510 PUBLICATION

Primitive neuroectodermal tumours/extra-osseous Ewing's sarcoma. Ten years of experience at Portuguese Institute of Oncology – Porto

José Dinis, Narciso Oliveira, Isabel Azevedo, Deolinda Pereira, Helena Rodrigues, Machado Lopes, M.C. Azevedo. *Portuguese Institute of Oncology, Porto, Portugal*

Peripheral primitive neuroectodermal tumours (pPNET) and Ewing's sarcoma (ES) are rare small round cell tumours. ES may arise in the soft tissues and is then refered to as extra-osseous Ewing's sarcoma (EOES). Both pPNET and ES/EOES have a specific chromossome translocation between chromossomes 11 and 22 – t(11;22) (q24;q12), suggesting a common cytogenetic event with different pathway of differentiation. Data on pPNET and EOES are rare.

We report a series of 14 consecutive patients, older than 15 ys (13 pPNET and 1 EOES) treated at the Porto Cancer Institute since 1988. Characteristics: median age 20 (15–42); 10 Males and 4 Females; 11 local and 3 with metastatic disease; 5 upper limb, 2 lower limb, 3 thorax, 1 lumbar, 3 pelvis. Chemotherapy was in all cases VADRIAC regimen.

Surgery (1 pt) and Radiotherapy (13 pts) were used for local control. It was observed 7 CR, 1 PR and 6 PD (response rate: 57.1%). Two years survival was 30% with a median survival of 13 months. At present 3 pts are alive and disease free with a follow up of 11, 15 and 87 months, respectively.

Multidisciplinary approach seems essential in improving treatment results in these rare tumours. The optimal chemotherapy schedule and timing of local therapies is still to be assessed.

511 PUBLICATION

Soft tissue sarcomas: Results of a retrospective study

M. Julieta Silva, M. Rosário Valsassina, Filomena Santos, M. Cândida Trindade, M.B. Patricio. *Department of Radiotherapy, Instituto Português de Oncologia de Francisco Gentil, Centro de Lisboa (IPOFG-Lisbon), Portugal*

Purpose: To evaluate the importance of Radiotherapy for treatment of soft tissue sarcomas and determine factors influencing disease and patient survival.

Type of Study: Retrospective analysis of 142 patients' files afflicted by primary, metastatic or recurrent soft tissue sarcoma, referred for irradiation to Radiotherapy Dept. of IPOFG Lisbon, between 1979 and 1991. Patient age and gender, primary localisation and histological type of the tumour, disease stage, modalities of therapy, extend of surgical excision, radiation dose, survival and relapse time of the disease were evaluated.

Results: 68 patients were males and 74 females, age ranging 1 to 86 y. Most of the tumours were primary, located to extremities. Histologically fibrosarcomas, neurogenic sarcomas and rabdomyosarcomas predominated. Prior diagnosis, the disease was present between 1 and 120 months. In 76% of cases ^{60}CO was used. Post surgical radiotherapy followed or not by chemotherapy was performed in the majority. Survival varies according to age (better after 50th), tumour localisation (extremities 46%, other areas 54%), disease stage (earlier without dissemination, the better), tumour type, extent of resection (larger the better), type of therapy and radiation dosage (better for >60 Gy).

Conclusions: Therapeutic efficacy depends on various factors and radiotherapy provided good effects in cases of soft tissue sarcomas, beeing effective in preventing relapses.

512 PUBLICATION

Orthotopically transplanted human synovial sarcoma xenografts in nude mice

S. Crnalic[1], L.-Å. Brostrőm[1], L. Boqvist[2], R. Löfvenberg[1]. [1]*Department of Orthopedics,* [2]*Department of Pathology, Umeå University Hospital, Umeå, Sweden*

Purpose: An experimental tumor model with subcutaneously transplanted human synovial sarcoma xenografts has been established in our laboratory. The purpose with the present study was to establish a new human spontaneous metastasis model using orthotopic transplantation of histologically intact synovial sarcoma tumor tissue into the thigh muscles of nude mice.

Methods: Intact tumor pieces, obtained from the 3rd and 7th serial passages of two different subcutaneously growing human synovial sarcoma xenografts were implanted into the distal thigh in close proximity to the knee joint in 46 nude mice. The animals were sacrificed and autopsied 4, 8 and 11 weeks after transplantation and examined macroscopically and microscopically for local tumor growth and metastases.

