution of primary carcinoma associated with *active* tuberculosis mainly in lung, intestines and lymph-nodes.

Breast .....	10	Æsophagus .....	13
Uterus .....	10	Stomach .....	39
Cheek .....	1	Liver .....	8
Jaw .....	2	Pancreas .....	3
Tongue .....	1	Bowel .....	4
Pharynx .....	1	—	—
		Total .....	92

In addition, after excluding the well-known tendency to epithelioma formation superimposed on long-standing lupus, he collected the cases in which tuberculosis and cancer existed in the same organ with the following distribution of the lesions.

Breast .....	7	Stomach .....	3
Uterus .....	1	Small bowel .....	3
Larynx .....	2	Large bowel .....	4
Lungs .....	20	Liver .....	2
Æsophagus .....	4	Rectum .....	3
		—	—
		Total .....	49

Moak's description<sup>8</sup> of carcinoma of the prostate in a case of pulmonary tuberculosis with subsequent distant involvement of lung, bronchial lymph-nodes, adrenal, liver and spleen by both processes, and Warthin's<sup>9</sup> report of a breast cancer with axillary metastases into a node already the seat of active tuberculosis show clearly the ability of cancer metastases to flourish in soil already involved in tubercle formation. The literature contains a great number of similar isolated reports and Broders<sup>10</sup> from his own material showed twenty cases of coëxistence of active tuberculosis and cancer, in six of which the two processes were to be observed in the same microscopic field.

The observations recorded above would appear to indicate that the two disorders coincide sufficiently often to show that there is no specific antagonism. Nevertheless, believing such an antagonism to exist, there have been

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made isolated attempts to tuberculinize patients with carcinoma considered hopeless from any other therapeutic viewpoint. McCaskey,<sup>11</sup> in 1902, was the first to suggest this and, although citing possible improvement in one case, gave no detailed report. Dabney<sup>12</sup> in 1916 again attempted this method of therapy, and of six patients injected, noted marked improvement over a three-month interval in a young woman with an oesophageal cancer. No further clinical attempts were carried out until Delbet and Monod in 1920,<sup>13, 14</sup> in a fairly extensive and carefully conducted series of cases studied the thermal reactions in various types of cancer patients with graduated doses of tuberculin. In addition they studied the effect of tuberculin injected locally into cancer tissue, but were unable to demonstrate in either procedure any conclusive findings save the expected thermal rise. More recently statistical studies of post-mortem material have led biometricians<sup>15</sup> to feel that an antagonism was demonstrable between the two processes, and in consequence still another attempt has been made by Pearl, Sutton and Howard<sup>16</sup> to tuberculinize carcinoma patients in the hope of altering the progress of the malignancy.

### CONCLUSIONS

1. Of 1,850 verified intracranial tumors fifty-seven (3.0 per cent.) are metastatic, and of these forty-four (2.3 per cent.) are carcinomas.
2. Of forty-four metastatic intracranial carcinomas, one-fourth are primary in the breast.
3. The average age of patients with intracranial metastases from the breast is fifty-one years, the oldest being sixty-five, and the youngest thirty years old.
4. The onset of intracranial signs after primary focus in the breast averages over three and a half years, the interval ranging from three months to twelve years.
5. The course from the appearance of intracranial symptoms is rapid, fatality ensuing on an average of six months, and operative interference is survived on an average of six weeks, the longest period being five months.

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