

The neurology of metastatic chorion carcinoma

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Summary

Although chorion carcinoma of the uterus is the seventh commonest in the comparative frequency of malignant tumours seen at the Cancer Registry of the University College Hospital, Ibadan, Nigeria (being exceeded in order of commonness by the reticuloendothelial tumours, carcinoma of the cervix, liver, breast, stomach and ovary), it is the most frequent source of tumour deposit of the brain in this hospital.

Between 1960 and 1969, 197 Nigerians with chorion cancer of the uterus were admitted to UCH; in twenty-five of them the nervous system was involved during the course of their disease. The neurological involvement presented as acute cerebrovascular accident in fourteen, encephalitis in five; as primary intracranial space-occupying lesion in three cases and in one patient, as cord compression. There were no obvious neurological features in two cases in which necropsy revealed brain metastases.

Involvement of the nervous system carries a poor prognosis in chorion cancer of the uterus.

Résumé

Bien que le carcinome du chorion de l'utérus soit au 7e rang de fréquence des tumeurs malignes enregistrées à l'University Teaching Hospital d'Ibadan, Nigeria (après les tumeurs réticule-endothéliales, le cancer du col de l'utérus, du foie, du sein, de l'estomac et de l'ovaire), il constitue la source la plus fréquente de dépôt tumoral du cerveau dans cet hôpital.

Entre 1960 et 1969, 197 Nigériennes atteintes de cancer du chorion ont été admises à l'U.C.H. 25

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d'entre elles ont présenté des complications neurologiques en cours de maladie, dont 14 un accident cérébrovasculaire aigu, 5 une encéphalite, 3 une lésion intracrâniale primaire expansive, et 1 une compression de la moelle. Il n'y avait pas de caractères neurologiques évidents dans 2 cas ou l'autopsie a révélé des métastases cérébrales.

Les complications neurologiques entraînaient un pronostic défavorable dans le cancer du chorion de l'utérus.

At the Cancer Registry of the University College Hospital (UCH), Ibadan, Nigeria, chorion carcinoma of the uterus is the seventh commonest malignant disease on record (Table 1), but it is responsible for about 70% of all the brain metastases in Nigerians who attend this hospital (Adeloje & Odeku, 1969). Isolated examples of cerebral involvement in chorion epithelioma of the uterus were noted until 1910 when Inglis & Bruce reported five cases of this complication; since then, the neurological characteristics of metastatic chorion cancer have been highlighted by a number of authors (Cary, 1913; Brews, 1939; Acosta-Sison & Espaniola, 1941; Dockerty & Craig, 1942; Vaughan & Howard, 1962; Aguilar & Rabinovitch, 1964; Tupasi *et al.*, 1968). This paper is a brief account of the neurological presentations of metastatic chorion epithelioma of the uterus as seen at Ibadan, Nigeria.

Materials

Between 1960 and 1969, 197 Nigerian women with chorion carcinoma of the uterus were treated at the University College Hospital, Ibadan. The twenty-five (12.2%) of them who developed evidence, clinical and pathological, of involvement of the central

nervous system during the course of their malignant disease formed the subject of this paper.

TABLE 1. Ratio of relative frequencies of some tumours seen at the Cancer Registry, UCH, Ibadan, 1960-1966

International class no.	Type and site of tumour	Ratio of relative frequency
200-202	Reticuloendothelial tumours (Reticulum cell sarcoma. Adult lymphosarcoma. Burkitt's lymphoma. Hodgkin's disease. Reticulosis.)	19.2
171	Carcinoma of cervix	9.9
155	Carcinoma of liver	7.5
170	Carcinoma of breast	5.3
151	Carcinoma of stomach	4.1
175	Carcinoma of ovary	3.2
173.2	Chorion carcinoma of uterus	3.1

Findings

General features

The twenty-five women with neurological involvement whose ages varied from 20 to 45 were all in the child-bearing span of life. Twelve were in the third, eleven in the fourth and the remaining two were in the fifth decade of life.

Twenty of them presented with vaginal bleeding as the inaugural evidence of chorion cancer, the bleeding occurring either after normal deliveries (five cases) or after abortion (fifteen cases) of a normal foetus or of an hydatidiform mole. In four patients, respiratory symptoms were the initial presentation, and the last patient was admitted as suffering from a primary intracranial space-occupying lesion without any indication of the presence of chorion-epithelioma.

Onset of neurological manifestations

Twelve patients developed CNS signs within a year of the onset of their systemic disease, eight between 12 and 24 months and two after 2 years. In the patient admitted with the diagnosis of primary intracranial space-occupying lesion, histological examination of specimen removed at craniotomy revealed chorion cancer and in the remaining two patients neurological involvement was clinically silent, but necropsy revealed tumour deposits in parietal and occipital lobes of the brain.

In eighteen cases, pulmonary symptoms antedated the CNS manifestations.

Neurological features observed in the series

These are summarized in Table 2.

Limb paresis was often sudden in onset, but it was of the stuttering type in a few cases. There was the tendency to gradual recovery of motor function, but rarely the weakness was recurrent.

Convulsions were either of the generalized or focal type; they tended to be repetitive when each attack preceded another 'cerebrovascular accident', and the frequency of the fits was considerably increased terminally among those who died.

Headache had a localizing character and when persistent, it was severe and intractable.

