

Neoadjuvant Chemotherapy in Nasopharyngeal Carcinoma

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Summary:

Back ground: nasopharyngeal carcinoma is rare in Iraq and the treatment of this tumor is usually by radiotherapy and chemotherapy.

Objectives: this study was conducted to estimate the effect of neoadjuvant chemotherapy in Iraqi patients with nasopharyngeal carcinoma

Patients and methods: This study included sixty patients already diagnosed with nasopharyngeal tumors who attended the department of oncology in Baghdad teaching hospital during the period from January 2009 to December 2010, 50 patients of them were treated by using combination chemotherapy in the form of Paclitaxel, 5-Fluorouracil and cisplatinol for 4 courses prior to radiotherapy. Neoadjuvant chemotherapy was given due to advanced stage at presentation and due to long waiting list for radiotherapy which takes at least 6 months. 10 patients were excluded from the study due to different reasons.

Results: About half of the patients had partial response to neoadjuvant chemotherapy, only 8 patients (16%) had complete response, 12 patients (24%) did not show any response and 5 patients (10%) have progressive disease during the course of neoadjuvant chemotherapy.

Conclusion: Neoadjuvant chemotherapy is beneficial in the management of Nasopharyngeal Cancer regarding local control and overall response rate.

Key words: Nasopharyngeal Carcinoma, radiotherapy, neoadjuvant chemotherapy, concomitant chemoradiation.

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Introduction:

Carcinoma of post nasal space is more common in south Asia like China, Korea and Japan due to Epstein Barr Virus infection which is considered as causative agent. (1) In Iraq carcinoma of post nasal space is a rare malignancy and it forming only 1% of all malignancies according to Iraqi cancer registry and about 7.2 % of head and neck cancer. (2) Squamous cell carcinoma is the predominant pathological type worldwide and usually is poorly differentiated. Radiotherapy is the corner stone and the main method in the management of carcinoma of nasopharynx. The role of surgery is very limited; it's just used to establish the diagnosis by taking biopsy as post nasal space is a blind space. (3) There are different ways to improve the results of radiotherapy by using chemotherapy; either in the form of neoadjuvant chemotherapy or chemoradiation which is now the standard method in the management of carcinoma of post nasal space. The applications of 3D conformal radiotherapy and Intensity Modulated Radiation Therapy definitely improves the results by giving higher dose of radiation to the primary site of tumor and decrease the dose of radiation to adjacent normal structures like eyes, parotid glands, brain stem and spinal cord. (4)

In this study we tried to focus on the result of using neoadjuvant chemotherapy as a new experience in Iraq.

Neoadjuvant chemotherapy is given before definitive radiotherapy aiming to decrease an increasing local control by radiotherapy.

Different protocol had been used for neoadjuvant setting like (5- fluorouracil and Cisplatin) or (5- fluorouracil, Cisplatin and folic acid) (3,4). In this study I used combination of chemotherapy in the form of Paclitaxel (Taxol), 5- fluorouracil and Cisplatin for the first time in Iraq as neoadjuvant chemotherapy before definitive radiotherapy.

Patients and methods:

The study comprised a total of 60 patients with tumor of post nasal space who were managed in Baghdad teaching hospital / oncology unit, during the period from the first of January 2009 to the end of December 2010. They were all clinically diagnosed and histologically proved to have post nasal carcinoma. They were evaluated regarding histological types, clinical presentations, staging, methods of treatment, and results. The Patients were treated both in Medical City/Baghdad Hospital/Oncology Unit; where they received their chemotherapy and at the Institute of Radiotherapy and Nuclear Medicine; where they received their radiotherapy. Neoadjuvant chemotherapy was given to 50 patients out of 60 patients. The remaining 10 patients were excluded due to different pathology other than squamous cell carcinoma like (non Hodgkin Lymphoma or adenocarcinoma) or presented with advanced stage, or due to their poor performance status.

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Chemotherapy was given as combination of the following:

Paclitaxel (Taxol) 175mg/m² i.v infusion Day 1.
 5 Fluorouracil (5FU) 600mg/m²i.v infusion Day 1.
 Cisplatinol (Platinol) 60mg/m²i.v infusion Day 1.
 The above combinations were given every three weeks for 4 cycles to be followed by radiotherapy.

Radiotherapy Techniques:

3D conformal radiotherapy was given to 15 patients (30% of the cases).

70 Gray/32Fraction for 6.5 weeks were delivered to post nasal space.

50 Gray to the neck node.

Booster dose to residual disease.

CT Simulation was done to all of those 15 patients.

2D radiotherapy was given to 25 patients (50%).

65 Gray/30Fraction for 6 weeks to post nasal space.

50 Gray/25Fraction to neck nodes.

Palliative Radiotherapy was given to 10 patients (20% of the cases) due to advanced disease and poor general condition. They were given only 40Gray/20Fraction for 4 weeks.

(These are internationally accepted radiotherapy doses for management of nasopharyngeal carcinoma) (3,4,11) .

