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Combination chemotherapy as the first line in the management of locally advanced epidermoid carcinoma of the head and neck region in Nigerians

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Summary

Of cancer patients in Nigeria, 92% report at a late stage before treatment. Those with tumours of the head and neck region in particular, pose serious problems with management. Their advanced disease means that they are often inoperable and results of treatment by radiation are poor because the dose is limited to what the tissues can tolerate and also because the larger the tumour volume involved, the less the amount of radiation dose possible, so the response is poor. The problem is made worse by inadequate radiotherapy facilities. At the time of the study only one moderately equipped radiotherapy centre served the whole of Nigeria (with a population of 100 million) and neighbouring Ghana, Sierra-Leone and the Cameroons. There is usually a patient waiting list of about 3–4 months at any time, thus making prompt treatment impossible. These local problems and the search for an alternative approach led to this prospective study, which took place between 1980 and 1984. Two hundred and five adult patients with histologically proven, and locally advanced, epidermoid carcinoma in the head and neck region were given combination chemotherapy with Vincristine, Bleomycin and Methotrexate as the first line of management. There was a tumour regression rate of 68% (complete + partial), such that further treatment with surgery, radiotherapy, or a combination of both was then possible.

Résumé

Quatre-vingt-douze de malades cancer au Nigéria se present trop tard pour la traitement. Ceux avec les tumeurs dans les régions de la tête et le cou pose les problèmes grave de l'administration où a cause du gravité de leur maladies il ne pas possible de fait un opération et les resultats du traitement par radiation sont pauvre parceque la dose a restreinte a ce que les tissus peuvent tolérer. Un autre raison est que les tumeurs plus grand demande un montant moins de radiation et par cousequence la reponse pauvre. La problem se mit plus grave par les installations radiotherapie inadéquate, où une centre radiotherapie servir la nation de 100 million peuples plus autre pays de l'Afrique occidentale comme Ghana, Sierra-Leone et Cameroun. Ces pays n'ont pas les installations radiotherapie. Il y'avait toujours un liste d'entente de malades de 3 a 4 mois chaquefois, un situation qui fait la traitement rapide impossible. Ces problemes locales et la recherche pour les alternatif aboutir a entréprise cet étude prospectif entre 1980–1984. 205 malades adultes avec carcinoma epidermoid de la région de la tête et le cou démontrée par l'analyse histologique ont reçu traitement chemotherapy combiné de vincristino, Bleomycin, Methotrexate comme le premier ligne de l'administration. Il y'avait un taux deregression du tumeurs de 68% (Compleet + partiel) tel que la traitement supplementaire avec opération, radiotherapie cu un combinaison de tous les deux etait possible.

Introduction

Tumours of the head and neck region account for 16% of all tumours seen and managed at the oldest radiotherapy unit in Nigeria, situated at

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the Lagos University Teaching Hospital. These tumours rank third after carcinoma of the cervix (26.3%) and carcinoma of the breast (24.2%) [1]. Of all tumours seen, 92% present with late and advanced metastatic disease [1]. Patients with tumours in head and neck region usually present with huge unilateral or bilateral neck nodes and disease so severe that surgery and radiotherapy are not technically possible in most cases. At the time of the study, Nigeria, with a population of about 100 million people, had only one moderately equipped radiotherapy centre, which catered for about 5000 cases each year who were referred from all over Nigeria, and the neighbouring West African States of Ghana, Sierra-Leone and the Cameroons.

There is usually an average waiting list of 3–4 months before patients are given radiotherapy. The late presentation and the inevitable and unacceptably long patient waiting list for palliative radiotherapy led to the search for an alternative approach whereby chemotherapy was offered as the first line of management. The primary aim is to debulk the tumour before further treatment with surgery, radiotherapy or both. Although overall patient survival may not necessarily be influenced by this approach, there is worthwhile palliation of the patients' symptoms, and improved quality of life as a result of the disappearance of the massive swellings on the face and neck of these patients.

Patients and methods

Two hundred and forty-six patients, aged 16 and above, who presented with advanced histologically proven epidermoid carcinoma in the head and neck region between 1980 and 1984, were included in this study. Only 205 patients were found evaluable. Reasons for exclusion from analysis included lack of histological proof of epidermoid origin in 19 patients; long distance from referral centre, making follow-up impossible (10 patients); those who had less than four courses of chemotherapy due to financial constraints or other reasons (seven patients); poor general condition (four patients) and drug reaction (one patient).

Baseline investigations on admission to the study included a full haemogram, platelet count, assessment of urea and electrolyte

levels, and liver function tests. Radiological investigations included X-rays of the skull and chest. A full clinical examination with the recording of all measurable lesions was done, and clinical photographs were taken before and after at least four courses of chemotherapy whenever possible.

The chemotherapy regime employed was a combination of Vincristine 1.4 mg/m² (max 2 mg), Bleomycin 10 mg/m² and Methotrexate 30 mg/m², given intravenously once every 3 weeks, subject to a satisfactory blood count with Hb over 10 g/dl, WBC over 3000/mm³, and a platelet count over 100,000/mm³.