Results: All mice developed local tumors histologically similar to the primary human tumors as well as the subcutaneously growing tumors. Metastases were observed in lung, liver, spleen and lymph nodes.

Conclusion: This new spontaneous metastasis model of human synovial sarcoma in nude mice, may resemble the clinical situation and could thus be useful for studies on local tumor growth, metastasis formation and therapy.

513 PUBLICATION

Cooperative study of soft tissue sarcoma: First results

T. Brodowicz, C. Wiltschke, M. Krainer, P. Ritschl, R. Windhager, W. Dobrowsky, R. Pötter, G. Amman, S. Lang, M. Salzer-Kuntschik, R. Kotz, C.C. Zielinski. *Departments of Oncology, Pathology, Radiationtherapy & Orthopedics University Hospital, Vienna, Austria*

In the present study we investigated the efficacy of an adjuvant chemo- and/or radiotherapy on wide-marginal or radical locoregional operable soft tissue sarcomas (STS) without distant metastases. Cytostatic chemotherapy (IFADIC) consisted of 1.5 g ifosfamide/sqm (d1–4), 25 mg adriblastin/sqm (d1–2) and 200 mg DTIC/sqm (d1–4) augmented with G-CSF (5 mcg/kg d5–13), q14d. According to Enneking 66 patients were randomized, receiving either IFADIC or a combination of IFADIC with radiotherapy (51Gy) or in case of radical surgery only IFADIC or observation. Overall 24 (60%) out of 40 evaluable patients in group C achieved a complete remisson (CR), 3 (7.5%) patients a partial response (PR), 3 (7.5%) patients stable disease (SD) whereas 8 (20%) patients developed recurrences (PD) and 2 of them died. In the "radiotherapy only" group, 15 (58%) out of 26 patients achieved a CR and 5 (19%) patients showed PD out of which 1 died. Disease free survival for patients who underwent chemotherapy was not significant better in both subgroups. We conclude that the addition of adjuvant chemotherapy did not result in a benefit for patients with wide-marginal or radical locoregional operable STS.

514 PUBLICATION

Localised soft tissue sarcomas. Treatment results and prognostic factors

Dana Cernea[1], V. Cernea[2], A Rancea[2], M. Muresan[2], N. Todor[1], N. Ghilezan[2]. [1]*Oncological Institute "Ion Chiricuta",* [2]*Department Radiotherapy, Cluj-Napoca University of Medicine and Pharmacy, Cluj-Napoca, Romania*

Purpose: To assess the results of the combined modality treatment and analyze the prognostic factors.

Methods: 82 patients (pts.) were treated between 1987–1993. Median age was 44 years, and male/female ratio 48/34. Topography: 47 patients-lower limb, 17- sarcomas of the trunk, 9- upper limb, 7 head and neck, 2 retroperytoneal. T category distribution: T2-34, T1-25, T3-23 pts. Surgical Treatment: 89% (72) of patients have wide excision, 3% simple excision, 2% compartimental excision and 1% amputation. Postopeative radiotherapy was administrated with standard fractionation, median dose was 55 Gy for all T categories.

Results: The median follow-up was 42 month. Actuarial survival at 5 years for the whole group- 40%. T1 pts. survive 54% at 5 years and T2-33% ($p < 0.04$). Survival according to location of the tumor (proximal vs. distal) is 47% and 15% respectively. ($p < 0.05$). According to histological grade actuarial survival was 61% for G1, 35% for G2 and 15% for G3. Local control (LC) at 5 years was 78%. LC is an important prognostic factor: survival at 5 years with local control is 55% vs. 22% without LC ($p < 0.01$). The main cause of therapeutic failure was metastatic disease.

Conclusions: Combined conservative surgery and postoperative irradiation provide good local control in adult soft tissue sarcomas. The main prognostic factors are: histological grade of the tumor, T category, local control of the primary. Improvements in therapy must include chemotherapy for the control of micrometastatic disease.

