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Malignant melanoma of unknown primary site (MUP). Systematic review of the literature with emphasis on survival and prognostic factors

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Background: Although more than 90% of melanomas have a cutaneous origin, occasionally it is discovered fist as a secondary deposit without evident primary site. The aim of this study was to systematically review published literature and analyse data on incidence, survival and prognostic factors.
Materials and Methods: We searched MEDLINE, (search terms *Melanom*, unknown origin, unknown primary, indolent, occult)* and the abstracts from ESMO and ASCO congresses of the last 4 years and perused the references of the retrieved relevant articles.
Results: Altogether, 38 peer reviewed articles and two abstracts were analysed. 4283 patients with MUP were reported along with 135,831 patients with MKP; any site included. The incidence of MUP from these studies is 3.15%. MUP patients harbouring nodal disease had a median overall survival ranging between 24 and 127 months compared to 165 months in matched control populations, 5-year survival rate between 28.6% and 75.6% and 10 year survival rate between 18.8% and 62.9%. MUP patients with visceral disease had median survival times between 3 and 13.2 months, and 5 year survival rates between 5.9% and 18%. Presence of tumour regression in metastatic sites and low nodal burden were associated with favorable outcome. Potentially curative surgical treatment offered survival advantage in comparison to patients with residual metastatic foci. MUP patients who received adjuvant chemotherapy or radiotherapy seemed to fare worse compared to patients observed, while there was no consensus on the impact of age and gender on prognosis.
Conclusions: This is the first review to bring together the information of eighty eight years and to analyse all the potential information accumulated. Although a well know entity no consensus is reached to describe MUP presentation, management or prognosis.

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Changes of ferritin and CRP levels in melanoma patients treated with adjuvant interferon a (EORTC 18952) have no prognostic value on treatment outcome

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Background: Adjuvant therapy with interferon α (IFN) is disappointing in melanoma patients with only a minority benefiting treatment. A predictive marker selecting responders does not exist. It was shown that IFN induced an increase in ferritin and a decrease in CRP levels, however, an association with treatment response was not studied.
Material and Methods: Patients participated in the EORTC 18952 trial comparing adjuvant treatment with intermediate high dose (10 MU) IFN for one year and intermediate low dose (5 MU) IFN for two years to no treatment. Ferritin and CRP levels were determined by enzyme-linked immunosorbent assay; before treatment, after induction treatment, at 3, 6, 9, 12, 16, 20 and 24 months. Ferritin levels are influenced by sex and age; therefore ratios of increase/decrease (compared to pre-treatment value) were calculated for both ferritin and CRP. Cox regression analyses and landmark methods at end of induction and 6 months were used to evaluate the association between ferritin, CRP and distant metastasis free survival (DMFS).
Results: Baseline ferritin and CRP levels were determined in 138 patients. Among these, 7 patients had high ferritin levels (higher than 300 ng/ml for men, 150 ng/ml for women younger than 50 and 300 ng/ml for women older than 50), 14 patients had high CRP levels at baseline (higher than 10 μg/ml) and were excluded from further analysis. Baseline ferritin levels for the observation group ($N = 21$) and the IFN group ($N = 96$) were not significantly different ($p = 0.92$). However, ferritin ratios were significantly higher in the IFN-treated patients as compared to the observation group, at end of induction ($p = 0.0003$) and at 6 months ($p = 0.009$). Landmark analyses at end of induction and at 6 months indicated that a higher ferritin ratio was not correlated with improved outcome in patients treated with IFN ($p = 0.72$ and $p = 0.72$ respectively). No difference between the treatment groups in CRP ratio was observed during the study period. Furthermore, no association between CRP ratios and DMFS was found.
Conclusions: Administration of adjuvant interferon α in melanoma patients induced increased ferritin levels but no significant changes in CRP levels. Ferritin and CRP ratios have no prognostic value regarding DMFS.

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Electrochemotherapy treatment of metastatic cutaneous cancer

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Background: Electrochemotherapy (ECT) is a tumour ablation modality combining administration of a poorly permeable cytotoxic chemotherapeutic drug with an electric pulse in order to facilitate drug delivery into the cells. Exposure of tumour cells to electric pulses increases the cytotoxicity of bleomycin 300 fold. ECT has been successfully used in treatment of metastatic malignant melanoma and non-melanomatous cancer. In July 2007 a national referral base was established at James Cook University Hospital (Middlesbrough, UK) to evaluate the potential benefits of ECT treatment in cancer patients.
Material and Methods: Approval was granted by the clinical effectiveness subcommittee for treatment of metastatic skin and subcutaneous lesions, palliation of bleeding or painful lesions and primary treatment in cancers not amenable to surgical excision or conventional treatments. Training and accreditation was obtained from Herlev University Hospital, Copenhagen. A single operator administered ECT and patient data and outcomes were prospectively collected.
Results: Eighteen patients received ECT treatment. Pathologies included nine malignant melanomas, three breast cancers, two BCCs, an SCC, a uterine leiomyosarcoma, an angiosarcoma and a CLL infiltrating a keloid scar. Eleven patients were treated with general anaesthesia; seven with local anaesthesia and conscious sedation. All were day cases. A total of 133 lesions were treated. Treatment lasted an average of 19 minutes. The average post-operative pain score was 2/10. No systemic complications occurred. Three patients presented with localised skin infection following treatment, a skin rash and severe pain after a second scalp treatment in one patient each. Based on the RECIST criteria six patients showed complete resolution of their lesions, seven patients had a partial response, one had progressive disease and four stable disease.
Conclusion: Electrochemotherapy treatment has shown promising early results in eighteen patients presenting with metastatic disease, including radio-recurrent lesions. The treatment was well tolerated. All patients were prepared to have further treatments. Long-term outcome results, in a large pooled patient population, are required to establish the place and palliative benefits of ECT for patients with metastatic disease.

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Acral melanoma: histopathological prognostic features of 6 cases

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Background: Acral melanoma represents 3 to 15% of all cutaneous melanoma. In Morocco, this location is predominant. The aim of our work is to study clinicopathological features and prognosis of acral melanoma in the region of Fez in Morocco.
Materials and Methods: This is a retrospective study of 6 cases of acral melanoma diagnosed in anatomocytology's laboratory, at Hassan II University Hospital of Fez, during the period of 5 years (2005−2009).
Results: The mean age of the patients was 60 years, the sex-ratio was 2, and the most commonly involved location was plantar region (83.4%). The concept of trauma was found in half of our patients. The most common histological type was Nodular melanoma (83.4%). The mean Breslow thickness of tumor was 4.6 mm. Clark's level was III in 83.4% of cases. Ulceration was found in 83.4% of cases. The mean mitotic index was 7.6 mitoses/10 fields. Diagnosis of acral melanoma was raised at a late stage in our patients, 66% were stage III or IV. The treatment was based on surgery in 66% of cases. At 2-year follow up, 34% have died of melanoma and 16% were lost of view.
Conclusion: Acral melanomas is the most common location of cutaneous melanoma (54%) in the region of Fez and is characterized by its poorer prognosis.