520 PUBLICATION

Treatment of malignant hipbone tumors

G.M. Vedzizhev, B.G. Vedzizhev. *Medical Radiological Research Center of RAMS, Obninsk, Russia*

Purpose: The results of therapy for malignant hipbone tumors were evaluated.

Methods: 27 patients were operated on. 25 patients had primary malignant tumors and 2 had metastases. There were 18 males and 9 females aged from 14–70 years. Chondrosarcoma was present in 18 cases, fibrosarcoma in 3, angiosarcoma in 2, metastases in 2 (lung cancer and hypernephroma), leiomyosarcoma in one and osteogenic sarcoma in one case. Autoplasty was performed in one patient, alloplasty in 2 patients, 24 patients without osteoplasty underwent operation. 10 patients received radiation therapy plus polychemotherapy.

Results: Recurrences occurred in 11 patients who were operated on again. 3-year survival made up 70%, 5-year survival – 40% and 10-year survival – 35%.

Conclusion: Sparing surgery is promising in therapy for malignant hipbone tumors.

521 PUBLICATION

Overexpression of p53 and MDM2 proteins in soft tissue tumors. The correlation with p53 gene mutations and searching for prognostic factors

J. Ryś[1], A. Kruczak[1], R. Schneider-Stock[2], A. Wasilewska[1], W. Szklarski[1], A. Gruchala[1], A. Sokołowski[1], D. Markiewicz[1], A. Roessner[2], A. Niezabitowski. [1]*Cracow Center of Oncology, Poland;* [2]*Institute of Pathology, Otto-Guericke University in Magdeburg, Germany*

The alterations of p53 gene are associated with removal of its negative growth control signals and with uncontrolled proliferation of cells. The mutant p53 protein has a much longer half-life time, accumulates in large amount in the nuclei of transformed cells and can be detected immunohistochemically. The prognostic value of p53 mutation, as well as the overexpression of mutant p53 protein in mesenchymal tumors is still controversial. Whereas some studies demostrated the correlation of p53 alterations with indicators of tumour aggressiveness, others did not confirm their role as a criterion of malignancy. The goal of present study is to evaluate 1) the frequency p53 gene mutation and the overexpression of p53 protein in soft tissue tumors, 2) the relationship of p53 alterations, proliferation activity, ploidy and others clinico-morphological parameters including disease-free- and overall survivals of patients.

Material and Methods: The study was performed on 70 soft tissue tumors from 63 unselected patients. For estimation of p53 mutations exons 5–8 of the p53 gene were analyzed by PCR-SSCP technique. For an evaluation of the immunohistochemical status 4 monoclonal antibodies against different epitops of p53 protein (DO-7, BP 53-12, p53–1801, and MCA 909) were used. The MDM2 expression was estimated immunohistochemically using two monoclonal antibodies produced by Oncogene and Novocastra. The evaluation of proliferative activity was based on Ki-67 (MIB) immunostaining. The influence on survival has been assessed by log-rank test and Cox proportional hazard model. Multiple model was also estimated with stepwise selection procedure.

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Prolonged survival with complete resection of lung metastases

S.E. İnanç[1], H. Onat[1], E. Darendeliler[1], H. Çamlıca[1], G. Kalaycı[2]. *Istanbul University;* [1]*Institute of Oncology;* [2]*Istanbul Medical Faculty, Div. Thoracic Surgery, İstanbul, Turkey*

We have reviewed the experience with resection of lung metastases (MTS). Between 1993–1996, metastatectomy (MTT) has been performed in 14 patients (pts) (renal cell carcinoma-RCC-3, germ cell cancer-GCC-1, soft tissue sarcoma-STS-4, osteosarcoma-OS-6). Lung MTS was the only site of recurrence in all but one patient with STS who also had a local recurrence that was resected. Two pts (1 RCC, 1 GCC) had MTS on presentation, and resection was performed following systemic treatment. Twelve pts developed MTS during follow-up, with seven presenting >12 months after the completion of treatment for the primary tumor. The median disease-free survival (DFS) before resection was 11.5 months (4–36). Eleven pts had one to 3 nodules and 3 had multiple nodules (12, 14, and 42) resected. One patient was unevaluable for response after MTT. Radiologic complete resection was achieved in 8 pts (%61.5); two pts with residual nodules after resection converted to complete response after additional chemotherapy. Two pts with STS developed lung MTS (one with a single large brain MTS in addition) after a disease-free period of 11 and 20 months, and were reoperated. The median follow-up is 36 months (13–71). Median DFS after MTT is 30 months (0–50), and the median survival has not been reached yet. Although the small number of pts precludes analysis, the long term survivors are the pts with MTS on presentation and those with long DFS before the emergence of MTS.