515 PUBLICATION

Extremity soft tissue sarcomas

M.E. Pitcher, R. Chandran, J.M. Thomas. *Royal Marsden Hospital, London, UK*

Soft tissue sarcomas provide challenges in diagnosis and treatment. We report our experience of limb and limb girdle sarcomas to highlight the

differential diagnosis, and emphasize the problem of local recurrence and mortality.

439 consecutive patients with primary and recurrent soft tissue sarcomas of limb and limb girdle have been treated at the Royal Marsden Hospital over the 6 year period 1989–1995. During this time 975 patients were referred with a presumed diagnosis of soft tissue sarcoma at any site, of whom 23% were found to have a benign soft tissue tumour and 7% had other malignancy.

There were 325 primary and 114 locally recurrent soft tissue sarcomas of limb and limb girdle. Amputation was performed in 21 cases (4.8%), as initial treatment in 10 (2%) and in 11 for failure of initial treatment or recurrence. By excluding those who were found to have have metastatic disease, those treated primarily with chemotherapy and those where surgical clearance was not possible we considered 354 (81%) disease free after treatment. This group has a local recurrence rate of 15.5% and a mortality of 30% (median follow up is 3.9 years). Isolated local recurrence rate (excluding those with simulataneous distant metastases) is 12 7%

These rates are comparable to other reported series but emphasize the aggressive biology of the disease and the need to develop effective adjuvant treatments.

516 PUBLICATION

In vivo scintigraphic imaging of somatostatin receptors in sarcomas – Possible applications

C. Giannakenas[1], H.P. Kalofonos[2], D. Apostolopoulos[3], A. Chondromaras[1], E. Tzorakolefterakis[4], T. Petsas[5], P.J. Vassilakos[3].
[1]Dept. of Nuclear Medicine, "St. Andreas" General Hospital, Patras; [2]Dept. of Oncology; [3]Dept. of Nuclear Medicine; [4]Dept. of Surgery; [5]Dept. of Radiology, University Hospital of Patras, Greece

Purpose: The aim of this continuing study is to investigate the efficacy of 111In-DTPA-Octreotide (OC) for the in vivo scintigraphic imaging of these relatively uncommon tumours.

Method: To date we have studied 14 patients with known sarcomatous lesions, M/F = 9/5, mean age 59 y. All the patients had at least one known lesion as demonstrated by other modalities e.g. CAT, U/S. Planar and in a few cases SPECT scintigraphy was performed at 48 hr and 22hr after the IV injection of 2.9–4.2 mCi of OC,. Histologic verification was obtained in all cases, (FNA or from surgically removed tissue).

Results: Positive (+) imaging was observed in 12/14 cases (85.7%): fibrosarcoma = 1+, embryonic rhabdomyosarcoma = 1+, (HIV-) Kaposi sarcoma = 1+, leiomyosarcomas = 2+/1−, liposarcomas = 2+, uterine sarcomas = 2+, osteosarcomas = 2+, chondrosarcomas = 1−, and neurogenous sarcoma = 1+. Both negatives were false negative. Occult lesions were demonstrated in two of the patients.

Conclusions: OC appears to have properties which may lead to a new indication in localising primary and secondary lesions and possibly as a tumour marker for radioimmunoguided surgery. The latter aspect is under trial in this continuing study.

517 PUBLICATION

Therapeutic concepts for loco-regional recurrences in soft tissue sarcomas of the extremities

P. Klein, B. Reingruber, L. Pahlke, W. Haupt, W. Hohenberger.
Chirurgische Universitätsklinik Erlangen, Germany

Between January 1983 and January 1994, 39 patients were treated for recurrences of soft tissue sarcomas at the extremities at the Chirurgische Universitätsklinik, Erlangen. Patients with distant metastases were not considered in this study. The primary operations had been performed externally in 82% of cases, 18% had been pre-treated in our hospital, the latter represented our recurrence rate of 7.1% after operations for primary tumours.

Treatment consisted of biopsies, no surgical treatment or R1/2 resections (n = 5); wide radical excisions (n = 13); compartmental resections (n = 11); amputations (n = 10).

Results:

	Cumulative 5-year survival after primary operation	Cumulative 5-year survival after operation for recurrence	Re-recurrence rate
Biopsy, no or R1/2 resection	0.4	–	100% progression
Wide radical excision	0.74	0.73	23.1%
Compartmental resection	0.61	0.64	9.1%
Amputation	0.7	0.73	30%

All curative treatment groups had similar survival both after the primary operation as well as after the operation for recurrence. The mean survival in the non-curative ('biopsy, no surgery and R1/2') group could be improved by radiotherapy.

