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THE HUMORAL IMMUNE RESPONSE OF FELINE MAMMARY TUMOR

By

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ABSTRACT

Feline mammary tumors (FMT) are the third common tumors in cats after skin tumors and lymphomas. The main diagnostic tool of FMT is the imaging technique and histopathology that shows difficulties in application like time consuming and the high cost. The aim of the present investigation is to find a new easily, rapid and of low-cost diagnostic tool laboratory evaluation of humoral immune response in normal and FMT cases. From the obtained results, it could be concluded that the using of autoantibodies is recommended as a rapid, easily and low-cost diagnostic tool of feline mammary tumor which is the human counterpart of breast cancer.

Keywords:

Feline, Humoral Immunity, Mammary Tumor, Tumor Markers.

INTRODUCTION

The occurrence of spontaneous tumors in some animals make them suitable models for the study of tumorigenesis, for the improvement of diagnostic tools and for the development of successful therapies for the human counterpart **(Cannon, 2015).** Moreover, the shorter lifespan and faster progression of cancer in model species allows a quicker trial completion and data collection. Amongst the animal models used in comparative oncology, cats (Felis catus) are emerging as an excellent organism, a conclusion supported by different perspectives **(DeMaria *et al,* 2005)**. Unlike the usual laboratory animals, such as rodents, cats (and dogs) share the same environmental risk factors as humans, with cancer occurring

naturally **(Cekanova and Rathore 2014)**. FMT shares a broad Clinicopathological, demographical and epidemiological similarity with the human breast carcinoma (HBC) **(Thomas, 2015).**

The traditional clinical/pathological factors as the number of regional lymph nodes with metastases, tumor size and tumor grade tend to be forgotten as they require tumor tissue for their determination which seems to be difficult in most cases. Recently the most widely used are the molecular diagnostic tools but these tests are expensive and indeed prohibitively expensive in many countries. Clearly, it would be desirable to have strong and clinically validated, inexpensive and simple circulating prognostic biomarker tests **(Nicolini *et al*, 2018)**. Autoantibodies (AAbs) to tumor-associated antigens (TAAs) have been identified in the circulation of patients with cancer. TAAs have been identified to elicit circulating AAbs in breast carcinoma: p53, MUC-1, heat shock proteins (HSP-27, HSP-60, and HSP-90), HER2/neu/c-erb B2, GIPC-1, c-myc, c-myb, cancer-testis antigens (NY-ESO-1), BRCA1, BRCA2, endostatin, lipophilin B, cyclin B1, cyclin D1, fibulin, insulin-like growth factor binding protein 2 (IGFBP-2), topoisomerase II alpha (TOPO2α), and cathepsin **(Piura and Piura, 2010)**. Proliferating cell nuclear antigen antibodies (PCNA) detected in serum of Small-cell lung carcinoma and Hepatocellular carcinoma **(Vermeersch *et al*, 2009).**

The aim of the present study is to evaluate the diagnostic efficiency of autoantibodies of P53, MUC-1, C-MYC and PCNA tumor associated antigens (TAAs) in feline mammary tumors (FMT) through using rapid, easily and low-cost ELISA technique.

MATERIAL AND METHODS

In the present investigation, 32 serum samples were collected from cats suffering from mammary tumors. Through clinical examination and x-ray Fig. (1) in the surgery clinic of faculty of Veterinary Medicine Cairo University and six serum samples from clinically normal cats during the period of august 2018 till January 2020. Detection of autoantibodies was through house ELISA protocol as previously described in **(u *et al*, 2012)**. Statistical analysis of the results through calculation of cut off value equation mean+2SD, making Receiver operating characteristic (ROC) curves and detection of AUC t±o each of the four autoantibodies (P53, MUC-1, PCNA and C-MYC) alone.

