P2320

Metalloproteinases expression and metastatic cutaneous melanoma dissemination

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Introduction: The formation of metastasis is a multistep complex process, including the degradation and remodelling of the basement membrane and the extracellular matrix. The matrix metalloproteinases (MMPs), play a essential role in that process.

Objective: The aim of that work is to assess the predictive value of MMPs in melanoma metastasis formation, and in addition to investigate if their presence is related with positive sentinel lymph node.

Material and Methods: We have studied the immunoexpression of different MMPs (MMP-1, MMP-2, MMP-9, MMP-13), in 40 specimens of melanoma. Initially we have compared the immunoexpression in 10 melanomas with regional lymph node and/or distant metastasis, with 10 melanomas without metastasis and similar clinicopathological characteristics. On the other hand we have studied 20 more specimens of melanoma where we have practiced sentinel lymph node study, 10 negative and 10 positive cases. For the immunohistochemical studies, the biotine-estreptavidine-peroxidase technique has been used, and we have assessed the percentage of stained cells in 10 high magnification fields.

Results: The results demonstrate that among the different studied MMPs, the MMP-2 is expressed in a statistically higher percentage of cells from melanomas that metastasize by haematic via. None of the MMPs has demonstrated to be useful to predict positivity of the sentinel lymph node technique. References: Nelson, AR, Fingleton B, Rothenberg ML, et al. Matrix Metalloproteinases: biologic activity and clinical implications. J Clin Oncol 2000;18:1135-49.

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P2321

Evaluation of clinical and quantitative ABCD characteristics of pigmented skin lesions in the diagnosis of melanoma

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Background: Over 20 clinical sites contributed data on biopsied pigmented skin lesions (PSL) to create a database for the development of a system for non-invasive diagnosis of melanoma. This digital dermoscopy database consists of multi-spectral images of these lesions, patient and lesion information, and histological diagnoses by the study dermatopathologists. The lesions in the database are characterized by the study exclusion criteria: no lesions smaller than 2 mm or greater than 22 mm; no previously excised or biopsied lesions; no erosions or clinical ulceration; and others. PSLs were biopsied to: rule out melanoma (75%), to rule out other skin cancer, or due to patient's concern. To diagnose melanoma clinically, examining dermatologists may have used characteristics of melanoma such as clinical ABCD (Asymmetry, Border irregularity, Color variegation, Diameter >6 mm), evolving over time, patient's concern, regression, and "ugly duckling."

Objective: To characterize quantitatively PSLs in the digital dermoscopy database, to evaluate the relationship of these features to melanoma, and to compare quantitative vs clinical characterization.

Methods: The following quantitative characteristics of PSLs were defined using the pigmented area of the lesion: A — asymmetry; B — irregularity of the border; C — distribution of lesion reflectance in the red spectral band (700 nm); and D — maximum dimension. A characteristic was considered to be absent if its numerical value was less than a threshold value. For each characteristic, the threshold value was independently selected to maximize the diagnostic accuracy for malignant melanomas (MM) and high-grade dysplastic nevi (HGDN), on a set of 993 PSLs (including 182 MM and HGDN) from the digital dermoscopy database. Then, the entire database of 1520 PSLs (including 224 MM and HGDN) was characterized by the number of quantitative ABCD (qABCD) characteristics. Quantitative and clinical ABCD characteristics were compared on a subset of lesions with clinical images.

Results: 98% of lesions in the database had 1 or more qABCD characteristics, regardless whether the reason for biopsy was to rule out melanoma or other. All 224 MM and HGDN in the database had 1 or more of qABCD. However, 18% of these (41 cases) had only 1 such characteristic; in 40 of these cases the only characteristic present was color variegation. Clinical and quantitative ABCD characteristics of PSLs were strongly correlated.

Conclusions: PSLs without any qABCD characteristics may be unlikely to be melanoma. Dermatologists may also be using criteria other beyond clinical ABCD (e.g., gestalt, dermoscopic features, etc.) when identifying lesions suspicious for melanoma. Augmentation of diagnostic specificity may be possible through quantitative lesion image analysis with digital dermoscopy systems.

