

PS171

Neuroimaging analysis of rare brain metastases from prostate cancer



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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 metastases 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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PS177

Studies towards the synthesis of dicarboxylic acid metabolite of mitoxantrone



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Aim: The objective of this work was to synthesize 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-naphthoquinoline 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 H₂O₂ 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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