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2 **Multiple tumors (papillary Carcinoma and fibro-adenoma) in the mammary**
3 **gland of camel (*Camelus dromedaries*) in Sudan**

4

5 **Abstract:**

6 **Aims of the Study:** to report the different types of tumors in the udder of camel (*Camelus*
7 *dromedaries*) for the first time in Sudan.

8 **Place and Duration of Study:** the study was undertaken in the department of pathology,
9 veterinary research institute, ministry of animal resource and fisheries, Khartoum, Sudan in 2009.

10 **Study Design:** sample was obtained from Tumboul abattoir in Al-Gazeera State, gross,
11 histopathological and immunohistochemistry study were done in the udder tissue of 9-year-old
12 Butana heavy weight ecotype, early pregnant, non lactating she camel.

13 **Methodology:**The macroscopic picture of two masses in the udder tissue were seen and
14 described then histopathological lesions on tissues were studied using H & E stain. Lastly
15 Immunohistochemical staining was done using estrogen and progesterone antibodies.

16 **Result:** Multiple mammary neoplasms were detected in the udders of she-camel. One was
17 diagnosed as a papillary carcinoma and the second as fibroadenoma [fibroadenomatous
18 hyperplasia].

19 **Conclusion:** mammary tumors were detected in Sudanese camel and completely confirm by
20 using histopathological methods.

21 **Keywords:** multiple tumor papillary carcinoma fibroadenoma camel Sudan.

22 **1. Introduction:**

23 Camels are well adapted to survive in arid zones and are able to with stand thirst and survive on
24 thorny desert shrubs. In the Sudan they are multipurpose animals representing an important
25 source of food (milk and meat), clothing, shelter and transportation for bedwins. Camels' milk and
26 urine have proven to have therapeutic effects against certain diseases [1,2,3]. Mammary glands
27 masses are common in bitch and cat, but are rare in other domestic animal species [4]. Such
28 lesions were commonly detected in bitches and described as benign tumors was: adenoma,
29 papillary adenoma and benign mixed tumors; or malignant tumors such as acinar or ductal
30 adenocarcinoma, papillary adenocarcinoma, medillary adenocarcinoma, squamous cell carcinoma
31 and malignant mixed tumors [5,6].

A mammary gland neoplasm was detected at necropsy in a 9-year-old ovariectomized Holstein cow with a history for one year of an enlarged left hindquarter that contained multiple cysts [7]. The histological diagnosis was multicentric papillary cystadenoma was reported [7, 8] it was also reported in ewes [9, 10], nany goats [11] and in zoo animals [12].

Mammary neoplasia is rare in Camelids, it was first reported as carcinoma in mixed mammary tumor in a 13-year-old female *llama*. Histopathological examination revealed tubulopapillaryacinar or solid nest-like clusters of neoplastic epithelial cells surrounded by whorls and sheets of proliferation of epithelial cells and classified as a mixed tumor. Positive confirmed diagnosis is by Immunohistochemical staining of neoplastic epithelial cells with anti-cytokeratin antibody, metastasis to regional lymph nodes was not reported [13].

In Sudan choroid plexus papilloma was diagnosed during investigation in to dromedary herds owned by nomadic pastoralist, Northern Darfur State, western Sudan for neurological diseases in 2010 [14].

Four types of mammary neoplasia in the dromedary camel were reported. These include: Fibrosclerosis, Intraductal fibroma which composed of papillary over growth protruding into the duct lumen, adenocarcinoma consisting of tubular arrangement as well as solid and/or squamous structure. Pleomorphism and mitotic activity were common. Plasma cells and lymphocytes were present in varying numbers around the tumor cells. The stroma was moderate and in some areas sclerotic [15].

2. Materials and methods:

Case history:

During survey of udder affection of slaughtered she-camel at Tumbool slaughter house from January to December /2009, Tumbool town, Al-Gazeera State, Sudan. Tumbool is about 130 k southeast of Khartoum. From the total number of samples ($N=150$) of she-camel udder tissues, one was showed tumor masses it was a 9-year-old Butana heavy weight ecotype, an early pregnant, non lactating she camel was slaughtered. Tissue specimens from tumor were fixed in 10% formalin, processed routinely in paraffin wax and 5-6 μ sections were prepared and stained with haematoxylin and eosin (H&E).

