

Adenocarcinoma among sheep and goats in Kuwait

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ABSTRACT

Record of clinical, endoscopic and histopathological features of enzootic nasal adenocarcinoma (ENA) among sheep and goats in Kuwait was mentioned in addition to evaluation of surgical interventions. One sheep and three goats were affected with enzootic nasal adenocarcinoma. Clinically, all cases were suffered from persistent seromucous nasal discharge, head shaking, muzzle licking, dyspnea, exophthalmia and frontal protrusion. Two goats were presented with unilateral fleshy mass protruded from the nostril and the 3rd goat was diagnosed after slaughtering and postmortem examination. The affected sheep was subjected to nasal upper respiratory tract endoscopic examination and endoscopic resection of the tumor mass. The two goats were treated surgically via total excision. The nasal tumors were subjected to histopathological examined. Endoscopic examination showed soft touch, pinkish-white tumor masses in the nasal cavities with distortion of the turbinate and the medium septum. According to clinical and pathological findings, the tumor has been defined as a low grade papillary nasal adenocarcinoma. This is, to our knowledge, the first report of ENA in Kuwait. However, such association requires confirmation by direct and/or indirect viral investigation. Endoscopic resection of ENA showed successful result as less invasive method comparing with traditional surgical procedures.

INTRODUCTION

Respiratory diseases represent the most serious small ruminant problem worldwide and can be a significant reason of death and productivity reduction. Different surgical affections of the upper respiratory tract of sheep and goats were previously mentioned included nasal foreign bodies, sinusitis associated with the larvae of *Oestrus ovis*, retropharyngeal lymph node abscessation, and benign or malignant nasal tumors (Jesse et al., 2019). The recorded small ruminant nasal tumors were adeno-papilloma (nasal polyps), adenomas, adenocarcinomas, lympho-sarcomas (goats), and squamous cell carcinomas (sheep) (Wilson, 2016, He et al., 2017 and Santana de Cecco et al., 2019).

Enzootic nasal adenocarcinoma (ENA) is an economically important highly contagious neoplasm of sheep and goats, associated with the oncogenic retroviruses; enzootic nasal tumor virus (ENTV) 1 and 2, respectively. It is naturally occurring worldwide and seems to be highly

distributed in countries with significant small ruminant-production except in Australia, New Zealand (De las Heras et al. 1998) and Great Britain (Sharp and De las Heras, 2000). The first case of the disease was described by Cohrs in 1953 (Švara et al., 2006). ENA has been reported in many countries like Canada, Spain, France, Slovenia and China (McKinnon et al., 1982, Ortún et al., 2003, Švara et al., 2006 and Wang et al., 2016) and more recently in Turkey (Ozmen and Serpin, 2016), Algeria (Sid et al., 2018), and southern Brazil (Santana de Cecco et al., 2019). ENA diagnosis in small ruminants is mainly based on autopsy and histopathology, and recently, there are many literatures studied real-time PCR as an available method for ENTV-2 detection (Walsh et al., 2014 and Apostolidi et al., 2019). According to authors' knowledge, there are no available literatures studied using of nasal endoscopy (Rhinoscopy) for diagnosis of ENA. There is one review article mentioned endoscopy and x-ray as confirmatory tools of diagnosis without description of their findings (Švara et al., 2006).

Enzootic nasal adenocarcinoma arises as tumoral proliferation of the secretory epithelial cells of the ethmoid turbinate area of the nasal cavity either unilaterally or bilaterally (Walsh et al., 2013 and Sid et al., 2018), and grossly, the tumors are soft, whitish or pinkish-red in color and can partially or completely obscure the nasal cavity (Walsh et al., 2010). No records of tumor metastases to the regional lymph nodes, brain or other organs (Yi et al., 2010). Until now, there are no effective approaches for early diagnosis of ENA and the affected animal could be only diagnosed after evolution of clinical symptoms. Actually, as it is problematic to differentiate between animals with a hidden infection and healthy ones, the virus spreads among the herds, and can infect several animals and threaten the whole population and consequently raises the economic losses (Wang et al 2016).

