VERIZONA PUBLISHER
Publishing Your Ideas

www.verizonaonlinepublishing.com
Vol: 2, Issue: 1

Journal of Cancer Epidemiology & Treatment

Nasopharyngeal Cancers: The Evolution of Great Success

Muhyi Al-Sarraf, MD, FRCPC, FACP

National and International Consultant and Speakers, Naples, Florida, USA

***Corresponding author**: Muhyi Al-Sarraf, MD, FRCPC, FACP, National and International Consultant and Speakers, Naples, Florida, USA; Email: mealsarraf@aol.com

Article Type: Editorial, **Submission Date:** 01 August 2017, **Accepted Date:** 15 February 2018, **Published Date:** 06 March 2018.

Citation: Muhyi Al-Sarraf, MD, FRCPC, FACP (2018) Nasopharyngeal Cancers: The Evolution of Great Success. J Can Epi Treat 2(1): 1-3. doi: https://doi.org/10.24218/jcet.2018.19.

Nasopharyngeal carcinoma (NPC) is rather rare malignancy in North America and Europe, but it occurs in much higher frequency in the Far East, Middle East and North Africa. It could be considered endemic in these most/all areas/countries. Many etiological factors contribute to this distribution, including genetic, viral, cultural, etc. Migrants from these high endemic areas into other countries, the high incidence of NPC may continue through the third generation.

Patients usually present with high stage disease, locally and with regional lymph nodes involvements and the incidence of systemic metastasis are usually higher than other head and neck cancer sites.

NPC is highly sensitive to radiotherapy (RT) and chemotherapy (CT), but the five years cure rate and/or survival was low.

Before 1975 patients with stages III and IV nasopharyngeal cancers where treated with total radiotherapy (RT). In spite of good initial response to the total RT alone, the overall 5 years survival was less than 40%. Many of these surviving patients had recurrent or systemic disease.

The introduction of platinol (Cisplatin) about the mid 1970 in patients with responsive testicular cancer, let to the evaluation of this agent in these patients with NPC. Cisplatin combined with RT, Pre, concurrent or post, improved the five year survival in these patients to about 50-55% [1-6].

The combination of 5 fluorouracil and platinol (PF), are very synergetic in these patients with head and neck cancers and especially NPC. PF was evaluated in recurrent disease, and later in previously untreated patients. Only two courses of PF where used followed by surgery and/or RT[1,2].

Three courses of PF followed by total RT in these patients with stages III and IV NPC produced overall five year survival about 75% [5,6].

The intergroup study was carried on comparing total RT only to Cisplatin concurrent with RT followed by three cycles of PF in the combined arm proved the superiority of the combined arm, and became the standard of care[7-16].

In spite the huge improvement of survival in these patients with locally advanced NPC, it was rather toxic, and not all patients completed their designed total treatment.

Taxol/Taxotere was found to be effective and active in patients with advanced head and neck cancers, including those with NPC disease.

So, the combination of: Taxotere, Platinol, and 5FU 120 hour infusion, where tested in these patients with H&N cancers by investigators from few and selected institutions. This combination was doable, with expected toxicities and very active in these limited patients[8,17,20].

This lead to the Intergroup trial comparing the standard PF to the new TPF in patients with stages III and IV locally advanced H&N patients, followed by concurrent Carboplatin with total RT in both arms[16-19].

The three agents combination arm where highly superior to the two agent standard PF, and so become the standard of care.

Unfortunately, the TPF arm was very toxic, led to delay of the CT therapy, and modification of the dosage of certain agents.

Some of these side effects where serious (hematologic, nausea and vomiting, stomatitis, fluid imbalance, renal, etc.) and others where permanent (hearing loss, peripheral neuropathy).

This led us to modify the active and the new standard TPF. This very active and successful modification, led to up to 99% completely their total treatment, and more important their induction CT treatment and followed by the total CT+RT therapy[20].

We kept the agent Taxotere and dose of 75mg/m^2 on day one and every three weeks for three courses.

We changed the platinol, to Carboplatin AUC 5.0 IV on day one, and every three weeks for three courses,

And we gave the 5FU as 2,600mg/m^2 for 24 hours continuous infusion on days 1, 8, and 15.