A minimum of six courses were given. Assessment of response was done after the fourth course. Complete response (CR) was recorded when there was a total disappearance of all visible tumour, which was sustained for at least 6 weeks. Partial response (PR) was achieved with $\geq 50\%$ reduction in the sum of the products of the longest perpendicular diameters of the measurable disease. No response (NR) was recorded when there was no change in the size of any measurable lesion or $< 50\%$ reduction of measurable disease. Progression (P) was recorded when there was $< 50\%$ increase in the sum of the products of the largest perpendicular diameter of any measurable lesion.

Results

A total of 205 patients, 113 males and 92 females, were included in the study. The age ranged between 16 years and 75 years, with a mean of 45 years. Table 1 shows the distribution by site and frequency of the tumours under review. Carcinoma of the nasopharynx and the antrum accounted for 54.2% of all the tumours in the study. The presenting features included the presence of a huge unilateral or bilateral neck swelling in 72% (Fig. 1), visible swelling on face, nose or oral cavity in 45%. The primary facial swelling and neck nodes were ulcerated in 55% of the cases (113 patients). Some of the patients had malodour from these infected ulcers. The odour was well controlled with the topical application of metronidazole in a large number of these patients [2]. The cranial neuropathy was largely confined to patients with tumours of the nasopharynx. Fourteen patients

Table 1. The distribution by site and frequency of the tumours reviewed

Tumour site	No. cases	%
Nasopharynx	69	33.7
Antrum	42	20.5
Larynx	37	18.1
Oral cavity	22	10.7
Oropharynx	17	8.3
Metastasis (undetermined primary)	13	6.3
Others	5	2.4

(7%) required tracheostomy to relieve their respiratory distress. The other presenting features are as shown in Table 2. An analysis of the histopathology report showed that 45% had poorly differentiated squamous cell carcinoma while 21% had a well-differentiated lesion. There was no histological grading in 34%, reported only as epidermoid carcinoma. Results following chemotherapy alone are as shown in Table 3. A tumour regression rate (complete and partial) of 68% was obtained. The tumour regression is further enhanced by further treatment with radiation, surgery or a combination of both. The side-effects observed from chemotherapy are as shown in Table 4. The tiredness that usually occurred within 24 h of chemotherapy disappeared within 72 h. The

Table 2. Signs and symptoms at presentation

Symptom/sign	No.	Frequency % overall
Neck mass — unilateral	103	50
Neck mass — bilateral	45	22
Ulceration over head, neck swelling	113	55
Swelling face, nose or mouth	92	45
Foetor oris	52	25.4
Bleeding from tumour	35	17.1
Nasal obstruction	27	13.1
Cranial neuropathy	25	12
Anaemia	22	11
Poor nutritional state	22	11
Tracheostomy	14	7
Poor oral hygiene	8	4

Table 3. Tumour response to chemotherapy

Response	No.	%
Complete response	32	16
Partial response	107	52
No response	37	18
Progression	29	14

chemotherapy regime was well tolerated and treatment was discontinued in only one patient who had severe oral mucositis, lip oedema and some bleeding from the lips; which did suggest methotrexate toxicity.

Discussion

The late presentation for treatment by patients with head and neck cancers in Nigeria, coupled with the long waiting list before radiotherapy of these mostly inoperable tumours, led to this study on the evaluation of combination chemotherapy as a first line of management. The results obtained are very encouraging. Advantages obtained include a debulking of the tumour, thus making further treatment by surgery or irradiation possible. The patient also obtains a psychological boost through the gradual reduction in the size of his tumour. Other advantages gained from this approach include the possibility of enhancement of the effect of radiotherapy following adequate tumour regression, particularly with the non-interference with the vascularity of the tumour itself.

Table 4. Observed side-effects following chemotherapy

Side-effect	No.	%
Tiredness	72	35.1
Nausea	32	15.6
Vomiting	12	5.8
Fever	15	7.3
Leukopenia	27	13.1
Thrombocytopenia	34	16.6
Oral mucositis (severe)	1	0.5
Oral mucositis (mild)	7	3.4
Thrombophlebitis	5	2.4



Fig. 1. Partial response to chemotherapy: (a) before, (b) after treatment. Near complete response to chemotherapy: (c) before, (d) after treatment.

Effective single agents that have been used against epidermoid carcinoma in the head and neck region include methotrexate, cis-platinum bleomycin, 5 fluoro-uracil, hydroxy-urea, the vinca alkaloids, cyclophosphamide and doxorubicin. Combination chemotherapy has been shown to provide a better result than single agent chemotherapy, although the survival may not necessarily be improved [3]. Response rates to combination chemotherapy are also known to be higher in previously untreated patients than in those patients treated after failure of local therapy [4,5].

This chemotherapy regime was well tolerated, with a response rate of 68%. Treatment was withdrawn in only 0.5%. Thus, this approach is particularly suitable in Nigeria, considering the local problems. The drugs used in combination are also regularly available, and the prescribed regimen is simple and with adequate guidelines can be safely administered even at peripheral hospitals. The patients may then be reviewed at the specialist hospital at prescribed intervals where more specialist treatment such as radiotherapy or surgery are offered.

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