This type of tumor usually affects mature animals (2–4 years old) (Santana de Cecco et al., 2019). Clinically, the affected animals show persistent nasal discharge, dyspnoea, stertorous breathing,

and productive cough; open mouthed breathing (Ozmen, and Serpin, 2016 and Sid et al., 2018). The lesion of ENA may be presented either unilateral or bilateral mass associated with facial enlargement, skull deformations or exophthalmia with deviation of the nasal septum in advanced unilateral tumors (Santana de Cecco et al., 2019). Gradually, the animals lose weight with time and finally die within 90 days after the appearance of first clinical signs due to pasteurellosis or other complications (Švara et al., 2006).

The present study presented the first record of enzootic intranasal tumor among sheep and goats in Kuwait.

MATERIAL AND METHODS

A total number of 4 small ruminants (one sheep and three goats) were admitted to different clinics belonging to Public authority for agriculture affairs and fish resources - Kuwait City, Kuwait. The details of the cases were recorded in Table 1.

Table 1: The full descriptions of the recorded sheep and goats affected with enzootic nasal adenocarcinoma in Kuwait

Case number	Species	Breed	Sex	Age	Clinical descriptions
Case (1)	Sheep	Awassi	Male	2.5 year	Right unilateral persistent seromucous nasal discharge, head shaking, muzzle licking, dyspnoea, and frontal protrusion
Case (2)	Goat	Jamunapari	Female	2 years	Emaciation, off food, persistent seromucous nasal discharge, head shaking, and dyspnoea,
Case (3)	Goat	Pyrenean	Male	3 years	Presence of unilateral fleshy mass protruded from the left nostril, bloody nasal discharge, head shaking, and dyspnoea,
Case (4)	Goat	Anglo-Nubian	Female	2 years	Presence of unilateral fleshy mass protruded from the left nostril, persistent seromucous nasal discharge, head shaking and exophthalmia

Surgical excision of the nasal tumors was performed in two cases and the excised masses were subjected to histopathological evaluation. Tumors were collected, immediately fixed in 10% neutral buffered formalin, embedded in paraffin, cut into five mm thick sections, stained with

haematoxylin-eosin (HE) and examined microscopically.

Three cases were examined endoscopically to visualize the nasal cavity and upper respiratory tract. The endoscopic images were captured for

mare genital passage using Eickemeyer© (Germany) video-endoscope unit supplied with halogen light source (Vet Lux-150 Watt) and insertion tube (8.5 mm diameter, 1.5-meter length and 2 mm working channel). A video and several still frame images of nasal cavity were collected. One case was subjected to endoscopic resection of the ENA unilateral lesion. One case was slaughtered and subjected to postmortem evaluation.

RESULT

Four animals (one sheep and three goats) of different sexes and breeds were presented with

persistent sero-mucous nasal discharge, head shaking, muzzle licking, respiratory distress, exophthalmia and frontal protrusion with major facial deformation (Figure 1).

Endoscopic examination of nasal cavity was done in the sheep and two goats. The tumors appeared as soft touch, pinkish-white in color and they completely obstructed the nasal cavity; they were covered by clear mucous exudate. They were associated with inflammation, necrosis and distortion of turbinates and the medial septum (Figure 2A & B).



Figure 1: Clinical and gross examination of the cases affected with enzootic adenocarcinoma. A), B) A three years old Pyrenean buck affected with ENA showing unilateral protrusion of fleshy mass with nasal discharge, C) the same case after radical surgical removing of the intranasal tumor mass, D) A two years old Anglo-Nubian female goat suffering from unilateral fleshy mass protruded from the left nostril, persistent seromucous nasal discharge, E) and F) A two and half years old Awassi ram suffering from right unilateral persistent seromucous nasal discharge, head shaking, muzzle licking, dyspnoea, deformation of the frontal bone and facial asymmetry.

Surgical excision was performed in two goats according to owner request and endoscopic resection of the tumor was performed in the sheep using snare (Figure 2C). The 3rd goat was slaughtered, and the tumors were collected for histopathological examinations.

One goat was slaughtered, and complete necropsy was performed. After longitudinal cut of the head along the midline, bilateral, friable tumor masses were found in the caudal part of the nasal cavity closely attached to the mucous membrane of the ethmoid turbinates (Figure 3). No metastases were detected in regional lymph nodes, lung, brain, liver, kidney or other organs and tissues.