Results:

Thirty five patients were males (59%) while 25 patients (41%) were females with a male to female ratio of 1.2/1

The age ranged between 13 years and 75 years with a mean age of 44 years. Forty five patients (75%) presented with cervical lymphadenopathy (LAP), unilateral in 30 patients and bilateral in 15 patients (tab.1).

Nasal symptoms were present in 40 patients (66%) mostly obstructive in nature. Earsymptoms were present in 18 patients, mostly earache, throbbing headache in 16 patients, cranial nerve palsy in 12 patients, and only 6 patients presented with symptoms related to metastasis.

The results of biopsy and histopathological examination showed that the majority of tumors were Squamous cell carcinoma (56 patients 93%) (tab.2).

Forty-six patients (76%) presented with stage III and IV (tab. 3).

Partial response to chemotherapy was achieved in about 50% of patients (25 patients) while complete response was achieved only in 8 patients (16%). The rest of the patients followed a progressive course despite treatment.(table4)

The statistical analyses were done using SPSS program and data was analyzed using Chi square test.

Table (1) Clinical presentation of 60 patients with nasopharyngeal tumor

Signs & symptoms		Number of patients	percentage
Lymph Nodes metastasis	unilateral	30	50%
	bilateral	15	25%
Nasal symptoms	obstruction	20	33.3%
	bleeding	15	25%
	discharge	5	8.3%
Ear symptoms	Earache	10	16.6%
	Otitis media	6	9%
	deafness	2	3.3%
Headache(throbbing)		16	26%
Cranial nerve palsy		12	20%
Metastasis	bone	4	10%
	lung	1	
	liver	1	

Table (2) Histopathological results (5)

Histological type		Number of patients	percentage
Squamous cell carcinoma	Poorly differentiated	50	84%
	Moderately differentiated	5	4%
	Well differentiated	1	1.6%
Non-Hodgkin's lymphoma		2	3.3%
Adenocarcinoma		1	1.6%
Transitional cell carcinoma		1	1.6%

Table (3) Staging of patients with Squamous cell carcinoma of nasopharynx

TNM Classification	stage	Number of patients	percentage
T1N0M0	Stage I	2	3.5%
T2N0M0 T1N1M0	Stage II	12	21.4%
T3N0M0 T1-2N2M0	Stage III	36	64.2%
AnyT,N3, M0 Any T, Any N, M0	Stage IV	6	10.7%

*The Staging system was that of the American Joint Committee on Cancer (AJCC). AJCC Cancers Staging Manual, Seventh Edition (2010), published by Springer Science and Business Media, was employed(6)

Table (4) Response Rate following Neoadjuvant Chemotherapy according to the stage of disease.

	Stage I	Stage II	Stage III	Stage IV	Total
Complete Response	1	7	-	-	8(16%)
Partial Response	1	5	19	-	25(50%)
NO Response	-	-	10	2	12(24%)
Progressive Disease	-	-	1	4	5(10%)
Total	2(3.5%)	12(21.4%)	30(64.25%)	6(1.7%)	50(100%)

P Value <0.001 (Significant Results) **Discussion:**

Discussion:

Nasopharyngeal carcinoma is a serious disease, and it is fatal if not treated properly. EB viruses were claimed to be a causative factor, especially in south of Asia like china, Japan, Korea and others.(1) In Iraq the real cause is not known yet. So far, no viral studies have been performed to assess the rule of EBV in the pathogenesis of nasopharyngeal carcinoma. In accordance with other studies there is a slight male predominance.(7) . Most of the patients presented with advanced stage (Stage III and IV) 76% compared to 24% of stage one and two. This is due to the fact that the nasopharyngeal space is a hidden space and many of the symptoms and signs are non specific and sometimes misleading in way makes you think of other possibilities such as nasal obstruction, allergy rhinitis, otitis media and non-specific cervical lymph adenopathy due to other diseases.(7). Most of the patients presented with either unilateral or bilateral cervical lymph nodes metastasis. 75% of patients have lymph node metastasis because of the fact that the nasopharynx is a very rich area with lymphatics, and it is considered as the main lymphatic drainage station to the upper deep cervical group.as it is seen in many studies (3)(4)(7)(11). Radiotherapy is the milestone in the management of nasopharyngeal carcinoma, the idea of radiotherapy planning is to deliver high dose of irradiation to large field side. (4). There are different ways to improve the results of treatment; one of these is the application of cytotoxic drugs. Chemotherapy has a strong impact on local control, and disease free period. Yet this modality alone is not very effective in controlling the disease.(8)(9)(10) Chemotherapy is given in two ways: either as neoadjuvant chemotherapy; three to four cycles of combination chemotherapy in the form of TPF (Taxol, Platinol, and 5Florouracile) protocol followed by radiotherapy, or as a Concomitant Chemoradiation (chemotherapy given during the course of radio therapy).(4)

This is a new study, first done in Iraq, about the benefit of neoadjuvant chemotherapy before radiotherapy in the management of nasopharyngeal carcinoma using Paclitaxel(Taxol), 5FU, and Cisplatinol. And I found that using this combination is more effective than old protocol using 5FU, and Cisplatinol only.(3)(4)(7)(11)

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