CASE REPORT

Natural ovine pulmonary adenocarcinoma in an Egyptian sheep farm

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Özet

Radad K, Khalil S. Mısır'da bir koyun çiftliğinde ovine pulmoner adenokarsinoma. **Eurasian J Vet Sci, 2014, 30, 1, 39-43**

Ovine pulmonar adenokarsinoma koyunlarda retrovirüsün neden olduğu akciğer kanseridir. Mevcut vaka raporunun amacı Mısır'da bir koyun çiftliğinde hastalığın histopatalojik ve klinik tanımı yapmaktır. Çiftlikteki 4 adeti ölü ve 5 adeti hasta genç koyuna klinik, makroskobik ve histopatalojik değerlendirmeler yapıldı. Histopatalojik incelemeler için akciğer, mediastinal lenf yumruları, karaciğer, kalp, böbrek ve beyin dokusu örnekleri alındı. Örnekler %10 formalde tespit edildi ve ışık mikroskopta incelendi. İncelene hayvanlarda ağır kilo kaybı ve burunda mokuid akıntı gözlendi. Nekropside akciğer çok sayıda grimsi köpüklü sıvı ve pleural boşluk mukois sıvı birikimi gözlendi. Histopatalojik incelemede çok sayıda alveolar epitek kökenli kapsülsüz neoplastik odaklar tespit edildi. Neoplastik odak kübik ve sütun hücrelerden oluşmaktaydı. Bunlar düzenli papillar ve asiner şekilde belirlendi. Proliferatif hücreler küçük damar hücreleri ve fibroblast içeren yumuşak doku ile desteklenmiş olarak belirlendi. Neoplastic odaklarla ilişkili alveolar boşluklarda çok sayıda şişkin makrofaj varlığı belirgindi. Sonuç olarak ovine pulmonar adenokarsinomalar için kübik ve uzun hücrelerle kaplı alveolar epitelin transformasyonu ve burundan mukoid sıvı akıntısı patognomiktir.

Anahtar kelimeler: Adenokarsinoma, histopatoloji, akciğer, koyun

Abstract

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Ovine pulmonary adenocarcinoma is a naturally occurring retrovirus-induced contagious lung neoplasm in sheep. The current report aims to describe clinical and histopathological characteristics of the disease in an Egyptian sheep farm. In which, 4 dead and 5 sick young sheep were subjected to clinical, gross and histopathological examinations. For histopathological examination, tissue specimens were taken from lungs, mediastinal lymph nodes, liver, heart, kidneys and brain, fixed in 10% neutral buffered formalin and processed for light microscopy. Examined animals showed release of copious amount of mucoid fluid from their nostrils and marked loss of body weight. At necropsy, there were many solid grayish nodules exuding frothy fluid in the lungs and accumulation of mucoid fluid in the pleural cavity. Histopathological examination revealed presence of many non-encapsulated neoplastic foci originating from the alveolar epithelial lining. Neoplastic foci consisted of cuboidal and columnar cells that arranged in papillary and acinar forms. Proliferating cells appeared supported by loose connective tissue containing some fibroblasts and small blood vessels. Prominently, there was large number of swollen and ruffled macrophages in alveolar spaces adjacent to neoplastic foci. In conclusions, release of copious amount of mucoid fluid from nostrils and transformation of alveolar epithelial lining into cuboidal and columnar cells are pathognomonic for ovine pulmonary adenocarcinoma.

Keywords: Adenocarcinoma, histopathology, lungs, sheep.

