

I S — 1 Molecular genetic analysis of cervical carcinoma

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[Objective] Loss of heterozygosity (LOH) of some tumor suppressor genes is harbored on some chromosome region involving in the development of various cancer. To further clarify the carcinogenesis which may be involved in cervical carcinoma, we have investigated the LOH of TP53, p16, RB1, NM23, DPC4, PTCH, DCC and WT1 in the lesions of cervical carcinoma. **[Materials & Methods]** DNA samples from 36 cases of cervical carcinoma, and corresponding normal cells were extracted from formalin-fixed, paraffin-embedded tissues. The tissues were used after obtaining written consent from the patients. Histologically, 25 cases were squamous cell carcinoma (SCC), 11 cases were carcinoma in situ (CIS). LOH was analyzed using 8 DNA polymorphic markers. The correlations between LOH and clinicopathological parameters including clinical stage, histologic type, grade and lymph nodes metastases were statistically analyzed. **[Results]** Of 36 cases of cervical malignancies, LOH were detected in 12 cases (44%) in SCC, 2 cases (18.1%) in CIS. The rate of LOH of TP53, WT1, DPC-4, p16, NM23, and RB1 was 8.3 %, 13.9%, 13.9%, 5.6%, 11.1%, and 16.8%, respectively. Only one case showed LOH of DCC locus. The most frequently LOH of PTCH locus is detected in cervical cancer (25%). A significantly higher rate of LOH was observed in SCC than CIS. In addition, no significant correlation was found between the LOH of these tumor suppressor genes and clinicopathological parameters. **[Conclusion]** These results suggested that genetic alterations of these tumor suppressor genes are important for the development of cervical carcinoma.

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Combined Adjuvant Radio-chemotherapy in Patients with Cervical Carcinoma and a High Risk of Recurrence

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Therapies involving radical operation and radiation treatment for cervical carcinoma in stages I and II seem not to be sufficiently effective in certain patient subgroups. In general, combined chemo - radiotherapy has a high toxicity.

Twentyone-patients with at least 2 risk factors for recurrence were treated with an adjuvant chemotherapy after radical hysterectomy. The protocol consisted of 3 cycles of Ifosfamide 16mg/m² (d1-3) and Carboplatin (AUC4, d1) triweekly. For cell protection the patients received Amifostine 740 mg/m² d1- 3; this was followed by standard radiation therapy (percutaneous and afterloading). The dose determination of the substances, their toxicity and the DFS were investigated.

Patient data: average age 42.9y (range: 25-70); radical hysterectomy: 21, pT1b - 2a 12, pT2b: 9, pN1: 16, pN0: 5, G1 - G2: 18, C3: 3, squamous cell cancer: 16, adenocarcinoma, 5 Median number of cycles of chemotherapy: 2.8, Median observation time: 29.7 months (range: 6-36), median DFS: 19.5 months

Patients with a local recurrence: 4 (2 without radiation, 2 with grade 2, 3 with pT1bpN1, 1 with pT2bpN1)

Toxicity of chemotherapy and radiotherapy; Toxicity(OTC):23(anemia: grade 3-4; 3, grade 2; 10; leucopenia: grade 3 - 4; 3, grade 2: 1), no grade 2 or greater radiotherapy toxicity, no renal toxicity.

This combined adjuvant therapy was effective and showed relatively few side effects, which might be due to the use of Amifostine. To counteract the high rate of anemia, prophylactic administration of Erythropoietin might be attempted in a Phase-III study.