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RESPONSE KINETIC UNDER INITIAL CYTOSTATIC TREATMENT ACCORDING TO PROGNOSIS OF RHABDOMYOSARCOMA - A REPORT FROM THE CWS-81 STUDY OF THE GERMAN SOCIETY OF PEDIATRIC ONCOLOGY (GPO)

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Between 1981 and 1985, 290 patients with malignant soft tissue tumors were registered in the CWS-81 study. These patients came from 48 clinics in West Germany, 185 of them (63.8%) were rhabdomyosarcomas (RMS). The disease-free survival rate (DSF) for stage I is 83%, for stage II 64%, for stage III 52%, for stage IV 33% and for stages I-IV 57%. The median observation time is 27 months. The DSF rates by site of tumor are the following: paratesticular RMS 89%, RMS of the orbit 80%, urogenital RMS 67%, RMS of the head and neck (orbit excluded) 49%, abdominal RMS 37%, RMS of the extremities 23%.
We checked the prognostic significance of histologic subtypes (alveolar versus embryonal RMS), the influence of primary bone involvement, the influence of lymph node involvement, tumor diameter and the influence of tumor reduction per unit of time under initial cytostatic treatment. Tumor reduction per unit of time was the major hazard function affecting relapse-free survival time. Response under initial chemotherapy up to week 7 was classed into 4 groups: tumor regression complete (100% DSF rate), regression >2/3 but not complete (67% DSF rate), regression <2/3-1/3 (25% DSF rate) and tumor reduction <1/3 or tumor progression (27% DSF rate). This a very new and important aspect, valid for individual treatment strategy as well as for prognosis of therapeutic studies in the future.

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THE SIGNIFICANCE FOR RADIOTHERAPY WITHIN RHABDOMYOSARCOMA TREATMENT ACCORDING TO THE CWS-81-STUDY.

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290 children with rhabdomyosarcoma (RMS) were treated since 1981 according to the "Cooperative-Weichteil-Sarkom-Studie (CWS-81)". Initial therapy was chemotherapy with VACA (Vincristin, Adriamycin, Cyclophosphamid, Actinomycin D) for stage I-IIB followed by surgery and restaging. Stage I patients got only chemotherapy. Radiotherapy was given up to 40 Gy in case of microscopical residual tumor and up to 50 Gy if there was gross residual. Stage IIB and III patients not responding to initial VACA chemotherapy were irradiated up to 30 Gy with a change of chemotherapy to VAIA (Vincristin, Adriamycin, Ifosfamid, Actinomycin D). The therapy was completed by surgery and boost radiotherapy up to 50 Gy.
120 Children got adiuvant irradiation. These are the conclusions of the treatment results: 1) Limb lesions and alveolar type of RMS need radiation even if they were stage I cases. 2) Stage I and II RMS with bone involvement should be treated by additional radiotherapy up to 50 Gy. 3) Initial stage III cases being downstaged to I should get chemotherapy only. 4) Patients being downstaged to II need radiotherapy up to 50 Gy. 5) Embryonal rhabdomyosarcoma not responding to chemotherapy seems to be sensitive to additional radiotherapy in contrast to other histologic types.

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TREATMENT OF METASTATIC NEUROBLASTOMA WITH METAIODOBENZYL-GUANEDINE IN CHILDREN

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We treated 9 children withneuroblastoma with Metaiodobenzylguanedine (MIBG) in altogether 23 treatment courses. 4 of these had a relapse of neuroblastoma, 3 had never reached a remission in spite of very intensive therapy and 2 were treated during the 1st or 2nd remission. 5 of these children lost their bone pain and fever during the first 3 days of therapy. In 6 of 7 children with a manifest tumor the solid tumor part as well as the bone marrow-infiltration responded to the MIBG-therapy:Response extended from transitory decrease of the tumor mass to complete disappearance of great abdominal tumors. We also saw a stabilization of osteolytic lesions, a decrease of elevated serum catecholamines and a decrease of bone marrow infiltration. 5 of the 7 children with a manifest tumor died of the tumor progression 55 to 249 days after the begin of MIBG-treatment. 2 lived without evidence of disease up to 350 days after begin of MIBG-treatment after having transplanted with autologous bone marrow. All the children tolerated the therapy very well. For them and their parents the procedure seemed to be much less harmful than chemotherapy. Side effects were only seen as transitory bone marrow depression. No changes in blood pressure or adrenal function were observed.
Before using MIBG therapeutically we had demostrated,that it is a useful substance for scintigraphic imaging of neuroblastoma(J.Treuner et al,NucCompact 15,23,1984) and we had investigated the cytotoxicity and uptake in various neuroblastoma cell-lines(J.Buck et al,Cancer Res.in press). MIBG is a new therapeutic substance which's effect in neuroblastoma relapse patients could be proved and which seems to be very promising in close connection to bone marrow transplantation as well as at a more early moment in neuroblastoma therapy.

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SKELETAL INVOLVEMENT IN NEUROBLASTOMA: RADIOGRAPHIC PATTERNS AND DIFFERENTIAL DIAGNOSIS

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Among solid tumours in childhood neuroblastoma stands out by frequent and early dissemination in the skeleton which may cause symptoms before clinical manifestation of the primary tumour and require a roentgenological differentiation from other primary or secondary bone lesions in this age group, e.g. leukaemia, osteosarcoma, Ewing's sarcoma, Hodgkin's disease, histiocytosis X, Wilms' tumour, rhabdomyosarcoma and osteomyelitis.
In a review of the X-ray findings in 13 children (age range 1 to 12 years; median age 4.8 years) more than 40 skeletal lesions of neuroblastoma were analysed and compared with other skeletal lesions in this age group. Following patterns of skeletal involvement in neuroblastoma were revealed:

(1) multifocal, rapidly progressive dissemination in the skeleton,
(2) frequent localisation in the skull (9 of 13 pts.) in a combination of
    - multiple punctiform osteolytic areas,
    - widening of the sutures,
    - spicular new bone formation,
(3) bilateral, nearly symmetric dissemination, mostly in the femur, pelvis and humerus.

In children elder than 1 year the stage of disease at diagnosis is the most important prognostic factor. Skeletal involvement (stage IV-B following Evans et al., III-B/C following Hayes et al.) must be diagnosed early for selection of treatment (multi-agent-chemotherapy).

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