For two types of tumor Immunohistochemistry using dextrane polymer_hrp for estrogen and progesterone receptor was done.

3. Results:

3.1 Gross lesions:

The udder of the one she-camel was slightly swollen and hard in consistency. One quarter of the udder was markedly distended approximately 2 cm above the base of the teat. On cut surface, the udder presented two reddish fleshy masses. The larger one composed of hard non-encapsulated well circumscribed, hard on cut surface, bulging mass attached to the inner surface of the udder and communicated with stalk to other nodules at the base of teat which blocked the teat cannal. The second mass was 1.6×2cm diameter, cauliflower-like and loose in teat cannal.

3.2 Histopathological lesions:

The most striking change was complete distortion and destruction of normal udder architecture and the normal udder tissue was replaced by invasive of tumor tissue. Though, the microscopic picture of two masses were variable, but the predominant change of the small nodule at the base of teat present of arboriform papillary fronds, with a core of fibrovascular tissue heaving complex secondary and tertiary branches (fig 1).

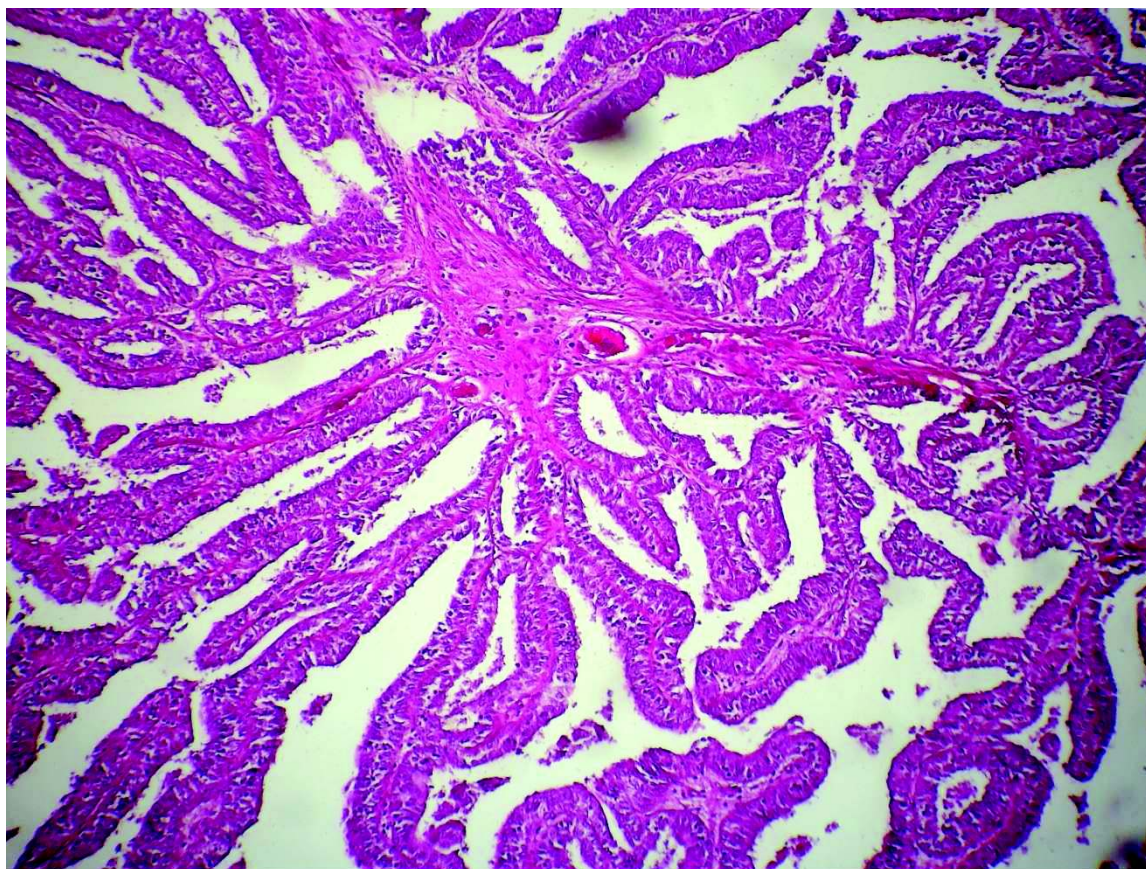


Fig 1: udder of she-camel with papillary carcinoma. Note, large fibrovascular core with congested blood vessels and complex branches, (H&E X10).

