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Neuroimaging analysis of rare brain metastases from prostate cancer

Juliana Macedo [1,*], Eduarda Carneiro [4],
Diana Ferreira [4], António Verdelho [5],
Luís Pedro Afonso [6], Joaquina Maurício [7],
Susana Maria Silva [2,3], Mavilde Arantes [2,3,4]

[1] Faculty of Medicine of the University of Porto,
4200-319 Porto, Portugal
[2] Unit of Anatomy, Department of Biomedicine,
Faculty of Medicine of the University of Porto,
4200-319 Porto, Portugal
[3] Center for Health Technology and Services Research
(CINTESIS), 4200-450, Portugal
[4] Division of Neuroradiology, Radiology Service,
Portuguese Institute of Oncology, Porto, Portugal
[5] Neurosurgery Service, Portuguese Institute of
Oncology, Porto, Portugal
[6] Pathological Anatomy Service, Portuguese Institute
of Oncology, Porto, Portugal
[7] Medical Oncology Service, Portuguese Institute of
Oncology, Porto, Portugal
E-mail address: ju.p.macedo18@gmail.com
(J. Macedo).

Aim: Our main study focus was to evaluate the incidence, imaging characteristics, and prognosis of parenchymal brain metastases originating from prostatic tumors.

Introduction: Prostate cancer is considered the second most commonly diagnosed cancer.[1] In addition, it is considered the fifth leading cause of cancer death amongst males.[2] A small percentage (2%) of patients with prostate cancer are found to be castrate-resistant and to develop brain metastasis, a rare complication which is associated to an advanced systemic state of the disease when the tumor has already spread to other sites.[3] Although, there is not much evidence on optimal management of these patients.[4]

Methods: A review of case records of prostate cancer patients within the IPO Porto data base from 2013 to 2015 was conducted in order to identify the patients with prostate cancer and evidence of brain metastases. As criteria of exclusion, cases transferred to other hospitals without follow up and cases that were incorrectly categorized were excluded.

Results: We screened 2194 patients with prostate cancer, with only one having evidence of brain metastasis. Additionally, one case was identified with bilateral orbital metastatic lesions. The patient with evidence of brain metastasis aged 48 years old. Magnetic resonance imaging showed six metastatic lesions, three infratentorial and three supratentorial. The largest lesion was found in the parieto-occipital region. These brain metastasis were detected 42 months after the initial diagnosis of prostate adenocarcinoma. In addition, by the time of brain metastasis detection, the patient already had bone metastatic lesion.

Conclusion: Brain metastases from prostate cancer are rare, with only a few cases described in the literature. Variable magnetic resonance imaging characteristics are described. Brain metastases are also associated with a poor prognosis, with a mean survival of 1–7.6 months.

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Studies towards the synthesis of dicarboxylic acid metabolite of mitoxantrone

Ivanna Hrynchak [1], Emília Sousa [1,2,*],
Maria de Lourdes Bastos [1,2,3], Madalena Pinto [1,2],
Vera Marisa Costa [3]

[1] Laboratório de Química Orgânica e Farmacêutica,
Departamento de Ciências Químicas, Faculdade de
Farmácia. Universidade do Porto, Portugal
[2] Centro Interdisciplinar de Investigação Marinha e
Ambiental (CIIMAR), Universidade do Porto, Portugal
[3] UCIBIO, REQUIMTE (Rede de Química e Tecnologia),
Laboratório de Toxicologia, Departamento de
Ciências Biológicas, Faculdade de Farmácia,
Universidade do Porto
E-mail address: esousa@ff.up.pt
(E. Sousa).

Aim: The objective of this work was to synthetize the dicarboxylic acid metabolite of mitoxantrone (MTX) to further investigate its cardiotoxicity in H9c2 differentiated cells.

Introduction: Drug metabolism can result in active or toxic metabolites that can lead to side effects, namely cardiotoxicity.[1] MTX, an antineoplastic that belongs to the synthetic anthracenediones,[2] is used to treat breast cancer, acute leukaemias, and acute lymphomas in adults.[3] Nowadays, it is also used to treat aggressive multiple sclerosis. One of the most frequent and relevant MTX side effect is cardiotoxicity. Previously, we found the MTX-naphthoquinoxaline metabolite (NAPHT) to be less cardiotoxic than MTX.[4] One of the main human MTX metabolites was identified as the dicarboxylic acid resulting from the oxidation of the terminal hydroxyl groups of the side chains.[5] However, its putative cardiotoxicity was not yet assessed. Herein, the synthesis and structure elucidation of the dicarboxylic acid metabolite will be presented.

Methods: The total synthesis of the metabolite involved five steps, starting from chrysazin. The enzymatic reaction was accomplished through the horseradish peroxidase (HRP)-catalysed H_2O_2 and the studies of the oxidative reactions involved sodium tungstate, chromium trioxide, sodium nitrite, and potassium permanganate.

Results: In order to obtain the carboxylic derivative, several approaches were undertaken, namely, total synthesis from a commercial available anthraquinone, as well as enzymatic and oxidative reactions from MTX. Different derivatives were obtained. The structure elucidation of the intermediates was established by spectroscopic techniques and the characterization of the dicarboxylic acid metabolite is ongoing.