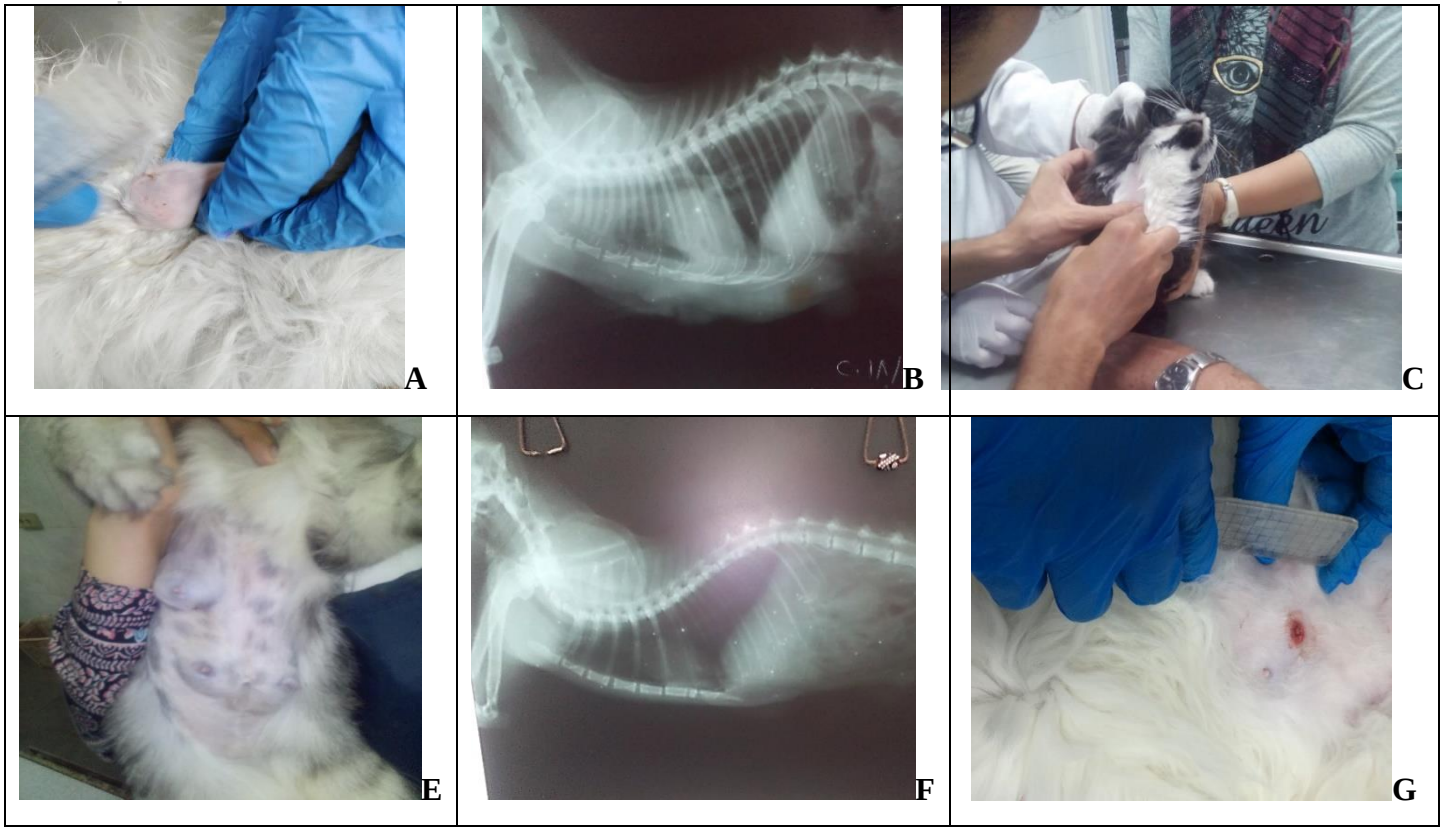
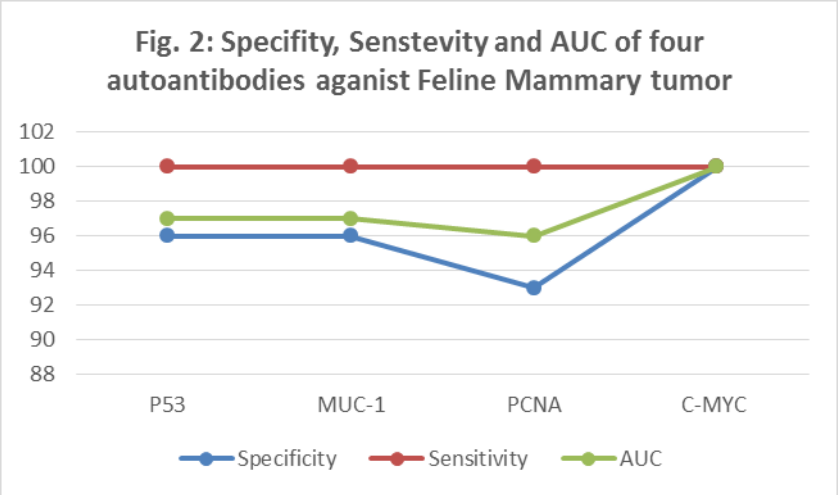


