Preradiation Peplomycin for Advanced Squamous Cell Carcinomas

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Summary: Locally advanced non-operable head and neck cancers are primarily treated with radiotherapy. Chemotherapy is given as a palliative measure on its own or in conjunction with radiation treatment. In this study, peplomycin (a new bleomycin derivative) is used as a single agent for the purpose of preradiation tumour shrinkage. Its acute side effects on its own and in combination with radiation are assessed. It is found to cause significant tumour shrinkage on its own and the acute toxicity is acceptable. Radiation therapy which followed did not aggravate acute toxicity.

Introduction

Squamous cell carcinoma of the lips, oral cavity and oropharynx as a group, rank fifth after nasopharynx, cervix, breast and lung as seen at the Institute of Radiotherapy and Oncology, General Hospital Kuala Lumpur. The average number of registered cancer cases annually since 1975 is 3000. The average number of lips, oral cavity and oropharynx as a group over this period is 300 ie. 10% of all cancers. Of these, ethnic Indians make up 40% of the cases although they comprise only 20% of registered cases. With few exceptions, the histological type is squamous and at presentation are beyond curative resection. Some are post surgical recurrences. In this situation, radiotherapy is given either to palliate pain, fungation, ulcerations, bleeding or related problems.

In some cases, a radical attempt at cure is made. The results of treatment in locally advanced disease with or without nodal involvement is unsatisfactory. (See table 1). The five year survival for T3 No and T3 N1-3 is only 10% and 5% respectively.[1]

STAGE	5-YEAR SURVIVAL
TINO	76%
TINI-3	66%
T2NO	53%
T2N1–3	35%
T3 NO	17%
T2N1–3	5%

Table 1:
Tumour stage and Survival for Oral Cancers treated between 1966–1970, Christie-Holt radium institute-Manchester.

However, there is a case for treating these cases. Growth restriction, tumour shrinkage and symptom relief are as important as cure itself if the patient is destined to succumb to the disease. This is more so if the treatment does not cause unacceptable morbidity and improves the quality of life.

The use of chemotherapy, pre or post radiation for locally advanced head and neck tumours have been evaluated in many studies. (P.M. Stell et al, 1983).[2] The conclusion is that ultimate survival is not improved although worthwhile responses can be obtained with improvement of the quality of life. Such treatment is a fair trade off if its morbidity is minimal and acceptable.

Common agents found to be effective include Vinblastine, Bleomycin, Methotrexate and Cisplatimun. These are often used in combination such as in the VBM regime (O'Connor A.D. et al, 1979).[3]

In this study peplomycin is used as a single agent prior to radiation therapy. Peplomycin was first studied in 1974 and later introduced into clinical use after its anti-tumour activity was established. Its activity is comparable to bleomycin but is said to be more potent with early appearing tumour effect and effective in nodal secondaries. In animal studies, late pulmonary toxicity is less.

Material and Methods

Eleven patients with locally advanced non resectable squamous cell carcinoma of the head and neck and one patient with squamous perile carcinoma were included in this study. All patients have a full physical examination, a clinical staging of tumour, CXR, blood count, liver function test, blood urea and electrolytes and histological verification of the tumour. Peplomycin was given 15 mg 1/v twice a week by slow infusion over one hour for three weeks (ie: a total dose of 90 mg of peplomycin). Table 2 gives the patient breakdown.

No	Age in Years	Sex	Race	Site	Stage (TNM)
1	71	F	Ind.	Cheek	T4 NO
2	55	M	Mly.	Cheek	T3 N0
3	67	F	Mly.	Cheek	T4 N1
4	48	F	Ind.	Cheek	T3 N1
5	50	M	Mly.	Scalp	T4 N0
6	73	M	Ch.	Penis	T4 N2
7	57	M	Ch.	Tongue	T4 N1
8	55	F	Ind.	Palate	T3 N0
9	65	M	Ind.	Floor of Mouth	T4 N1
10	60	F	Mly.	Floor of Mouth	T4 N1
11	61	F	Ind.	Tonsil	T4 N2
12	63	M	Mly.	Cheek	T3 N2

KEY: F = Female M = Male
Ind. = Indian Mly. = Malay Ch. = Chinese

Table 2:
Age, Sex, Race and Tumour Site and Stage

Upon completing 90 mg of peplomycin at the end of three weeks, all patients were given radiotherapy to the primary tumour site using a 6 MeV linear accelarator. (Patient No, 9 and 10 defaulted radiation treatment for reasons not related to

toxicity and therefore not assessible). The remaining 10 patients completed radiotherapy to a dose of 6000 cGy. Response was assessed using tumour shrinkage as the index. This was done using direct measurement after completion of peplomycin therapy but before radiation treatment and subsequently upon completion of radiotherapy.

Results

Complete resolution after peplomycin therapy was seen in one case (tongue carcinoma). Five cases showed 50% reduction of tumour bulk. Two cases showed 25% regression while two cases did not show any significant regression and these were the scalp and the penile carcinoma. After proceeding to radical radiotherapy of the five cases that had 50% regression after peplomycin, four achieved complete regression. The remaining five did not have any further significant response.

Peplomycin in the dose and methods used did not give any significant systemic toxicity. There was no acute adverse reactions. The marrow was not affected. One patient had nausea needing simple antiemetic. Radiation therapy which followed immediately, did not produce the anticipated severe acute radiation reaction in the treated volume.

Patient No.	Tumour Site	Response	Leukopenia	General Symptoms
1	Cheek	50%	Nil	Nil
2	Cheek	25%	Nil	Nil
3	Cheek	50%	Nil	Nausea
4	Cheek	25%	Nil	Nausea
5	Scalp	Nil	Nil	Nil
6	Penis	Nil	Nil	Nil
7	Tongue	100%	Nil	Nil
8	Palate	50%	Nil	Nil
9	Tonsil	50%	Nil	Nil
12	Cheek	50%	Nil	Nil

Table 3: .
Tumour Response and Toxicity after Peplomycin

Discussion and Conclusion

The role of chemotherapy in the adjuvant setting for early head and neck cancers has not been established. Its role in palliation however is significant and improvement of the quality of life is achievable with an acceptable morbidity if carefully employed. Useful agents like Cis platinum, Methotrexate and Bleomycin are often employed for this purpose. Synchronous chemotherapy using methotrexate and radiation has been reported to give worthwile response in advanced tumours (R.C.S. Pointon et al 1983).[4] Any form of effective chemotherapy of a simple nature with minimal morbidity when combined with radiation is worthwhile. In this respect it could be said that peplomycin use in the way described is well tolerated, easy to administer and response is seen in half of the cases treated. Tumour regression before the commencement of radiotherapy makes the radiation planning less formidable and radiation tolerance is better due to the smaller volume of irradiated tissue.

The long term effect especially on the lung, is not assessable. This would not be too important if the ultimate prognosis interms of survival is not altered by the treatment. If the aim in this situation is to improve the qualify of life with minimal morbidity, then this can contribute towards that aim.

References

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