Histology and Histopathology
From Cell Biology to Tissue Engineering

P04 - Histopathological analysis of growth of implanted VX2 liver tumor

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The rabbit VX2 model of cancer has been widely used to demonstrate the efficacy of treatments against liver tumors. It is an anaplastic squamous cell carcinoma derived from Shope papillomavirus infection in rabbit. The tumor can be serially transplanted from one animal to another by allograft implantation and may grow in almost any grafted organ. Although there are many articles related to the VX2 model, basic research articles are very few and give a sparse description of the tumor [1]. The aim of this study was to explore the tumor characteristics focus on the early stages of growth.

A total of 12 New Zealand white rabbits were used in the present study. In each animal, 1 mm^3 of thawed VX2 tumor was implanted into the middle lobe of the liver. Two rabbits were sacrificed at 2, 4, 8, 11 ,14 and 17 days after implantation and the implanted lobes were collected and fixed in 10% formalin. Procedures were approved by the Animal Experimentation Ethical Commission, University of Zaragoza (permit number: PI35/22). Formalin-fixed tissues were trimmed, the volume of the tumors was determined and samples were processed according to standard histopathological procedures. In addition, tissue sections were stained with Masson`s trichrome stain, and processed for immunohistochemistry (IHC) using the following primary mouse monoclonal antibodies: anti-cytokeratin 7 (CK7), anti-actin (SMA), anti-vimentin and anti-p53. All antibodies were obtained from Dako/Agilent (CA, United States).

Macroscopically, a well-demarcated white lesion was observed under the hepatic capsule. Lesion enlarged rapidly from 6 mm^3 at day 2 to 400-600 mm^3 at day 17. On days 2 and 4, the lesion was characterized histologically by the presence of the implanted tissue composed of necrotic cellular debris and residual connective septa. IHC for p53 and CK7 revealed scattered foci of tumor cells in the periphery of the implanted tissue. The lesion was outlined by a thin rim of vimentin-positive cells which included activated hepatic stellate cells (SMA-positive cells). On Masson`s trichrome stain sections, there was no staining of the collagen at the interface between the liver and implanted tissue. On day 8, the lesion was characterized by the presence of residual implanted tissue surrounded by a thick ring of high density of vimentin-positive cells. The ring of cells was composed of thin sheets of tumor cells surrounded by large fibrous septa containing SMA-positive cells and dense immune infiltration. A fibrous capsule located between the cellular rim and liver parenchyma was observed in both cases. From day 11, the following events were observed: i) the implanted residual tissue progressively decreased; ii) spontaneous necrosis was present and increased with tumor size forming cystic cavities; iii) the fibrous septa and the immune infiltration into the tumor decreased drastically; iv) a fibrous capsule with variable immune infiltration was present in all cases.

Information on implantation techniques and VX2 tumor growth is abundant, but to our knowledge, histopathological characteristics at very early stage after its implantation have not been previously reported. The current study may lead to a more complete understanding of tumor biology, which is essential for the design of experimental studies.

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