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78 The fronds were covered with single or multi-layers of pleomorphic poorly orientated overlapping
79 cells that appeared as pseudostratification. Bullring and necrosis of the papilliferous growth
80 stratification of the nuclei and leucocytes infiltration were frequently observed. The nuclei were
81 vesicular forming the empty look appearance and some with margined chromatin (fig 2).

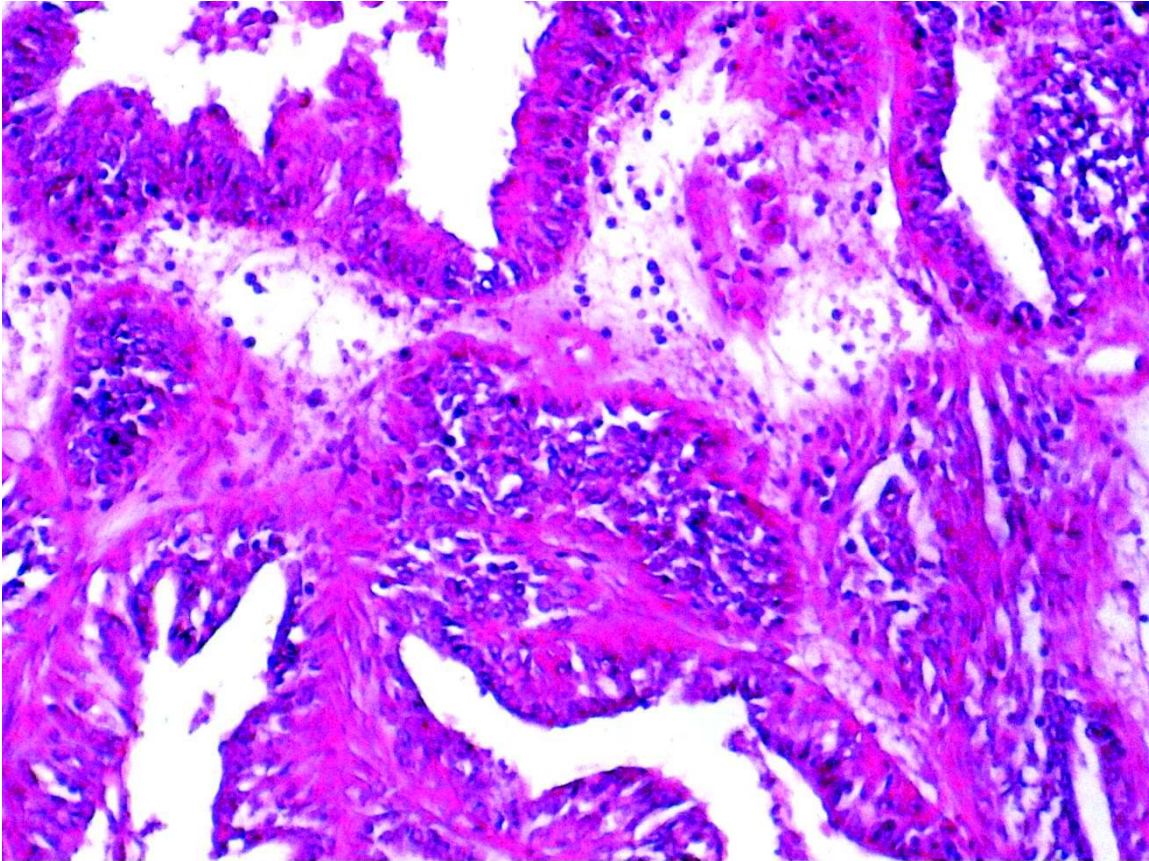


Fig 2:
Udder of she-camel with papillary carcinoma, Note, pleomorphic poorly orientated
overlapping cells with vascular nuclei, bulling and necrosis of neoplastic cells and
infiltration of leucocytes, (H&E x40).