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NON-MELANOMA SKIN CANCER

P2400

Carcinoma cuniculatum arising in focal plantar keratoderma

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There have been isolated reports of cancers arising in keratodermatous skin but only in severe or diffuse keratoderma, eg. Unna-Thost hyperkeratosis. This is probably the first case report of carcinoma cuniculatum arising in focal plantar keratoderma. A 60-year-old man presented with a 4-month history of a painful, non-healing lesion on the ball of his foot. He had attempted to remove a long-standing callus at this site without success and the area had become ulcerated and malodorous. He reported several callosities of both feet for as long as he could recall. Examination revealed 5 circumscribed areas of symmetrical keratoderma on each sole over pressure points. The index lesion was a 5 cm^2 indurated, tender, pink plaque with multiple openings. Secondary infection of a callus was presumed but there was no improvement with antibiotics. An MRI of the foot showed several focal coalescing soft tissue masses in the skin with displacement of the underlying bone and involvement of the capsule of the metatarsophalangeal joint and plantar musculature. An incisional biopsy revealed irregular acanthosis and hyperkeratosis with foci of invasive squamous cell carcinoma (SCC). A below-knee amputation was performed and showed tumor thickness of 11mm with no evidence of lymphovascular or perineural invasion. There has been no local or distant recurrence after 1 year follow-up. Carcinoma cuniculatum is a rare subtype of verrucous carcinoma usually affecting the sole of the foot. It is an SCC which invades locally causing destruction of adjacent structures including bone. Metastases are rare. The diagnosis may be delayed due to the initial banal clinical features and indolent course often mimicking a viral plantar wart. However, progression to a fungating plaque eventually occurs. Superficial biopsies may show non-specific features, giving false reassurance. A deep incisional biopsy is mandatory. Surgery is the treatment of choice with wide local excision. Radical amputation is indicated in advanced cases but Moh's micrographic surgery may help preserve normal tissue.

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P2401

Comparative analysis of immunohistochemical features in basal cell carcinoma

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There has been no general agreement in classifying basal cell carcinoma (BCC), and little is known about the immunohistochemical profiles in each subtypes of BCC. BCC is a locally invasive tumor, but its aggressive forms tend to recur and metastasize. MMP-2 degrades extracellular matrix, and thus it plays an important role in tumor invasion. MT1-MMP is expressed on tumor cell surface, controls the interaction of tumor cells and stroma, and plays an important role in the activation of MMP-2. In this study, we have compared the histopathological subtypes of BCC by immunohistochemical study. We also focused on identifying representative markers of growth in the aggressive forms of BCC by assessing MMP-2, MT1-MMP, Wnt-1, β-catenin, α-SMA and p53 expression. For the immunohistochemical staining of BCC specimens, tissue microarray technique was used. The total 66 samples were divided into 6 subtypes: 12 nodular, 14 nodular infiltrative, 10 micronodular, 11 infiltrative, 10 morphea-like and 9 metatypical. Nodular subtype was classified as non-aggressive and the remaining subtypes as aggressive. The following results were obtained after immunohistochemical staining with antibodies to MMP-2, MT-1 MMP, Wnt-1, β-catenin, α-SMA. (1) In aggressive forms of BCC, a significant increased expression of Wnt-1, β-catenin, α-SMA was observed. (2) The expression of β-catenin was increased in all 5 aggressive subtypes than nodular subtype. In comparison to the nodular BCC, the expression of Wnt-1 was increased in the morphea-like BCC. The expression of α-SMA was increased in the micronodular, morphea-like and infiltrative BCC than nodular BCC. (3) The individual expressions of MMP-2, MT1-MMP were not statistically significant. However, in comparison to the nodular BCC, the co-expressions of MMP-2 and MT-1 MMP were increased in all aggressive forms of BCC except for infiltrative BCC. In conclusion, the interaction between MMP-2 and MT-1 MMP seems to have a role in developing aggressive forms of BCC.

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P2402

Confocal reflectance mosaicing of basal cell carcinomas in skin excisions to potentially guide Mohs surgery

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Mohs surgery for the precise excision of basal cell carcinomas (BCCs) is a tedious and slow procedure, requiring multiple excisions that must each be guided by the examination of frozen histology. Confocal reflectance microscopes may enable rapid detection of nuclear morphology in BCCs directly within fresh surgical excisions with minimal need for histology, and thus may expedite Mohs surgery. Previously, washing skin excisions with acetic acid for several minutes demonstrated brightening of nuclei and detectability of BCCs. However, rapid detection will require short washing times. Experiments to determine nuclear brightening with clinically-relevant acetic acid concentrations (1%, 2%, 3%, 5%, 10%) and washing times (30 sec, 1 min, 2 min, 3 min, 5 min) show that concentrations of 5% and 10% require only 30 seconds, whereas 2% and 3% require 2 minutes, and 1% requires more than 5 minutes. With our 30X, 0.9 NA objective lens, the field of view is 0.5 mm, whereas Mohs excisions are of size 10-20 mm. To observe large areas of an excision, a 2-dimensional sequence of images is captured and stitched in software to display a mosaic with a larger field-of-view. At present, 30x30 images are stitched together to display a field-of-view of 15x15 mm with 2000 pixels, which is equivalent to 2X magnification in histology. At present, this requires 9 minutes compared to the 20-45 minutes required for preparing Mohs frozen histology. For mosaicing over large areas, a tissue fixture was developed, to mount and precisely control the flatness, stability, tilt and sag of Mohs excisions. Further research will be toward correlation of mosaics to histology for the main histologic subtypes of BCCs, using the optimum concentration of 5% and washing time of 30 seconds.