Microscopical examinations showed neoplastic cells arranged in tubular and papillary structures (Figure 4B). Neoplastic cells were mostly cuboidal and occasionally columnar, with distinct cell borders and a moderate amount of eosinophilic cytoplasm. The nuclei were uniform, round to oval, with clumped chromatin pattern and several small nucleoli, located centrally or in the basal parts of the cells. Mitotic figures were rare (Figure 4B). The stromal fibrous connective tissue was infiltrated by numerous lymphocytes, plasma cells and macrophages and varied from scattered to more abundant in some areas (Figure 4B).

DISCUSSION

According to annual agricultural statistics presented by central statistical bureau of state of Kuwait in 2016-2017, the total number of sheep and goats bred within different Kuwait's governorates were 684220 and 209686 respectively while the estimated population of state of Kuwait in 1/1/2019 was 1,335,712 Kuwaitis (Central Statistical Bureau, 2019). The fact which indicates that there are one sheep and one goat for each two and six Kuwaitis respectively. These ratios give an impression of the great importance of small ruminants within the Kuwait society.

On the other hand, enzootic nasal adenocarcinoma in sheep and goats may be an economically critical contagious tumor of the nasal mucosal glands with a prevalence that may reach 10% in some localities (De las Heras *et al.*, 2003). Based on the

available literature, the present study is the first report of ENT in Kuwait and it is logic to record such highly contagious neoplasm associated with the oncogenic retroviruses as it widely distributed in many countries and Kuwait is one of the extensively small ruminants importing country all over the world.

In the current research, there were four cases (one sheep and three goats) recorded as patients suffering from enzootic nasal adenocarcinoma which based in diagnosis on characteristic clinical presentation and examination, autopsy and histopathology. The results which agree with those mentioned in several previous articles (Wang *et al.*, 2016, Ozmen and Serpin, 2016, Sid *et al.*, 2018 and Santana de Cecco *et al.*, 2019). In the present study, rhinoscopy, as unique diagnostic tool, was used which considered noninvasive accurate method for diagnosis of difficult cases especially those with small size intranasal masses which did not extended outside the nostril. This result was parallel to those recorded in a previous review, in which the authors mentioned endoscopy as confirmatory tools of diagnosis without description of their findings (Švara *et al.*, 2006).

The clinical symptoms developed during the neoplasm evolution included constant sero-mucous nasal discharge and signs of upper respiratory obstruction as nostril flaring, dyspnoea and mouth breathing. These signs are frequently reported in previous articles (Wang *et al.*, 2016, Ozmen and Serpin, 2016, Sid *et al.*, 2018 and Santana de Cecco *et al.*, 2019). Regarding the present results, exophthalmia, skull deformations, facial asymmetry as well as emaciation, were reported in our cases, which considered as concurrent findings with other studies (Wang *et al.*, 2016, Ozmen and Serpin, 2016, Sid *et al.*, 2018 and Santana de Cecco *et al.*, 2019).

The histopathological findings in the sheep and goats were diagnostic and like those described previously (De las Heras *et al.*, 2003, Wang *et al.*, 2016, Ozmen and Serpin, 2016, Sid *et al.*, 2018 and Santana de Cecco *et al.*, 2019). In the present study, we observed papillary adenocarcinoma which considered as a low-grade adenocarcinoma with papillary lesions as the most common subtype of histopathological lesions (Aydogan and Ozmen,

2016 and Abdulrasoul et al. 2018). Other subtypes lesions were recorded as mucinous, tubular, and acinar patterns which also present in the tumoral tissues (Wilson, 2016). The neoplastic cells were cuboidal or columnar with round or oval nuclei with very low mitotic index. This type of carcinoma originates from the serous gland cells in ethmoidal turbinate as previously described by Abdulrasoul et al. (2018).

In the current study, successful surgical interventions were applied resulted in satisfactory postsurgical situations as presurgical septic rhinitis (due to secondary bacterial infection) completed after surgery and required systemic antibiotic and anti-inflammatory for several days (7-10 days) in addition to antihistaminic drugs. On the other side, surgical rhinoscopy was applied for radical resection of the intranasal tumor in one case with excellent results.