Mental changes included irrational behaviour, disorientation, depression, lack of cooperation with the nursing staff. The changes were either subtle personality changes or, rarely, consisted of frank, blatant and disturbing psychotic behaviour.

While any of these four common features may occur first, in some patients, a striking sequence of events was observed. This consisted of the appearance of mental changes first, which was succeeded by convulsions or headaches and finally the occurrence of limb weakness.

The following neurological 'syndromes' were noticed.

(1) *The clinical picture of acute cerebrovascular disease* was noted in fourteen patients. This was the first form of neurological involvement recorded in

TABLE 2. Neurological features of metastatic chorion cancer

Manifestation	No. of patients
Limb paresis	13
Convulsion	11
Headache	9
Mental changes	8
Neck pain/stiffness	7
Sphincter disturbance	4
Dysphasia	2
Painful flexion contractures	2
Papilloedema	2
Deafness	1
Hoarseness of voice	1
Blurred vision	1
Numbness of the hand	1

this disease (Inglis & Bruce, 1910). That it was the commonest mode of presentation in this series was hardly surprising in a lesion which is very vascular. Indeed, carotid cerebral angiography performed in one patient showed leakage of contrast material in the locus of the metastatic tumour deposit. The cerebrovascular disease may be a single event in which the neurological deficits either improved or more often, progressively worsened until death supervened. It may on the other hand present as 'multiple strokes' with partial recovery occurring initially until an extensive apoplexy finally fatally overwhelms the patient.

(2) *Those presenting as encephalitis.* Features of diffuse cerebral involvement without any neurological deficits were recorded in five patients who presented with confusion, restlessness, generalized headaches and convulsions. Death in the five patients occurred between 3 days and 3 weeks after onset of neurological manifestations and at necropsy widespread minute lesions were found in the brain, and in three patients, naked eye examination of the uterus showed no evidence of the primary disease.

(3) *The brain deposits in three patients presented as solitary, intracranial space-occupying lesions.* One of them had carotid cerebral angiographic and ventriculographic studies which confirmed the space-occupying lesion for which a craniotomy was performed. The histological examination of the haemorrhagic tumour removed confirmed metastatic chorion cancer.

(4) *There was one instance of cord compression.* The woman had multiple secondaries in both lungs; one lesion at the apex of the left lung spread directly to the first, second and third dorsal vertebrae to cause an extradural cord compression at the same level.

(5) *Neurological involvement was asymptomatic* in two cases in which necropsy examination showed tumour deposits in the parietal and occipital regions of the brain.

The methods of treatment employed consisted of blood transfusion, cancer chemotherapy and surgery. Multiple courses of blood replacement were given to patients as a result of severe blood loss or of anaemia following the administration of cancer chemotherapy. The latter consisted of the use of methotrexate, 6-mercaptopurine and actinomycin D. Total hysterectomy with or without bilateral salpingo-oophorectomy was performed in a few cases of excessive uterine bleeding.

Results of treatment

In about 50% of the patients, neurological complications manifested for the first time after the institution of cancer chemotherapy.

Three patients so far have survived; one for three months and then was lost to follow-up, and two for 4 years and 7 years respectively. The twenty-two deaths occurred within 1 week to 10 months after the first evidence of neurological involvement. The average duration of chorion cancer in the twenty-five patients was 14 months, but in the presence of neurological involvement, death occurred on an average of $2\frac{1}{2}$ months after the onset of neurological manifestation.

At necropsy, most of the brain metastases were found supratentorially and often in the parieto-occipital region of the brain in that compartment.

Discussion

Vaughan & Howard (1962) referred to the patterns in which the involvement of the central nervous system by metastases from chorion epithelioma of the uterus may manifest. The presentation of 'acute cerebrovascular accident' was the commonest in literature; next the picture of diffuse cerebral involvement which may mimic encephalitis, and lastly the presentation of a solitary intracranial mass lesion with the appropriate neurological deficits. These three patterns were noted in our series in which there were in addition the presentation of cord compression and the neurologically asymptomatic disease.

In those with acute cerebrovascular accident, the haemorrhage may occur within the substance of the brain (Vaughan & Howard, 1962) into the ventricular system (Beasley & Williams, 1962), the subarachnoid (Seal & Millard, 1955) and the subdural space (Acosta-Sison, 1956). Zander, Rossel & Curchod (1961) reported the case of a woman who presented with a solitary right parietal mass and was alive 14 months after the neurosurgical removal of the metastatic deposit. In cases without evidence of an expanding lesion, Bagshawe (1969) incriminated an embolic phenomenon due to the temporary growth of tumour tissue in the brain as the probable cause of cerebrovascular disease in such instances.

Once metastases appear in chorion cancer survival is shortened (Novak & Seah, 1954) and cases with brain metastases are invariably fatal (Vaughan & Howard, 1962). The long survival of 7 years in one of

our cases is very extraordinary, and the possibility of another cause besides brain deposit, namely cerebral ischaemia from severe blood loss, is worthy of consideration to explain the convulsions she had on her admission to hospital.

Cancer chemotherapy does not appear to alter the inexorable course of chorion cancer complicated by intracranial metastases. Indeed Bagshawe (1969) even observed that after cancer chemotherapy intracranial lesions which were previously silent may become symptomatic, presumably as a result of the physical changes induced in or about these metastases by such treatment.

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