course of alternating 6-hour CDDP 25 mg/m² and 18-hour ADR 20 mg/m² infusions (120-hour continuous infusion, total dose CDDP 125 mg/m², ADR 100 mg/m²).

Results: Complete and partial response was achieved in 42.3%. In 2 weeks after chemotherapy all patients were operated. Good histological response (necrosis more than 70% tumor cells) was in 57.7% of cases. 3 courses of adjuvant chemotherapy CAP were used in patients with good histological response. In that group local recurrences were 13.3%, metastasis – 26.7%, 3-years survival – 82%. In the group of patients with poor histological response frad following figures: local recurrences – 45.5%, metastasis – 45.5%, 3-years survival – 47%.

Conclusion: So neoadjuvant approach to treatment of soft tissue sarcomas with long-term continuous i.a. chemotherapy can improve survival and its quality.

506 PUBLICATION

Soft tissues granular cell tumor: Disease description and treatment

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Purpose: This retrospective study was designed to characterize this rare disease and determine the best treatment.

Methods: We have review 12 charts (10 women, 2 men) of patients treated between 1980 and 1995. Thirteen soft tissues granular cell tumors were found. Average age was 35 years (from 12 to 55 years), and all were in good health.

Results: Lesions were located in the breast area 5 times, on the thoracoabdominal area 7 times, and once on the arm. Once there was a suspect lymph node in the drainage area. Always subcutaneous, the lesion was attached to the skin twice, averaging size of 12.5 mm. In 3 patients, it was recurrence (always after a previous incomplete resection). The fine needle aspiration reported malignant cells 60% of the time. The macroscopic examination revealed a white, firm, homogeneous, and uncapsulated mass. The frozen section misdiagnosed a malignant lesion 1 on 7, and was good 6 on 7. Most part of the time, the paraffin diagnostic was relatively easy but 3 times, electronic microscopy and immunohistology were needed to do the diagnosis. All lesions were benign. All patients were treated with microscopically complete local resection. No recurrence was observed after a median follow-up of 4 years. One patient had an unrelated cutaneous basocellular 5 years later.

Conclusion: Soft tissue granular cell tumor presents as a small subcutaneous lump, sometimes infiltrating the skin or associated with benign lymph node histiocytosis. It is a benign lesion, sometimes difficult to identify. Fine needle aspiration and frozen section examination are not good diagnostic tools in this condition. Microscopic complete surgical excision is the goal of the treatment because if incompletely excised, recurrences rates are high. In case of recurrence, we recommend a 1 cm resection margins.

507 PUBLICATION

Phase II study with Docetaxel (Taxotere) as second line treatment of advanced soft tissues sarcomas in adult

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A recent phase II study (ASCO 1994) showed that Docetaxel is active in adult soft tissue sarcomas as second line treatment warranting studies on first line efficacy and/or inclusion in combination. To confirm these data we started a multicenter phase II study with Docetaxel administered at the dose of 100 mg/m2 in a 1-h infusion q 3 weeks with corticosteroid premedication and without antiemetics as a second line chemotherapy in relapsed or metastatic soft tissues sarcomas. 37 pts, median age 43 yrs (20–65), WHO performance status 0: 19 pts, 1: 11 pts, 2: 6 pts, 3. 1pts entered the study. Histological subtypes were: fibrosarcoma 2 pts, malignant fibrous histiocytoma 4 pts, leiomyosarcoma 9 pts, liposarcoma 2 pts, rhabdomyosarcoma 2 pts, synovial sarcoma 8 pts, malignant schwannoma 4 pts, miscellaneous and unclassified sarcomas 6 pts. Twenty four pts have had one line of chemotherapy, 9 pts two lines, 4 pts four lines. Three pts are not evaluable for response: 1 pt had early death due to malignant disease, 1 pt died before response evaluation, 1 pt was unfit for evaluation. The responses observed were as follows: partial remission 1 (3%, C.I. 95% 0–17), stable disease 10, progression 23. CTC grade ≥3 leucopenia occurred in 76% of pts, and neutropenia in 90% of pts, while CTC grade ≥3 trombopenia was observed only in a pt. Fever and documented infection were noticed in 20% and 33% of pts respectively. No severe anaphylactoid type reaction and sensory neurotoxicity were observed. Nail changes and skin reaction were noticed in <20% of pts. Peripheral edema and fluid retention occurred in 2 pts. A pt died due to toxicity.

According to this phase II study, Docetaxel seems to be devoid of activity in adult soft tissue sarcoma and thus, in particular, its inclusion in first line chemotherapy would not seem justified.

Supported in part by the Associazione Italiana per la Ricerca sul Cancro

508 PUBLICATION

Treatment response in childhood rhabdomyosarcoma (RMS) related to apoptotic and proliferation fraction

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Purpose: Proliferation fraction analysis does not take into account the fraction of cells undergoing apoptosis. Relationship between proliferation fraction and outcome is often tenuous. We compared apoptosis corrected proliferation fraction with treatment outcome in rhabdomyosarcoma.

Methods: Of 30 consecutive, unselected cases of rhabdomyosarcoma (M: 18, age 3 m–16 years; F: 12, age 2 m–15 years), pre-treatment, routinely processed archival tissue was used for analysis of S-phase (cDNA defined mono-clonal antibody against Ki-67 antigen MM1, Novacastra, UK) and apoptosis (DNA in-situ labelling of apoptotic DNA fragments, Frag-EL, Cal-Biochem, USA). Quantisation of fractions: blinding, systematic random sampling.

Results: Mean apoptotic fraction: 51.3% (7–90%), no difference between subtypes. Apoptosis corrected S-fraction: 43.7% in survivors (n = 13) and 74% in non-survivors (n = 16) ($p < 0.01$, Wilcoxon). High proliferation fraction (>40%) predicted poor outcome in 15/16 cases (sensitivity 94%); 15/20 cases of high proliferation rates had unsuccessful treatment (specificity 75%).

Conclusions: 1. Apoptosis affects a variable proportion of cells in rhabdomyosarcoma. 2. Apoptosis corrected proliferation fraction is an accurate predictor of treatment outcome in childhood RMS.

509 PUBLICATION

Local hyperthermia in the treatment of soft-tissue sarcomas

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Purpose: It is evident that local electro-magnetic hyperthermia enhances the efficacy of radiation therapy in the clinic. However up to the present time the optimal combination of irradiation and local hiperthermia has not been established.

Methods: 138 pts with inoperable soft-tissue sarcomas have-been treated with preoperative radiation therapy. In 92 pts radiation therapy was combined with local hyperthermia (thermo radiotherapy – TRT); 46 pts received only radiation therapy (RT). Radiation therapy was given twice a week with a single dose 4–5 Gy; total dose 30–42 Gy. Local hyperthermia was carried out on apparatus working with frequency 460 Mhz. Temperature inside the tumour during 60 min was maintained in the range of 41–45°C. Local hyperthermia was provided by two variants; just before irradiation or 3–4 hrs after radiation exposure.

Results: In 2–3 weeks after TRT complete or partial tumour regression was observed in 50 pts, and after RT – in 12 pts 46% of pts who received TRT weve undergone conservative surgery and only 27% after RT.

Conclusion: Local hyperthermia improves the results of preoperative radiation therapy in pts with soft-tissue sarcomas. The best results were seen in pts with hyperthermia 3–4 hrs after irradiation and the temperature inside the tumor above 43°C.