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P2403

Dermoscopic features of basal cell carcinoma of nipple in a patient with nevoid basal cell carcinoma syndrome

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Nevoid Basal Cell Carcinoma Syndrome (NBCCS) is an autosomal dominant disease characterized by the presence of multiple basal cell carcinomas, odontogenic keratocysts, palmoplantar pits, calcifications of falx cerebri, and other developmental skeletal abnormalities. Herein we report a 49-year-old NBCCS patient who suffered from a superficial basal cell carcinoma on the left nipple. The dermoscopic features showed groups of fine needle-like structures interconnected with fine black thread, surrounding the granular nodules of the nipple, and forming a circular arrangement; homogenous black pigmentation was also noted, which was quite different from the classic features of basal cell carcinoma. We also employed polymerase chain reaction and direct DNA sequencing method to analyze his PTCH gene and a novel C-to-A substitution in exon 5 was found, which results in premature termination at codon 135. Keywords: basal cell carcinoma, dermoscopy, NBCCS, PTCH gene.

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P2404

Does participation in an integrated transplant dermatology clinic impact the quality of life and anxiety level of transplant recipients?

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Background: As advances in the field of solid organ transplantation have improved patient and organ survival, providers and patients have become more concerned with quality of life (QOL) outcomes. This study investigates the impact of participation in an integrated transplant dermatology clinic on overall QOL and anxiety.

Methods: Transplant recipients attending the Emory Transplant Center Dermatology Clinic completed surveys during a baseline visit to the clinic and at 6 months. Liver transplant patients completed the QOL index for liver transplant (QLI); all other transplant patients completed the kidney transplant questionnaire (KTQ). All patients completed the STAI anxiety inventory, a skin specific QOL survey (Skindex-16) and a general health survey (SF-12). Data at 6 months was compared to baseline. A regression model was used to determine clinical predictors of QOL and anxiety.

Results: Of 33 patients who completed surveys at baseline, 25 (75.8%) returned surveys at 6-month follow-up. The study population consisted of 12 renal, 3 cardiac, 2 lung, 5 liver and 3 renal/pancreatic transplant recipients. Composite scores from the SF12 demonstrated a significant decline in mental function from baseline ($D = -7.16 \pm 9.61$, $P < .01$). The social/economic and family subscales of the QLI survey demonstrated an improved QOL from baseline ($D = 3.07$, $P = .16$ and $D = 4.26$, $P = .20$, respectively). Regression analysis revealed that QOL as measured by the KTQ fear subscale improved with a greater number of years since treatment (0.12, $P = .02$) and declined with increased skin cancer incidence (-1.54, $P < .01$); QOL as measured by the KTQ emotion subscale declined with increased age (-0.03, $P = .04$), and the appearance subscale was influenced by treatment regimen (-0.69, $P = .05$). Skindex-16 function subscale score was negatively influenced by years since treatment (2.07, $P = .04$) and the mental function scale of the SF12 was influenced by skin cancer incidence (0.87, $P = .05$).

Conclusion: Certain subscales of the QLI instrument indicate an improvement in QOL with P-values that approach statistical significance. Lack of statistical significance in these items may be due to a small sample size. By regression analysis, specific clinical factors, such as years since transplant and skin cancer incidence, appear to influence some subscales. These QOL measures will be reassessed in the same patients at 12 months to evaluate the effect of continued participation in the integrated clinic.

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P2405

Idiopathic angiosarcoma of the toe previously diagnosed as thromboembolic disorder

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Background: Angiosarcoma is a rare vascular neoplasm that usually occurs in chronic lymphedematous limbs, on the head or neck of elderly patients, or post-irradiation. We report the case of a 74-year-old female who presented with exquisitely tender, violaceous, edematous toes that upon biopsy showed angiosarcoma. To our knowledge, this is the first reported case of idiopathic angiosarcoma presenting on the toes.

History: This patient initially presented to podiatry 2 months prior to dermatologic evaluation for an ingrown toenail of the right hallux. After partial nail avulsion, unsuccessful treatment of presumed cellulitis, and an extensive workup by her vascular surgeon and primary physician, the only abnormality found was a 3.4-cm atheroma in her aortic arch, initially thought to be a source of thromboemboli to the toes. Intractable pain led the patient to pursue a dermatology consultation and a punch biopsy of the right hallux yielded the diagnosis of angiosarcoma. A technetium bone scan showed uptake on the right distal tibia, hindfoot, and forefoot near the first metatarsal, indicating the extent of the tumor. CT-scans of the chest, abdomen, and pelvis as well as an MRI of the brain did not show metastasis. An amputation of the right lower extremity was scheduled, and at the time of surgery, violaceous, tender patches similar to the primary lesions were found extending up the plantar foot, calf, and tibia. Intraoperative frozen sections of the anterior tibial skin also showed angiosarcoma, resulting in an above the knee amputation, which, histologically, revealed clear margins.

Conclusion: A review of the literature revealed rare reports of angiosarcoma of the lower extremity and no previous cases involving toes. This case is also unusual in that this patient's angiosarcoma was not classifiable into 1 of the 3 main categories of angiosarcoma: (1) it was not on the head or neck; (2) she did not have lymphedema; and (3) she had not been previously irradiated. Our patient is of additional clinical importance because her initial workup revealed internal pathology that suggested a different diagnosis, and further delay in the actual diagnosis might have led to a worse outcome. This illustrates the need to use an extensive differential diagnosis, especially when faced with difficult cases, and suggests that angiosarcoma be in the differential diagnosis of a tender, violaceous toe.

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