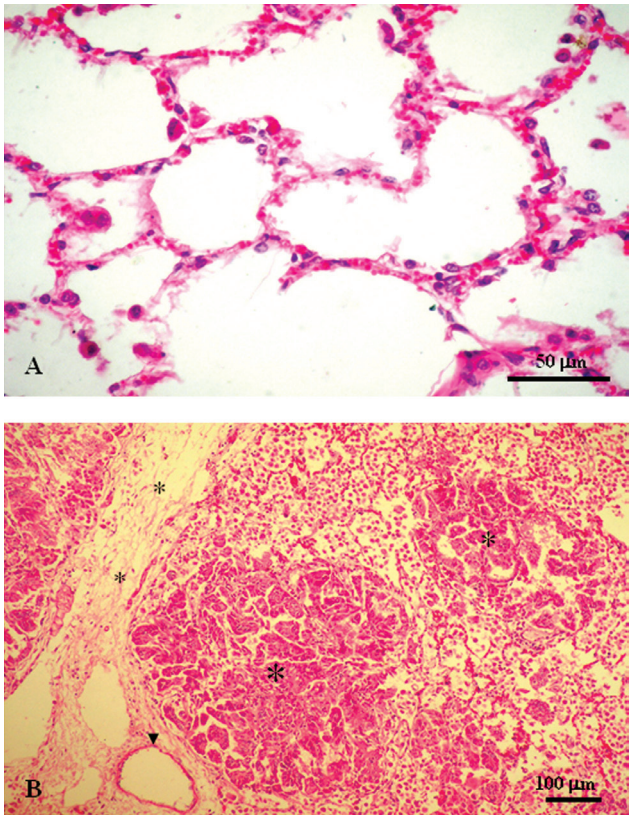

Figure 1. A) Normal histology for control lung showing normal alveolar epithelial lining. B) Lung showing focal areas of pulmonary adenocarcinoma consists of papillary and acinar forms of cellular proliferations. Papillary and acinar proliferations involve lung alveoli (asterisk). There are also dilatation of lymph vessels (arrow heads) and widening of interlobular septa (small asterisks).

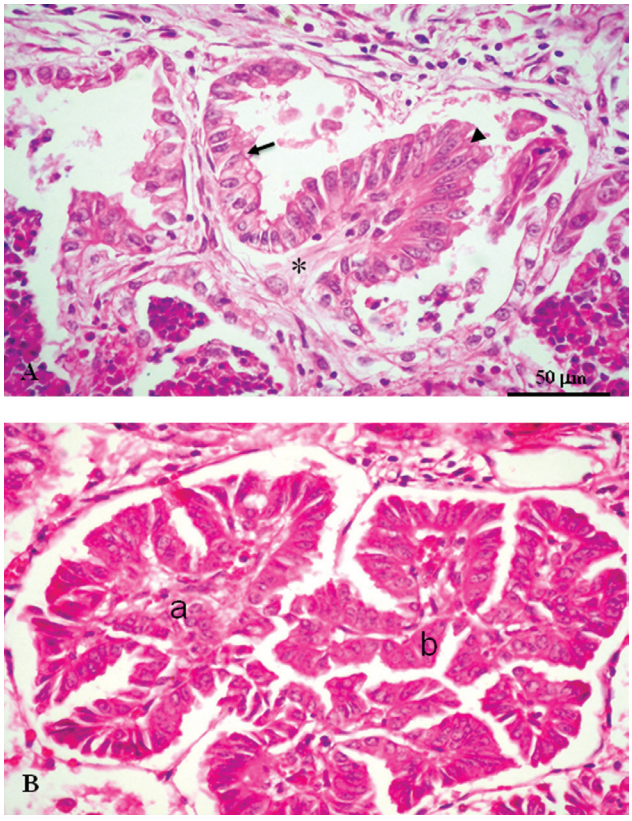

Figure 2. A) Alveolar epithelial lining showing columnar transformation (arrow), proliferation and papillary growth formation (arrow head). Epithelial proliferation is supported by loose connective tissue (asterisk). B) Two alveolar spaces (a, b) are completely occupied by tumor cells forming papillary forms.