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83

84 Focally micropapillary pattern with prominent papillary tufts were often observed. In some areas
85 the fibrovascular core was covered with single layer of flatten end epithelial and in other areas
86 covered with cuboidal to low columnar cells. The stromal connective tissue was variable in some
87 areas dense diffuse and in other showed myxomatous feature. The tumor displayed
88 fibroadenomatous hyperplasia. These areas composed of numerous irregular branching tubular

89 or ducts embedded in fibrous tissue stroma which varied from myxomatous with mild fibrotic
90 reaction to extensive fibrosis (fig 3).

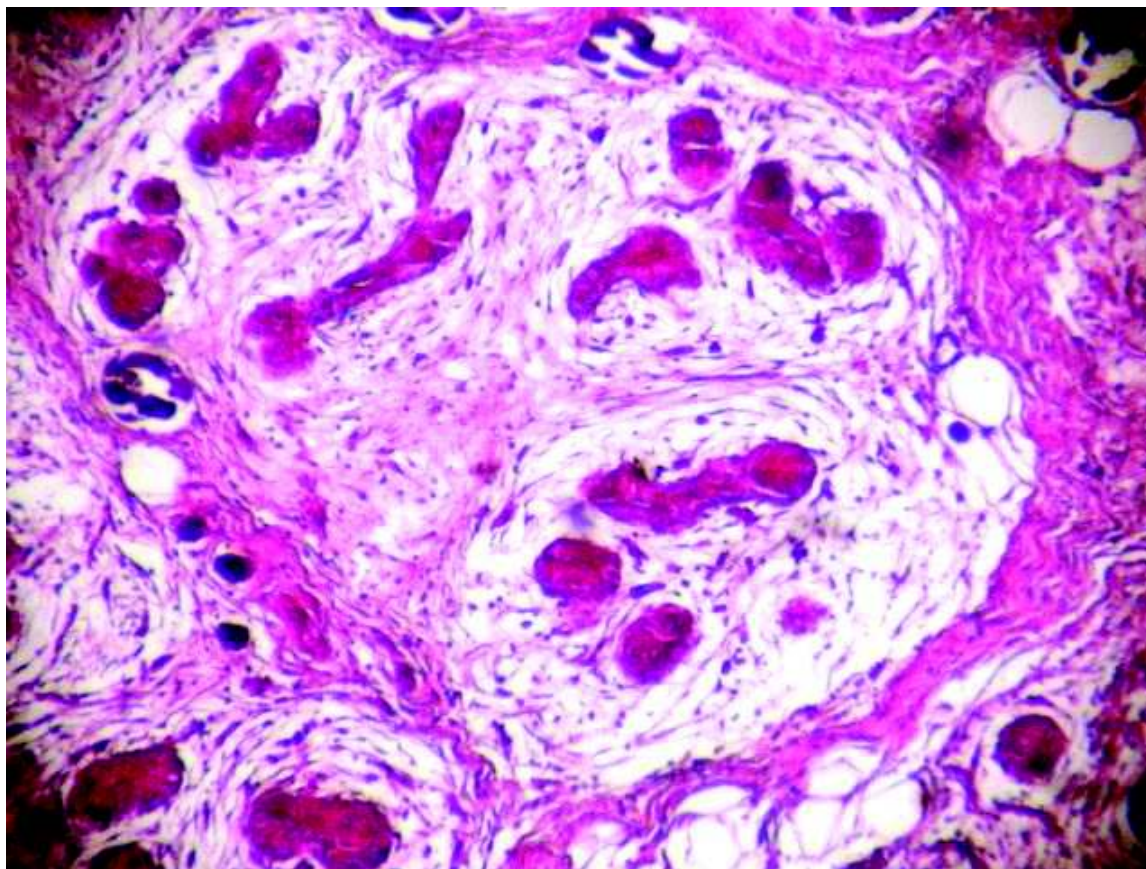


Fig 3:
udder of she-camel with fibroma, Note, irregular ducts entrapped in
fibrous tissue and calcium deposition (H&E x10).