Fig. (1): Clinical presentation of different cases suffering from mammary tumors, A) A case of 13 years old Shirazi queen suffering from mammary tumor at the right caudal thoracic mammary gland, B) The lateral chest radiograph of the same case showed no evidence of pulmonary metastasis, C) Blood sample collection from the jugular vein in a case of 14 years old mixed breed queen suffering from multiple mammary tumors at the right and left caudal abdomen and right inguinal mammary glands, Fig. (E). A case of 10 years old Shirazi queen suffered from mammary tumor at the right and left caudal thoracic and cranial abdomen mammary gland, F) The lateral chest radiograph of the same case showed no evidence of pulmonary metastasis, and G) A case of 9 years old Shirazi queen suffered from ulcerated mammary tumor at the left cranial thoracic mammary gland.

RESULTS AND DISCUSSION

The four autoantibodies P53, MUC-1, PCNA and C-MYC were detected in serum of diseased cats and not detected in serum of normal ones with specificity 96, 93 and 100 % respectively and sensitivity 100 % to all four autoantibodies and AUC 0.97, 0.97, 0.96 and one respectively Fig. (2).



Humoral studies have shown that cancer patients may develop immunity to abnormally expressed p53, as revealed by p53 autoantibodies in the blood and presence of circulating p53 autoantibodies at diagnosis of breast cancer being associated with reduced overall survival with poor prognostic factors such as high histological grade and the absence of hormone receptors **(Lenner *et al,* 1999) and (Mudenda *et al,* 1994)**.

Recent reports suggest that autoantibodies directed to aberrantly glycosylated mucins, in particular MUC1 and MUC4, are found in cancer patients. There is, however, limited information on the autoantibody levels before clinical diagnosis, and their utility in cancer screening in the general population **(Pedersen *et al,* 2014)**. Changes in the structure of O-linked glucans occur in all breast cancers resulting in the expression of glycoproteins that are antigenically distinct. Indeed, the serum assay widely used for monitoring disease progression in breast cancer (CA15.3), detects a glycoprotein (MUC1), but elevated levels of the antigen cannot be detected in early stage patients. However, since the immune system acts to amplify the antigenic signal, antibodies can be detected in sera long before the antigen. Autoantibodies to specific cancer associated glycoforms of MUC1 are found more frequently and at higher levels in early stage breast cancer patients than in women with benign breast

disease or healthy women. Association of strong antibody response with reduced rate and delay in metastases suggests that autoantibodies can affect disease progression **(Blixt *et al,* 2011)**.The anti-MDM2 and anti-c-Myc autoantibodies showed a significant increase of both autoantibodies in lung cancer patients compared to controls and were positively associated with IHC scores in 43 available lung cancer tissues. This indicates that serum levels of autoantibodies against these two TAAs might be useful in discriminating lung cancers from normal controls **(Li *et al,* 2016)**. Autoantibodies against c-myc appears to indicate the presence of early-stage breast cancers as a single marker or in association with p53, HER2, NY-ESO-1, BRCA1, BRCA2 and MUC1 autoantibodies **(Chapman *et al,* 2007)**. Elevated levels of c-myc, muc-1, p53 and c-erbB2 auto-antibodies were seen in 82% of primary breast cancer patients compared to normal **(Robertson *et al,* 2005)**.

Proliferating cell nuclear antigen (PCNA) antibodies usually studied as a diagnostic marker in systemic lupus erythematosus but also detected in serum of Small-cell lung carcinoma and Hepatocellular carcinoma **(Vermeersch *et al,* 2009)**. The current study revealed that PCNA antibodies association with feline mammary tumor with sensitivity 100% and specificity 93%.

CONCLUSION

The obtained results recommended that using autoantibodies as a rapid, easily and low cost diagnostic tool for feline mammary tumors which is considered the human counterpart of breast cancer.

Recommendation:

We recommended more interest in application of using autoantibodies as a diagnostic tool of FMT in large population number to give the green line to be used as a diagnostic tool in human.

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