Conclusion: The synthesis of the dicarboxylic acid metabolite was only achieved by the multistep approach. Future work will involve cardiotoxicity studies of this metabolite in H9c2 differentiated cells.

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Human papillomavirus in the etiology of oropharyngeal carcinoma

T. Kovacic [1,*], P. Stefanicka [2]

[1] *Faculty of Medicine, Comenius University in Bratislava, Slovakia*
[2] *Department of Otorhinolaryngology – Head and Neck Surgery, Faculty of Medicine and University Hospital in Bratislava, Slovakia*
E-mail address: tomas.kovacic93@gmail.com
(T. Kovacic).

Aim: The aim of this retrospective survey was to investigate the association of HPV status in patients with oropharyngeal cancer with tumour staging and other clinical features.

Introduction: Infection by human papillomavirus (HPV) stands for the most frequent viral carcinogenesis in the world. Over-expression of cell oncoprotein p16 is routinely diagnosed by immunohistochemistry (IHC) as the surrogate marker of viral activity.

Methods: Records from the oropharyngeal cancer patients treated in the Department of Otorhinolaryngology-Head and Neck Surgery in Bratislava from January 2013 to December 2016 were retrospectively analysed. Patients were divided, according to IHC results on oncoprotein p16, into p16 positive, considered HPV-positive, and p16 negative as HPV-negative. The incidence of oropharyngeal carcinoma, location, T and N staging, age, gender of patients was compared based on HPV status.

Results: From 129 oropharyngeal cancer patients with p16 examination were 52 (40%) considered as HPV positive. HPV positive group consisted of 45 (86.5%) men and 7 (13.5%) women. The primary tumour in HPV-positive patients originated from the palatine tonsil and base of the tongue in 96% of cases. The peak of occurrence of HPV-associated carcinoma was found between 50 and 59 years of age. HPV positive tumours were diagnosed in early T stage (T1/2) in 52%. Both HPV positive and negative patients were predominantly diagnosed with advanced-stage cancer, 90.4% in HPV-positive and 87% in HPV-negative group.

Conclusion: Early T stage in HPV positive carcinomas was approved, as well as more advanced regional spreading and prevalence of men and non-smokers. Wide variations in numbers of diagnosed patients during years of study may be caused by relatively small size of the studied group. Survey is focusing at HPV status as the most important prognostic factor in oropharyngeal cancer and systematized introduction of HPV status examination as progressive approach to effective and targeted therapy.

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The effects of cannabinoids in exemestane-resistant breast cancer cells

C. Almeida [1,2,3,*], T. Augusto [3],
G. Correia-da-Silva [3,4], N. Teixeira [4], C. Amaral [4]

[1] *Faculdade de Ciências, Universidade do Porto, Portugal*
[2] *Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Portugal*
[3] *Laboratório de Bioquímica, Departamento de Ciências Biológicas, Faculdade de Farmácia, Universidade do Porto, Portugal*
[4] *UCIBIO, REQUIMTE, Laboratório de Bioquímica, Departamento de Ciências Biológicas, Faculdade de Farmácia, Universidade do Porto*
E-mail address: cristina-almeida96@hotmail.com
(C. Almeida).

Aim: Considering that the development of resistance is the main reason for endocrine treatment failure, our group decided to explore the ability of three cannabinoids, Δ9-tetrahydrocannabinol (THC), cannabidiol (CBD) and anandamide (AEA), to reverse resistance to exemestane. The THC and CBD are phytocannabinoids derived from the plant Cannabis sativa (marijuana) whereas AEA is an endocannabinoid. For that, it was used LTEDaro cells, a long-term estrogen deprived ER+ breast cancer cell line that mimics resistance to exemestane.[1] These cells were treated with exemestane in combination with two phytocannabinoids, CBD and THC, and the endocannabinoid AEA.

Introduction: Exemestane is one of the aromatase inhibitors (AI) used as first line treatment for estrogen-receptor positive breast cancer in post-menopausal women. Exemestane acts by inhibiting aromatase, the enzyme responsible for the conversion of androgens to estrogens[2] and also by promoting apoptosis of breast cancer cells.[3] Nevertheless, despite its therapeutic success, this AI, after prolonged treatment, can induce acquired resistance, which causes tumor relapse. Therefore, it is important to find new strategies to overcome resistance in order to improve breast cancer treatment.

Methods: The presence of CB1 and CB2 in LTEDaro cells was confirmed by Western blot analysis and the effects of the combination of cannabinoids with exemestane were evaluated by MTT and LDH assays. Cell morphology was analyzed by Giemsa and Hoechst staining.

Results: Our results demonstrate that all the cannabinoids induce a decrease in viability of exemestane-resistant cells, in a dose- and time-dependent manner, without LDH release. These results indicate that the studied cannabinoids, mainly THC and AEA, revert the resistance to exemestane, probably by inducing apoptosis, as observed in Giemsa/Hoechst stain by the presence of typical morphological features of apoptosis.

Conclusion: This study highlights the efficacy of using cannabinoids as a potential adjuvant treatment to revert resistance to AIs.

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