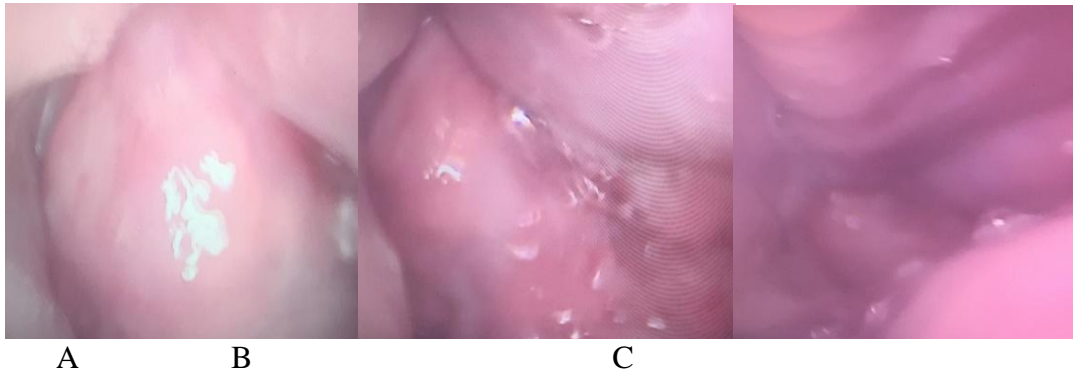


Figure 2: Findings of endoscopic examination of nasal cavity (rhinoscopy) in A two and half years old Awassi ram revealed presence of soft, pinkish-white in color mass which completely obstructed the nasal cavity; covered by clear mucous exudate, associated with inflammation, necrosis and distortion of the medial septum. A), B) before and C) two weeks after endoscopic resection of the intranasal tumor.



Figure 3: Sagittal section of the head of 2 years old Jamunapari female goat after slaughtering revealed presence of soft, pinkish-white in color mass which originated of the nasal mucosa at the level of the ethmoid turbinate.

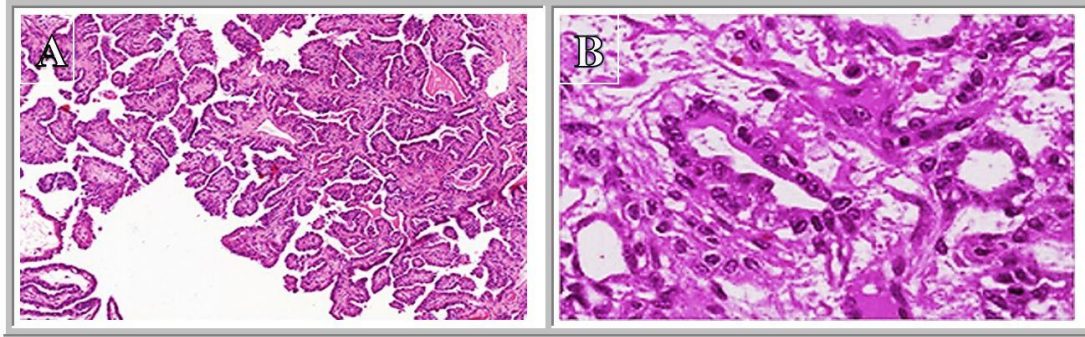


Figure 4: Histopathological finding of the nasal adenocarcinoma (HE, magnification X100). A) Papillary patterns of nasal adenocarcinoma with clear papillary projections, non-ciliated cells of the epithelial layer with thin oval nuclei and mononuclear cells infiltrating into the stroma. B) A cluster of neoplastic tubules with cuboidal cells and large round nuclei with clumped chromatin and small nucleoli. Stroma is infiltrated with mononuclear cells. (HE, magnification X400).

CONCLUSION

This is to our knowledge, the first report of ENA in Kuwait known to be associated with enzootic nasal tumor virus (ENTV) infection. However, such association requires confirmation by direct and/or indirect viral investigation. Endoscopic resection of ENA showed successful result as less invasive method comparing with traditional surgical procedures.

COMPETING INTERESTS

The authors declare no competing interests.

AUTHOR CONTRIBUTIONS

Khalifah Ali contributed to the collection of the data, clinical examination, surgical interventions and endoscopic examination and surgery.

Ahmed Osman contributed to the histopathological examination and interpretations.

Haithem Ali Mohamed Ahmed Farghali contributed to the conception and design of the work in addition to writing of the manuscript.

Ashraf Ali Eldesoky Shamaa contributed to the conception and design of the work in addition to revision of the manuscript.

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