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Comparative rat and human mammary histopathology

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Keywords

Histopathology, human, mammary gland, rat

Introduction

Animal model systems to study malignant and premalignant change are used by a number of investigators. For the correct interpretation of data in translational research, it is necessary to determine if the histopathology in these models is similar to that observed in human tissues.

Aims

To compare the histopathology of carcinogen-induced mammary gland lesions in the rat with those of the human.

Comments

Rat models of mammary carcinogenesis are used widely and their short latency period prior to tumour development makes them good models to study early, intermediate and late events associated with carcinogenesis. Here, the histopathological features of rat and human tumours of different stages were evaluated. While many of the features were similar, they were not always identical, particularly in the latter stages of carcinogenesis. Models of this type are useful research tools, but care must be taken when translating the results into human studies.

Methods

To induce breast carcinogenesis, 21 day old Sprague Dawley rats received intraperitoneal injections of 50 mg/kg 1-methyl-1-nitrosourea. Thirty five days after treatment, rats were euthanised. The cervical-thoracic and abdominal-inguinal mammary glands were excised and processed for histological examination. For comparison, sections of human breast samples were obtained.

Results

Breast tissue from humans and rats were categorised into six groups: normal, benign, hyperplastic, atypical ductal hyperplasia (ADH), carcinoma *in situ* (CIS) and carcinoma. The normal gland of both humans and rats was similar, with mammary acini lined with a single layer of luminal epithelial cells and a flattened myoepithelial layer. A wide range of benign lesions (fibroadenomas, micropapillomas) were observed in the human gland with some evidence of ADH and CIS in some fibroadenomas. In contrast, only a small number of benign lesions were seen in rats but these did not contain ADH or CIS. Hyperplasia was defined as an increase in the layers of epithelial cells lining the acini and ducts. In rats this was confined to standard hyperplasia while in humans more specialised hyperplastic lesions were seen, including hypersecretory and gynecomastoid hyperplasias. ADH was only seen in the human gland while ductal CIS (DCIS) was common to both. In rats cribiform and papillary DCIS predominated, with no evidence of microcalcification or elastosis (both common features in human DCIS). In human carcinomas, many subtypes were observed (eg ductal, lobular, medullary and tubular) each of which is associated with differing prognosis. By contrast, tubular, medullary or lobular carcinomas were not seen in rats. Similarly, lymph node involvement was frequent in human carcinomas but less so in rats.

Discussion

The rapid development of tumours in carcinogen-treated rats makes this an attractive model to determine the events involved in this process. This work has shown that while many of the histological features of normal, benign, pre-malignant and malignant breast lesions in rat and humans are similar, they are not identical. It is recommended that criteria already established for classifying human breast tumours should also be applied to the rat carcinogen model to allow a more relevent interpretation of data generated from such models.

References

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