THE ROLE OF P53 GENE IN LUNG CANCER WITH SPECIAL EMPHASIS ON HEREDITARY TYPES

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Lung cancer is the most common type of cancer affecting men and the fifth most frequent female cancer. The survival rate related to lung cancer is low, with the 5-year survival amounting to 10-13% in highly advanced countries. In Poland lung cancer survival does not exceed 5%.

The major causes of lung cancer incidence include tobacco smoking, environmental factors and genetic predisposition. The most frequent genetic modifications observed in lung cancer cells are mutations in the *myc*, *ras* and/or *erb1* genes.

The p53 gene has been located on the short arm of chromosome 17 and has been found to consist of 11 exons with the first one being non-coding. The analysis of its sequence in different species resulted in identifying five highly conservative regions, including exons 1, 4, 5, 7 and 8. The p53 has been classified as a suppresser gene.

The p53 protein is a nuclear phosphoprotein composed of 393 amino-acids. This protein is active in the two most important stages of the cellular cycle: during the transition between phases G_1 and S and between phases G_2 and M. The function of p53 can be described as ensuring the integrity of the genome by preventing replication of the damaged DNA and cell division. When the repair process fails, p53 triggers the apoptosis of cells. In addition to the regulatory function, p53 acts also as a transcription agent.

Mutations in p53 are responsible for 60% of cases of human lung cancer. The mutations are most often found in microcellular lung cancer (70%) and are less frequent in the cases of adenoid lung cancer (33%). The most common mutations related to lung cancers include: transversions of the G:C/A:T type, missense mutations, nonsense mutations and deletions. These mutations occur in as many as 100 various locations but the most characteristic ones for lung cancer are found in codon 157, 248 and 273. The hereditary mutations in p53 are associated with the Li-Fraumeni syndrome. This syndrome indicates a higher risk of developing different forms of cancer, including lung cancer. Genetic testing aimed at identifying the carriers of p53 mutations should be limited only to high-risk groups defined on the basis of a diagnostic pattern proposed by Lynch. In the families with one member affected by lung cancer the risk of developing lung cancer by first-degree relatives is four times higher compared to general population risk.

CONTINUOUS ACCELERATED IRRADIATION (CAIR) OF HEAD AND NECK CANCER - TREATMENT TECHNIQUE, TOXICITY AND 2-YEAR RESULTS

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Purpose

Evaluation of preliminary (2-year) treatment results of 7 days a week continuous accelerated irradiation (CAIR) in compare to convectional and concomitant radiotherapy.

Methods

One hundred and twenty eight patients with squamous cell carcinoma of oral cavity, oro- and hypopharynx and supraglottic larynx in stage T2-4 NO-1 MO were randomized between 3 groups: A (study-CAIR) - 51 pts, B (control-2) - 28 pts and treated by radiation therapy alone in 1994-96. In majority (81%) there were the patients in advanced clinical stage (T3+T4). Patient and tumour characteristic, radiation technique and volumes, total and fraction doses were exactly the same in 3 groups of patients. Only the overall treatment time was shorter by about 2 weeks in CAIR group comparing to control-1 because of the lack of weekend breaks. The overall treatment time in CAIR and control-2 group was exactly the same because in control-2 group the "CAIR weekend fractions" were given through the Tuesday and Fridays as a concomitant boost.

Results

One hundred twenty five patients (98%) completed the whole designed radiotherapy. Generally, 2-year local tumour control rate (LTCR) in CAIR arm was 87% and in control-1 and control-2 arms respectively 40% and 67% ($p<0.0001$ log rank). In aspect of tumour localization and stage the LTCR was significantly higher in CAIR arm than in controls and was respectively as follows:
75% vs 10% and 33% in oral cavity,
86% vs 36% and 70% in oropharynx,
88% vs 50% and 80% in hypopharynx and supraglottis;
100% vs 64% and 78% for T2,
94% vs 39% and 67% for T3,
66% vs 26% and 56% for T4.
There were 14% of grade III and IV radiation morbidity in CAIR arm and 4% and 10% in control-1 arms respectively.

Conclusion

The hight effectivness of CAIR fractionation reflects the net effect of not only the simple shortening the overall treatment time by 2 weeks but also the exclusion treatment weekend breaks.

MALIGNANT MELANOMA. RESULTS OF PALLIATIVE RADIOTHERAPY.

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Introduction

Radiotherapy of malignant melanoma is often performed in palliative therapy of recurrences, metastases "in transit", bones and brain metastases, to prevent bleeding and to control the pain. Because of existence of large "shoulder" in the radiation cell survival curve, high fraction doses are used.

Material and Methods

27 patients with local lymph nodes metastases or local recurrences of malignant melanoma were palliatively irradiated. This group included patients after surgical treatment and disqualified for second operation. They were irradiated with 9 MV photons or Co 60 gamma rays, fraction dose was of 6 Gy (2 fractions weekly), total dose was of 36 Gy (18 patients) or 48 Gy (9 patients).

Results

Total remission was achieved in 14 cases, partial remission in 8 cases, no remission we observed in 5 cases. 5-year survival rate was 40,7% (11 patients). In the group of patients irradiated with total dose of 36 Gy 5-year survival rate was 44,4% (8 of 18), in other group irradiated with total dose of 48 Gy 5-year survival rate was 33,3% (3 of 9).

Conclusion

Part of patients with malignant melanoma cured with palliative radiotherapy can survive over 5 year.