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93 These tubules were lined with multilayers of cuboidal epithelial cells (fig 4).

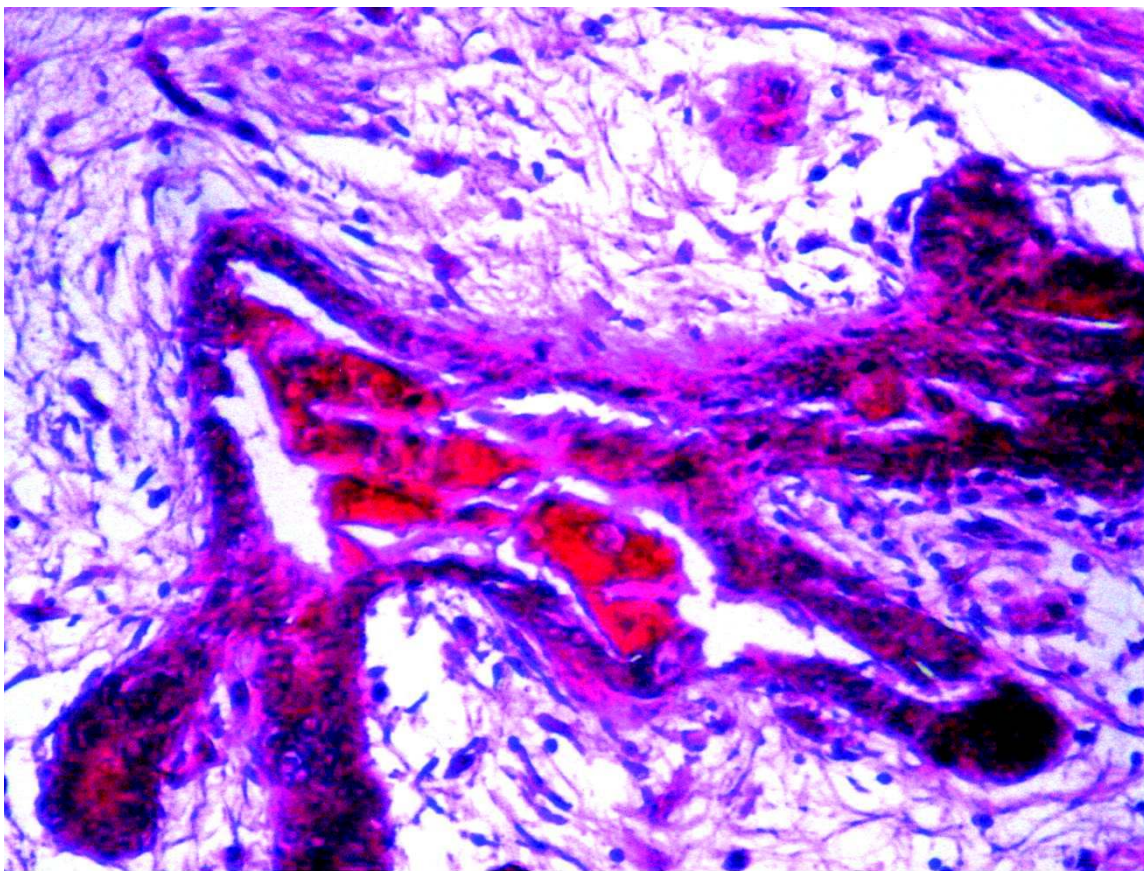


Fig 4:
udder of she-camel showed fibro adenoma (H&E x40).

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95 The arrangement of the layers was disorganized and revealed anisocytosis and anisokaryosis of
 96 cells and nuclei, respectively. In both the fibroadenoma and papilliferous growth calcospherites
 97 was observed in tubular, papillary component, fibrovascular core and epithelial lining. The tumor
 98 was metastasized in lymphatic vessels (fig 5).