523 PUBLICATION

Soft tissue sarcomas – Surgical tactics and multimodality treatment

P. Klein, L. Pahlke, B. Reingruber, J. Göhl, W. Hohenberger. *Chirurgische Universitätsklinik Erlangen, Germany*

Prior to any treatment, the malignancy has to be confirmed histopathologically. Smaller tumours may be removed by a diagnostic excision, i.e. complete removal of the tumour together with a small margin of uninvolved tissue. In larger tumours, a generous incisional biopsy producing >1 cm^3 of representative tissue should be performed under consideration of the definite surgical access.

The aim of any surgical treatment is a radical removal of the tumour with a histological confirmation of tumour free margins. To scrape the tumour out of its capsule is insufficient. Adequate tumour resection can in most cases be achieved by muscle group resection, wide radical excision or amputation of the affected limb. After wide radical excisions, adjuvant hyperfractionated radiation treatment was added in our series.

Between 1983 and 1993, 189 patients were treated for soft tissue sarcomas at the Chirurgische Universitätsklinik Erlangen. 90 of these were primary tumours. 59 patients had the sarcoma located at the extremities.

Adequate surgical treatment provided, the decisive prognostic factor in multivariate analysis is the grading of the tumour. 5-year-survival was above 70% if an R0 situation could be achieved; if not, survival was below 20%.

524 PUBLICATION

The multidrug chemotherapy: mitomycin C (MTC), vinorelbine (VNB), carboplatin (CBPT), mitoxantrone (MTT), calcium folinate (CF), 5-fluorouracil (5-FU) in the treatment of advanced breast cancer (ABC)

K. Szarlej-Wcislo, K. Zabkowska, M. Gomasiowa, C. Szczylik. *Department of Oncology Central Clinical Hospital Military Medical Academy, Warsaw, Poland*

Purpose: It has been accepted that multidrug chemotherapy is the most effective way of achieving a high number of remissions even in patients (pts) with ABC.

Methods: From December 1994 to November 1996 14 female pts with ABC after previous treatment (surgery, chemo-, hormono-, radiotherapy) were treated of the multidrug regimen. The study was designed to evaluate the feasibility, efficacy and toxicity of the multidrug regimen as follows: 1st week – 1st. day: CF 60 mg p.o. every 8 hours (hrs); 2nd day: CF 60 mg p.o. every 8 hrs. CF 150 mg/m^2 i.v., 5-FU 500 mg/m^2 i.v. MTC 5 mg/m^2 i.v. 2nd week – 1st day: CF. 60 mg p.o. every 8 hrs; VNB 50 mg/m^2 i.v. 2nd day: CF 60 mg p.o. every 8 hrs; CF 150 mg/m^2 i.v.; 5-FU 500 mg/m^2 i.v.; CBPT 50 mg/m^2 i.v. 3rd week – 1st day: CF 60 mg p.o. every 8 hrs; 2nd day: CF 60 mg p. o. every 8 hrs; CF 150 mg/m^2 i.v.; 5-FU 500 mg/m^2 i.v.; MTT 12 mg/m^2 i.v. Cycles were repeated every 5 weeks.

Results: In the investigated group of pts 77 cycles of such a chemotherapy have been delivered (median/patient: 5.5 cycles). 10 pts (71.4%) are alived, 4 pts (28.6%) died. In 15 cycles (19.5%) delay of chemotherapy was required because of grade 4 neutropenia was observed in 6 pts (42.9%) and 15 cycles (19.5%). Grade 4 infections was observed in 5 pts (35.7%). Nonhematologic toxicities included: phlebitis (2 pts), pulmonary thromboembolism (1 patient), ileus (1 patient), oral candidiasis (7 pts), nausea/vomiting (7 pts), diarrhoea (2 pts), reversible alopecia (8 pts). In the period of observation following responses: 6 CR (42.9%), IPR (7.1%), ISD (7.%), 2PD (14 2%). 1 patient died of toxicity (ileus) and 3 pts died of progression of ABC.

Conclusion: The multidrug regimen (MVCMtF) determines new challenge for the treatment of female pts with ABC.