518 PUBLICATION

Frequency of continuous cycling in childhood soft tissue sarcoma revealed by analysis of apoptotic fraction

L.M. Ball, C. Riddell, L. Resch, C.L. Lannon, M. Henry, J. Tam, K. Laybolt, A. Pyesmany, M. Yhap, D. van Velzen. *Departments of Haemato-Oncology and Pathology, IWK-Grace Health Centre, Halifax, N.S, Canada*

Purpose: In situ labelling for apoptosis specific DNA fragments (Frag-EL) allowed for the assessment of apoptotic rate and correction of immunocytochemically detected proliferation fraction in a representative series of paediatric soft tissue lesions.

Methods: Non-selected, consecutive, routinely processed diagnostic samples of 29 rhabdomyosarcoma (RMS), 14 Ewings sarcoma and 17 osteosarcoma, were studied for proliferation fraction by immunocytochemistry (cDNA defined monoclonal antibody for a subsegment of the Ki67 antigen, MM1, Novocastra, UK) and in-situ labelling of apoptosis derived DNA fragments (CalBiochem, USA) and routine image analysis (Quantimet 570C). Apoptosis corrected proliferation fraction was calculated as: Ki67 labelling % divided by (100 − apoptosis %).

Results: Apoptosis corrected proliferation fractions of 100%, indicating pathological continuous cycling, were found in 9/29 RMS (9/9 embryonal type), 0/14 Ewings sarcoma and 3/17 osteosarcoma with 6/10 cases deceased at assessment. Apoptotic fractions varied from 51% (7.5–89%) in RMS, 21% (1–58%) in Ewings sarcoma to 48% (23–84%) in osteosarcoma. Arrested or impaired apoptosis (fraction < 1%) was found only in Ewings sarcoma (6/14, 43%).

Conclusion: Proliferation fraction in childhood soft tissue tumours requires correction for apoptotic fraction when assessing relation to outcome.

519 PUBLICATION

Treatment results of synovial sarcoma

Zafer Koçak[1], Melahat Garipağaoğlu[1], Nazan Bozdoğan[2], Cengiz Kurtman[1], Binnaz Çelebioğlu[1], Mustafa Adlı[1], Ahmet Çakmak[1].
[1]Department of Radiation Oncology; [2]Department of Pathology, University of Ankara, Turkey

Background: Synovial sarcoma, a rare soft tissue tumor, arises from primitive mesenchimal tissue cells, characterizes high local recurrence rate. In this study it was evaluated synovial sarcoma patients in term of local control, survival and metastases characteristics.

Methods and Materials: Eighteen patients treated at Ankara University Medical School Radiation Oncology Department between 1979–1995 were evaluated retrospectively. Their ages were between 10–56, female/male ratio were 1/2. Localisations of tumors: truncus (n = 4), extremity (n = 14). Fourteen patients received primary treatment and four patients received salvage treatment after local relapse secondary to surgery. Their stage distributions were: Stage I (n = 2), stage II (n = 7), stage III (n = 8), stage IV (n = 1). Treatment types were: chemotherapy + surgery + radiotherapy (n = 11), radiotherapy + chemotherapy (n = 1) and surgery + radiotherapy (n = 6). Surgery was consisted of Total radiation doses were between 4000–6400 cGy.

Results: Three, 5 and 10-year survival ratios were 52%, 39.5% and 39.5% respectively. Pretreatment tumor volume (p = 0.007) and existence of macroscobic residue (p = 0.05) was found statistically significant effect on survival. Treatment failure was occurred in 10 patients (local relaps: 3, locoregional relaps: 1, distant metastases: 4, both local recurrences and distant metastases: 2). All patients that were received salvage treatment after recurrence secondary to surgery were relapsed again. Tumor grade, monomorphic-dimorphic subgroups, patients age, localization of tumor and using of chemotherapy were not found effect on prognosis.

Conclusion: Primary tumor volume and residual tumor volume were the most important prognostic factors. Treatment result was unsuccessful in patients group that received treatment after relapse secondary to surgery.