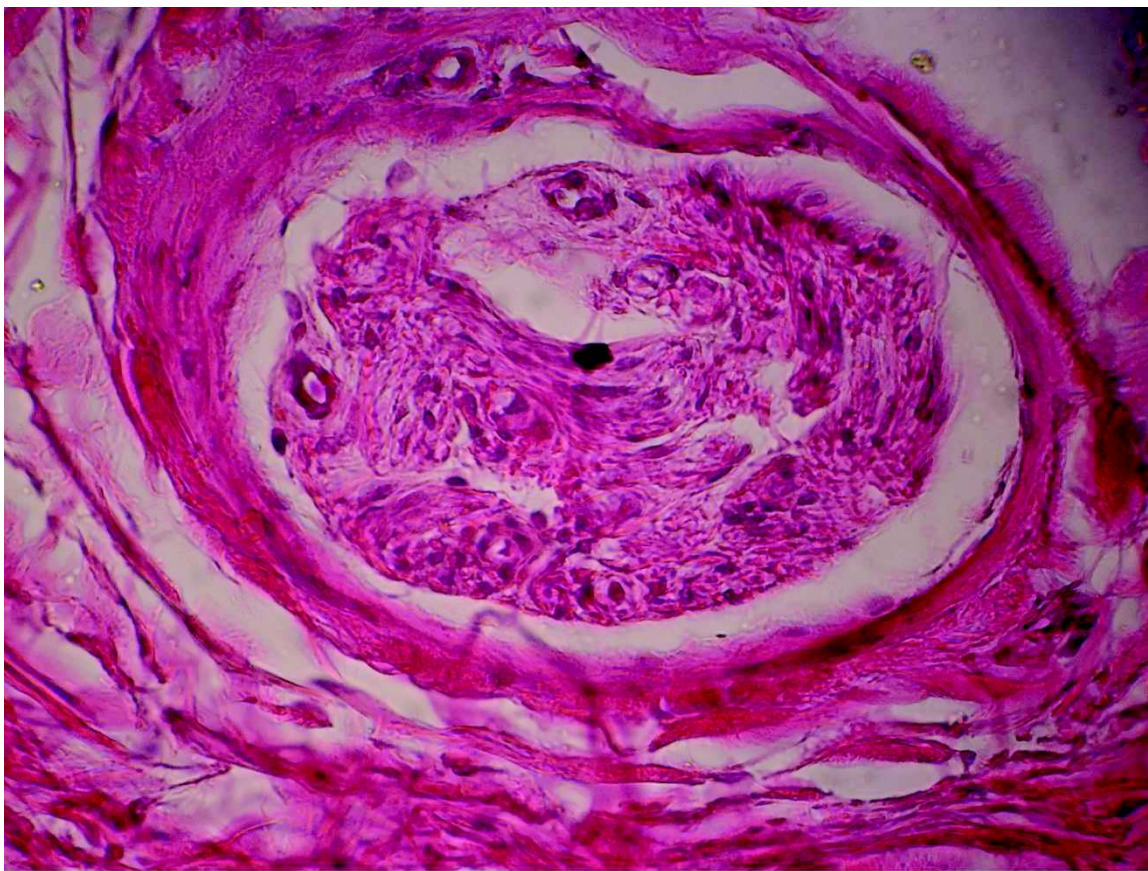


Fig 5:
 udder of she-camel show metastize, tumor cell inside lymphatic vessel (H&E x40).

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100 **3.3 Immunohistochemistry:**

101 The papillary section showed moderate positive result for estrogen receptor and negative
 102 progesterone (fig 6, 7) while the fibroadenoma section was negative for both receptors.

