Non-Small Cell Lung Cancer(NSCLC) - Spectrum, Management and Prospects

Itrat Mehdi (Pakistan Medical Research Council, PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Lung cancer is the commonest malignancy and leading cause of mortality in America and Europe with an overall 5 year survival around 13%, with an ever increasing incidence over the last 50 years[1-3]. The rise in incidence is more swift and alarming in females and more so in adencarcinoma variant[3]. The age-adjusted death rate has increased over the last few years[4]. Non-Small Cell Lung Cancer (NSCLC) constitute about 80% of lung cancers and its main distinct histological variants are squamous cell carcinoma, large cell carcinoma, adencarcinoma, and bron cho-alveo l ar carcinoma[5]. Para-neoplastic syndromes are commonly associated with lung cancer but less commonly seen in NSCLC[6]. In our population lung cancer is 7.9% of tumors in adult male and 1.1% of adult female tumors, with NSCLC accounting for 85.1%[7,8].

The major risk factors are cigarette smoking (number of cigarettes per day, duration of smoking, younger age at the onset of smoking, degree of smoke inhalation, tar and nicotine content of tobacco, use of filters). Passive smoking occupational care inogenic exposure(asbestos, arsenic, chromium. alkylatiiig agents, nickel, and mustard gas). Exposure ionizing radiation and mineral oils are other etiological factors[6].

Therapeutic options for NSCLC are surgery, radiotherapy, chemotherapy, and best support care either alone or in different combinations. Any therapeutic strategy employed should demonstrate at least 1 5% objective response rate, a definite survival benefit over best support care (BSC) alone and should improve quality of life[9-11] The criteria for selecting a treatment modality are tumor histology, clinical stage at diagnosis, age of the patient, performance status, expected survival, associated co-morbid conditions and patient's own choice or selection.

Surgical intervention with intent to cure/eradication is the prime option in stage I and II disase. A 5-year survival rate of 40% is reported in carefully selected cases undergoing curative resection[12], Surgery, pre-operative or adj uvant radiotherapy, neo-adjuvant and adj uvant chemotherapy can be used in stage III disease. in stage IV disease surgery is contra-indicated and radiotherapy, chemotherapy or best support care is instituted with a palliative intent[5,13]. Majority (70-80%) of NSCLC, due to late presentation, are either un-resectable or in stage IV making them inoperable at the time of diagnosis[4,14]. An extensive metastatic work up is essential before a surgical decision and yet there seems to be no way to detect micro/occult metastasis with the best available diagnostic tools. That is the reason why 30-75% operated cases later show metastasis[15]. Chemotherapy alone or combined chemotherapy is thus employed in majority of NSCLC. Neo-adjuvant chemo-radiotherapy is also suggested to have a role in management[16]. Poly-chemotherpy using double or triplet combinations is found to be better in NSCLC[17,18]. Many new promising chemotherapeutic molecules with consistent higher response rate (exceeding 25%) and significant survival and response benefit are now available like gemcitabine, ifosfamide, vinorelbine, CPT-II Paclitaxel and docetaxe[16,19]. Many other factors also contribute to this improved prognosis like patient selection, better support care, growth factors, more extensive screening tool (spiral CT, Positron emission tomography)[19]. A combination of gemcitabine and cisplatin has shown best median survival (8.1 month), one year survival rate 36%, Overall response rate 21%, time to progression 4.5 months and progressive disease as 50%. This is however a regimen with cinsiderable potential toxicity[20]. Encouraging survival benefit with triplet regimens is recently

reported but with higher toxicity profile and a more compromised quality of life[21], Second line chemothrerapy mostly has shown inconsistent and disappointing results with an exception of docetaxol[22]. Gene therapy with transfer of tumor suppresser genes (Wild-type p53 is reported feasible with low toxicity profile, having a therapeutic potential in times to come[23].

There is growing concern for optimal management of geriatric patients with lung cancer due to higher incidence in this particular age group and increasing proportion of geriatric population[24], Co-morbid conditions, reluctance to treat, common belief to have a less therapeutic gain, risk of enhanced toxicity due to declining physiological reserves are the major limitations in Oncologist's opinion whether or not to treat.

There has been relatively little and slow progress in survival, disease free survival, response to therapy and mortality over the last quarter of the century indicating the slow rate of progress in this lethal disease[25]. In-spite the availability of newer more active chemotherapeutic molecules and better understanding of lung tumor biology; the long-term survival remains low. Although the disease is a preventable one, the political and economic repercussions are the main drawbacks in prevention program all over the globe[6]. There is an obvious need to encourage the development of a health and disease oriented culture; where patient, family physician, health care workers and health authorities should work in a closely knitted system for a prompt and efficent health care delivery. Respiratory symptoms should never be ignored and must be thoroughly investigated in age group over 40 years especially in smokers. MRI is better than CT as a diagnostic aid but nodal staging potential is poor in both with only over I-cm lymph node detectable. FNAB, mediastinoscopy, sputum cytology and bronchoscopy have changed the bleak outlook at the outset, which was due to late presentation. The more early presentation will become a reality if it can be combined with health education, an integrated primary health care, better understanding and training at the end of primary health care physicians. Future directions will focus on newer less toxic molecules, optimal management in elderly patients, management in compromised performance status cases, salvage therapy with intact performance status cases, quality of life, quality adjusted survival, biologic response modifers[19] and hormones[26]. Except for unwilling or unsuitable patients there is no room for therapeutic nihilism.

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