Additional supportive medication(s) are given as needed.

All patients tolerated and completed their three courses. More important, mark reduction or abolishment of acute, subacute and delayed side effects.

These side effects of: stomatitis/mucositis, nausea and vomiting, fluid and electrolytes imbalance, renal, hearing, and peripheral neuropathy.

As important, the complete response rate to the three courses of this safe and effective combination chemotherapy was up in the high 90%.

We modified the concurrent chemotherapy given concurrent with radiotherapy, by giving Carboplatin AUC of 1.5 on the first day of RT, and then weekly during RT and for addition of 2-3 weeks after the RT was done. The reason for the additional Carboplatin was because the biological effects of RT where still on in the same period of time [20].

By using Carboplatin, and on weekly schedule, we reduced if not eliminated all possible side effects of platinol, especially the nausea and vomiting, renal, hearing and peripheral neuropathy. Patients lost minimum weight, and did not need hospitalization for further hydration or forced gastric tube feeding.

This total therapy produced 100% complete response and cure at five years.

With much improved and maintenances of organs function and quality of life.

In short, the total treatment of patients with locally and advanced NPC have evolved the last fifty years. We improved the local control; we eliminated the possibility of systemic involvement and the future recurrence. This resulted in the best survival possible for these patients with stages III and IV disease.

As important we improved the quality of life, and reduced/minimized the side effects of the agents used, and eliminated any subacute or delayed side effects. We reduced if not totally eliminated the need for hospitalization to support and maintain all body function.

In addition, the progress and huge success have been used with other epidermoid carcinomas of the different sites of the head and neck, with exact success and total results.

References

1. Kish J, Drelichman A, Jacobs J, Hoschner J, Kinzie J, Loh J, et al. Clinical Trial of Cis-Platinum and 5-FU Infusion as Initial Treatment for Advanced Squamous Carcinoma of the Head and Neck. Cancer Treat Rep. 1982; 66:471-474.
2. Decker D, Drelichman A, Al-Sarraf M, Crissman J, Reed M. Chemotherapy for Nasopharyngeal Carcinoma: A Ten-Year Experience. Cancer. 1983; 52:602-605.
3. Weaver A, Fleming S, Ensley J, Kish JA, Jacobs J, Kinzie J, et al. Superior Complete Clinical Response and Survival Rates with Initial Bolus Cis-Platinum and 120 Hour 5-FU Infusion before Definitive Therapy in Patients with Locally Advanced Head and Neck Cancer. Am J Surg. 1984; 148:525-529.
4. Al-Sarraf M, Pajak TF, Marcial VA, Mowry P, Cooper JS, Stetz J, et al. Concurrent Radiotherapy and Chemotherapy with Cisplatin in Inoperable Squamous Cell Carcinoma of the Head and Neck. RTOG Study Cancer. 1987; 59:259-265.
5. Al-Kourainy K, Crissman J, Ensley JF, Kish JA, Kelly J, Al-Sarraf M. Excellent Response to Cis-platinum based Chemotherapy in Patients with Recurrent or Previously Untreated Advanced Nasopharyngeal Carcinoma. Amer. J Clin Oncol. (CCT). 1988; 11:427-430.
6. Al-Sarraf M, Pajak TF, Cooper JS, Mohiuddin M, Herskovic A, Ager PJ. Chemo-Radiotherapy in Patients With Locally Advanced Nasopharyngeal Carcinoma: A Radiation Therapy Oncology Group Study. J Clin Onc. 1990; 8(8):1342-1351.
7. Al-Sarraf M, LeBlanc M, Giri PGS, Fu KK, Cooper J, Vuong T, et al. Chemo-radiotherapy vs Radiotherapy in Patients with Locally Advanced Nasopharyngeal Cancer: Phase III Randomized Intergroup Study (0099) (SWOG 8892, RTOG 8817, ECOG 2388). J Clin Oncology. 1998; 16:1310-1317.
8. Posner MR, Glisson B, Frenette G, Al-Sarraf M, Colevas AD, Norris CM, et al. A Multi-Center Phase I-II Trial of Docetexal, Cisplatin, and 5-Fluorouracil (TPF) Induction Chemotherapy for Patients with Locally Advanced Squamous Cell Cancer of the Head and Neck (SCCHN). JCO. 2001; 19:1096-1104.
9. Baujat B, Audry H, Bourhis J, Chan ATC, Onat H, Chua DTT, et al. Chemotherapy in locally advanced nasopharyngeal carcinoma: An individual patient data meta-analysis of eight randomized trials and 1753 patients. IJROBP. 2006; 64:47-56.
10. Al-Sarraf M. How We Wrote A Landmark Nasopharyngeal Intergroup Phase III Protocol In North America. Journal of Radiation Oncology. 2012; 1(4):415.
11. Al-Sarraf M, LeBlanc M, Giri PGS, Fu KK, Cooper J, Vuong T, et al. Chemo-radiotherapy vs Radiotherapy in Patients with Locally Advanced Nasopharyngeal Cancer: Phase III Randomized Intergroup Study (0099) (SWOG 8892, RTOG 8817, ECOG 2388). Classic Papers and Current Comments. 1999; 4:649-656.
12. Al-Sarraf M. Improving the Cure Rate and Overall Survival of Patients with Nasopharyngeal Cancers by Improving the Systemic Chemotherapy. Head & Neck. 2003; 25:447-450.
13. Giri PG, Al-Sarraf M, Nasopharyngeal Cancer. In Head and Neck Emerging respective. Ensley, Gutkind, Jacobs, Lippman, editors. San Diego, CA: Academic Press; 2003. 491-501 p.
14. Ali H, Al-Sarraf M. Nasopharyngeal Cancer. Hematology/Oncology Clinics of N. America. 1999; 13:837-847.
15. Al-Sarraf M, Reddy MS. Nasopharyngeal Carcinoma. Current Treatment Options in Oncology. 2002; 3:21-32.
16. Al-Sarraf M, LeBlanc M, Giri PGS, Fu K, Cooper J, Vuong T, et al. Chemo-Radiotherapy (CT-RT) vs Radiotherapy (RT) in Patients (PTS) with Advanced Nasopharyngeal Cancer (NPC). Intergroup (0099)(SWOG 8892, RTOG 8817, ECOG 2388) Phase III Study: Progress Report. Proc ASCO. 1998; 17:385a.