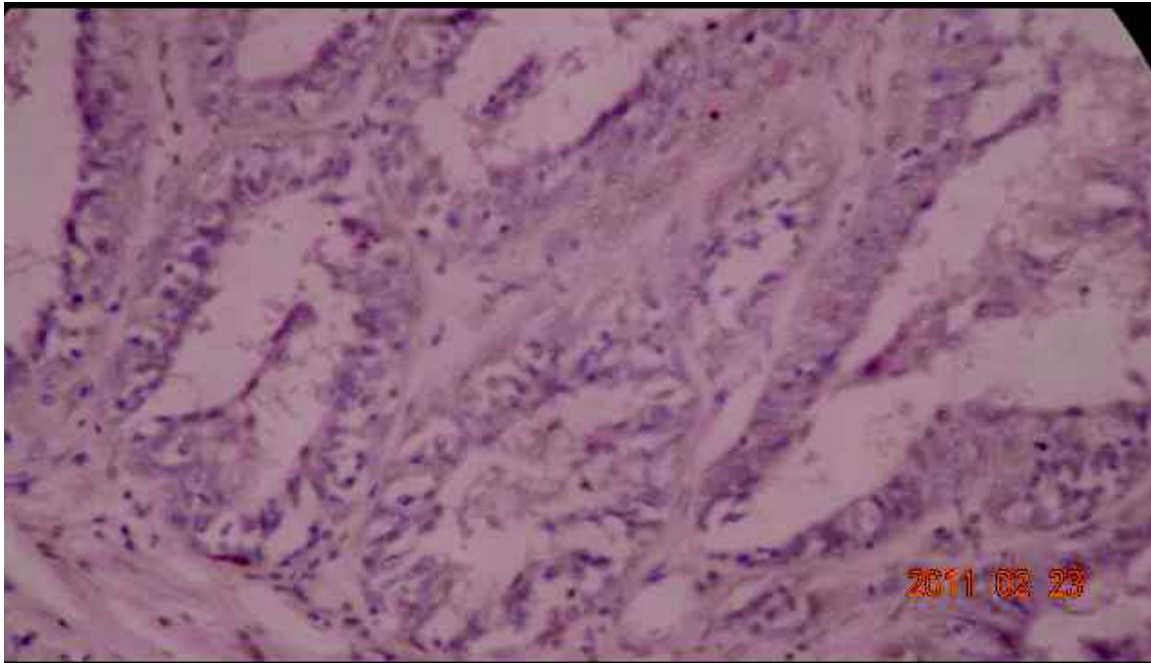


Fig 6:
udder of she camel with papillary carcinoma and negative for estrogen receptor,
immunostaining x40.

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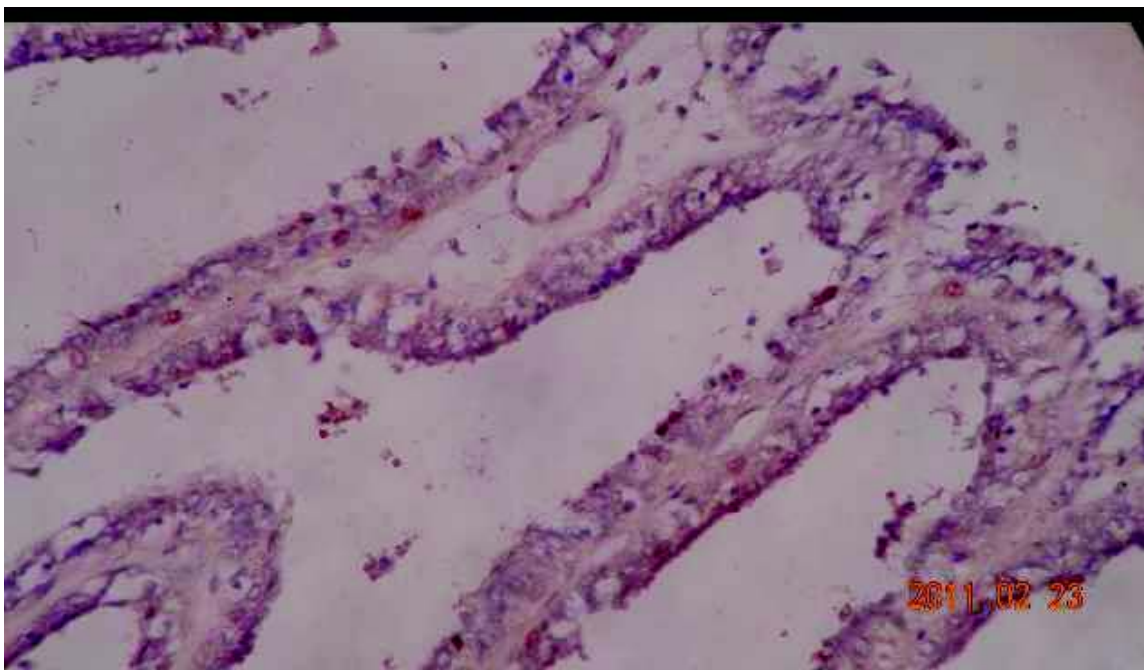


