Results: A missense mutation (p.D84Y; c.250G>T) was found in exon 2 of the CDKN2A gene. Segregation analysis of the variant was compatible with an association with the disease, since it was present in four affected family members. This mutation was predicted to affect protein function using SIFT and PolyPhen analysis. LOH analysis revealed one tumor with monoallelic loss and another with biallelic loss of the CDKN2A locus. We did not find BRAF and NRAS mutations in the tumors.
Conclusions: We show evidence that the p.D84Y missense mutation predisposes to melanoma since it is localized in a conserved domain and co-segregates with disease in this pedigree. These findings may have important implications for genetic counseling, molecular testing, and clinical management of Portuguese melanoma-prone families.

7012 POSTER

Photodynamic diagnostics of skin and mucosal lesions

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Background: Porphyrin-enriched tumor tissue irradiation with fluorescence excitation system leads to emission of pink-red fluorescence. This principle is used as a diagnostic procedure and is called photodynamic diagnosis (PDD). The aim of this work was to investigate the possibilities of PDD in skin and mucosal lesions diagnostics.
Material and Methods: Photodynamic diagnostics measurements were performed in 68 patients with malignant, premalignant and benign skin and mucosal lesions for detection of the foci of squamous cell carcinoma, basal cell carcinoma, primary and metastatic adenocarcinoma, chondrosarcoma. Two different photosensitizers have been used – intravenous injection of hematoporphyrin derivate (HpD) and the topical application of 5-aminolevulinic acid (ALA) induced protoporphyrin IX (PpIX). We used the simple and friendly fluorescence excitation system based on blue light emitting diodes. For the patients with advanced malignant disease, HpD was injected i.v. and 12−24 hours after the injection, malignant lesions were illuminated with violet-blue (405 nm) light for cancerous tissue detection. PDD for patients with T1−2 was carried on 3−6 hours after topical ALA application. The evaluated fluorescence data was correlated with cytological and/or histopathological tissue examination data.
Results: Red or red-pink fluorescence was observed in 72 malignant epithelial tumors; 43 of them fluorescent sharp, 27 – not so intensive. 2 malignant tumors – nasopharyngeal area chondrosarcomas – had no fluorescence. The most intensive red fluorescence was detected in thin superficial malignant lesions. From 165 benign lesions, very slight fluorescence has been detected in a few haemangiomas, paratracheal papillomas, one fragment of herpes zoster and some superficial open wounds with very intensive capillarity. Fluorescence of these benign lesions was different from malignant – not so red, bluer and less intensive. Nevi, papillomas, keratosis, scars and foci of psoriasis had no fluorescention.
Conclusions: Photodynamic diagnostics can be used for complete visualization of malignant lesions after the topical or systemic application of a tumour selective photosensitizer. It has been shown to be high effective in malignant superficial skin and mucosal lesions diagnostics. PDD may be required to optimise the detection of lesions in the post-PDT patients. Fluorescence detection following i.v. injection of HpD or topical application of ALA provides no difference.

7013 POSTER

Multicenter phase II study of chemo-immunotherapy in the treatment of metastatic melanoma

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Background: Combining chemotherapy and immunotherapeutic agents such as interleukin-2 and interferon alfa-2b may improve treatment results in metastatic melanoma [MM] patients compared with chemotherapy alone. This prospective study evaluated the potential efficacy of a bio-chemotherapy regimen followed by maintenance biotherapy for the treatment of MM.
Materials and Methods: Twenty-two patients with stage IV melanoma were treated for 5 consecutive days with cisplatin 20 mg/m^2, vinblastine 1.6 mg/m^2, and dacarbazine 160 mg/m^2 followed by pegylated ?-interferon 2b 50 ?g every week, subcutaneous interleukin-2 [IL-2] 1.8 M I.U. and oral 13-cis retinoic acid [13-cis-RA] 0.5 mg/kg, both given 5 days/week for 3 weeks each month. To eradicate minimal residual disease, maintenance biotherapy was continued in patients who achieved clinical benefit after 6 courses of bio-chemotherapy. The primary endpoint was response; secondary end-points were the evaluation of the immunological parameters, toxicity, progression-free survival [PFS], and overall survival [OS].
Results: Twelve patients [54.5%] achieved a response, and 7 [31.8%] maintained stable disease for at least 6 months on maintenance biotherapy. The median PFS and OS were 23.3 months and 45.7 months, respectively. The most important toxicities from chemotherapy were grade 3 and 4 neutropenia and thrombocytopenia in 41% and 18% of patients, respectively, while grade 2 autoimmune reactions were observed in 21% of patients after maintenance biotherapy. A prolonged enhancement of immunological function was observed in the 19 patients treated with maintenance therapy.
Conclusions: Six cycles of bio-chemotherapy followed by maintenance immunotherapy is well tolerated and shows significant activity in patients with MM.

7014 POSTER

Thin (<1 mm) and in-situ melanomas during 1989–2004 in Helsinki, Finland – clinical outcomes and prognostic factors

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Background: The prognostic factors associated with poor outcome in thin melanomas are not well known. Our purpose was to study the ratio and long term prognosis of thin melanomas in Helsinki region and to find out whether the tumor or patient characteristics that were studied were related with poor outcome.
Materials and Methods: The slides of Breslow thickness <1 mm, in-situ melanomas or lentigo malignae were reviewed, n = 301. The patient registries and the Finnish population registry were studied for the follow-up data.
Results: The mean age of the patients was 54.3 years, 58% were women. The mean follow-up was 6.7 years. There were 246 invasive cases (82%). 60.1% of all cases (n = 301) were of Clark level III, 18.6% were of Clark level II and 3.0% were of Clark level IV. Ten recurrent cases (4.1%) were invasive melanomas (<1 mm), three of which (1.2%) had died of melanoma. Four patients (1.6%) were alive with local recurrence, one with nodal recurrence and one with distant metastasis. One patient had died of coronary disease and was post-mortem diagnosed with metastatic melanoma. The group of in-situ melanomas and lentigo malignae (n = 55) contained one recurrent case with rapid nodal metastasis. The patient was diagnosed with nodal metastasis 13 days after the melanoma diagnosis, and had died of melanoma with distant metastasis one year later. The histological factors that were studied (Breslow thickness, tumor pigment, ulceration, solar elastosis and tumor-infiltrating lymphocytes) did not predict recurrence. The amount of pigment predicted overall survival, but tumor ulceration, the amount of lymphocytes and solar elastosis did not.
Conclusions: The treatment results in invasive melanomas (n = 246) were slightly better than expected (the recurrence rate was 4.1%). Pigment content of the tumor was the only prognostic factor for overall survival of the histological factors studied (pigment, ulceration, solar elastosis and tumor-infiltrating lymphocytes). These histological factors were not associated with disease recurrence. New prognostic factors are needed for staging thin melanomas.

7015 POSTER

The interest of raw data in dynamic contrast-enhanced ultrasonography (DCE-US) for the quantification of perfusion changes in in-transit melanoma metastasis (MM) treated by high doses of chemotherapy: does it predict the response?

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Background: To evaluate the performances of a new method of quantification of perfusion in DCE-US using the raw data for the prediction of tumoral response.
Materials and Methods: In this prospective study patients suffering from localised MM were included from march 2004. All of them were treated by high doses of chemotherapy (Melphalan +/− TNFa) delivered under isolated limb perfusion. B mode morphological imaging followed by functional examination using contrast agent injection (SonoVue, Bracco, Italy) and a perfusion and quantification software (VRI and CHI-Q, Toshiba, Japan) were performed before treatment and at D+1, D+7 and D+90. Contrast