17. Posner MR, Glisson B, Al-Sarraf M, Frenette Gp, McLaughlin WP, Norris CM, et al. A Multi-Center Phase II Study of Induction Chemotherapy with Taxotere (T), Cisplatinum (P), and 5-Fluorouracil (F) (TPF) for Curative Treatment of Locally Advanced Squamous Cell Carcinoma of the Head and Neck (SCCHN). Proc ASCO. 1999; 18:394a.

18. Al-Sarraf M, LeBlanc M, Giri PGS, Fu K, Cooper J, Vuong T, et al. Improved five years survival with chemo-Radiotherapy (CT-RT) vs Radiotherapy (RT) inpatients (PTS) with Advanced Nasopharyngeal Cancer (NPC). Intergroup (0099) (SWOG 8892, RTOG 8817, ECOG 2388) Phase III Study: progress Report. Ann Oncol (Suppl 4). 2000; 11:90.

19. Al-Sarraf M, LeBlanc M, Giri PGS, Fu K, Cooper J, Vuong T, et al. Superiotity of five year survival with chemo-radiotherapy (CT-RT) VS radiotherapy in patients (PTS) with locally advanced nasopharyngeal cancer (NPC). INTERGROUP (0099) (SWOG 8892, RTOG 8817, ECOG 2388) PHASE III Study: final report. Proc ASCO. 2001; 20:227a.

20. Al-Sarraf M, Bhalla P, Chen P, Jaiysimi I, D'Errico A. Feasibility and Effectiveness of Combination of Docetaxel, Carboplatin, and 5-FU Infusion (TCF) were Given on Outpatient Basis in Patients (pts) with Advanced Head and Neck Cancers (AHNC). Proc ASCO. 2003; 22:514.