Fig 7:
udder of she camel with papillary carcinoma and positive
for estrogen receptor. Note, variable nuclear stain brown
in color, immunostain x40.

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105 **4. Discussion:**

106 Multiple mammary neoplasms were detected in the udders of she-camel. One was diagnosed as
 107 a papillary carcinoma and the second as fibroadenomatous hyperplasia. The occurrence of
 108 multiple primary mammary tumors in an individual animal is common and well documented in
 109 bitches [16, 17, 18, 19], This phenomenon is rare in other animal species and was even less
 110 frequently in camel. The available literature included a single report of simultaneous seminoma
 111 and cholangiocarcinoma in an 18-year-old male camel [20]. Camiline papillary carcinoma of the
 112 mammary glands is meager [15]. This neoplasia, however, has been well documented in bitches
 113 and queens [16, 21] and in horse [22,23].

114 fibroadenomatous lesions known as cynonymous feline mammary hypertrophy or fibroepithelial
 115 hypertrophy are relatively common in dog and cat, but it is rare in herbivores [24]. A few individual
 116 cases, however, have been reported in a nanny goat [25]; a cow [26] and a lamb [27].

In this study benign neoplastic lesions were diagnosed as fibroadenomatous mammary hyperplasia according to the histological feature [21,16] The microscopic changes observed herein for fibroadenomatous hyperplasia were indistinguishable from those reported by other investigators [28, 29, 24, 27].

In camel no previous report available in literature. The relationship between these two neoplasms it present, was not established. Immunologic and low enzymatic defects predispose some breed of dogs to multiple tumors [30]. In human, irradiation or drugs used in the treatment of primary tumor may enhance the development of another neoplasm [31].

Negative immunostaining for the progesterone receptors may have resulted from a lack of cross-reactivity to the camel species with antibodies used in this study and that agree with other researcher [27]

Immunohistochemistry revealed the ductal epithelium to be positive for pan cytokeratin (AE1/AE3) and loose fibrovascularstroma was positive for vimentin and basal cells covered the ductal epithelium of alpha-smooth-muscle actin. Immunostaining for the estrogen and progesterone receptors was negative may have resulted from a lack of cross reactivity to the ovine species of antibodies used. A diagnosis of mammary fibroadenoma was made based on the histological and immunohistochemical findings [27].

The benign and malignant mammary tumors are positive for estrogen, progesterone or prolactin receptors to varying degrees [4].

From a comparative perspective, canine mammary mixed tumors and human pleomorphic adenomas of the salivary gland exhibit morphological and molecular similarities, suggesting a similarity in the pathogenic mechanisms involved in malignant transformation and histogenesis [32].

The lack of sufficient report of multiple neoplasm particularly in dromedary camel, make it difficult to draw conclusion about the interaction of these tumor. It is probable that, as in human, multiple neoplasm such as in the present case may represent a coincidence.

Conclusions:

1. Histopathology represent an important tool to detect and confirm different types of tumors.

- 148 2. Immunohistochemistry consider confirmative methods beside the histopathological
149 picture .
- 150 3. The lack of sufficient report of multiple neoplasm particularly in dromedary camel, make it
151 difficult to draw conclusion about the interaction of these tumor.
- 152 4. It is probable that, as in human, multiple neoplasm such as in the present case may
153 represent a coincidence.

154 **Recommendation:**

155 More studies were needed to check the available of different types of tumors in camels.

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