Ovine pulmonary adenocarcinoma (OPA), formerly sheep pulmonary adenomatosis and ovine pulmonary carcinoma, is a transmissible neoplastic disease of sheep (Fan et al 2009). The disease primarily affects both domestic and wild sheep, and does not occur in other livestock except goats, in which, the disease has been described in subclinical form (De las Heras et al 2003). OPA was first described as a cause of respiratory distress in sheep in South Africa in 1865. In that time, the disease was called "jaagsiekte", the name that is derived from the Afrikaans and means "chasing sickness". This is because affected animals show difficulty to breathe as if they are being chased (York et al 2003). Since then, OPA has distributed worldwide except in Australia and New Zealand (Griffiths et al 2010) and Iceland which has eradicated the disease (Maeda et al 2011). OPA is caused by the jaagsiekte sheep retrovirus (JSRV), a member of the genus *Betaretrovirus* in the family Retroviridae. JSRV induced neoplastic transformation of secretory epithelial cells of the lung, alveolar type II pneumocytes and bronchial Clara cells (Kycko and Reichert 2007). More specifically, it was reported that the JSRV genome is simple and not oncogenic, and the viral oncogenicity returns to the viral envelope protein (Leroux et al 2007). Administration of mice with JSRV Env protein induced similar histologic features of JSRV-induced OPA in sheep (Wootton et al 2006). JSRV Env protein activated PI3K-Akt and Ras-MEK-MAPK, the two main pathways involved in the transformation of lung cells (Kycko and Reichert 2007). Natural transmission of JSRV among sheep was reported to occur through several ways, most commonly, the aerosol route. In this context, Cousens et al (2009) reported that about 10^7-10^{10} copies of JSRV's RNA per 1 mL were found in the fluid released from the lungs of OPA-affected animals. Moreover, excreted JSRV in the milk and colostrums of affected ewes can transmit the virus into suckling lambs (Grego et al 2008). At present, OPA is considered a significant veterinary problem worldwide. In this context, York and Querat (2003) stated that the mortality in sheep due to JSRV in first-introduced flocks was 30-50% in the first year. Griffiths et al (2010) mentioned that however OPA has been recognized in sheep since the 19th century, there is no effective control

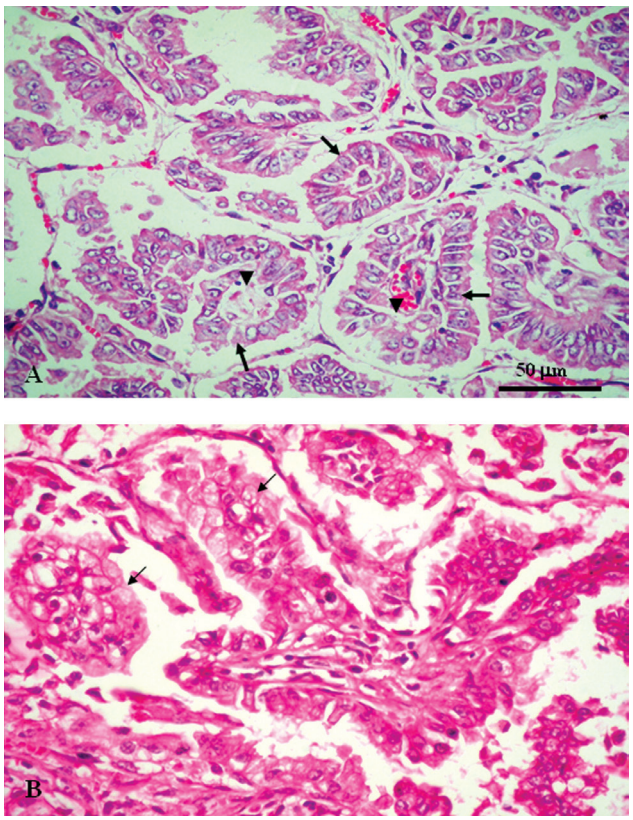

Figure 3. A) Lung showing OPA consists of acinar forms of proliferation (arrows). Acinar forms showing central fibrovascular core (arrow heads). B) Tumor cells showing more or less cytoplasmic vacuolation (arrows).

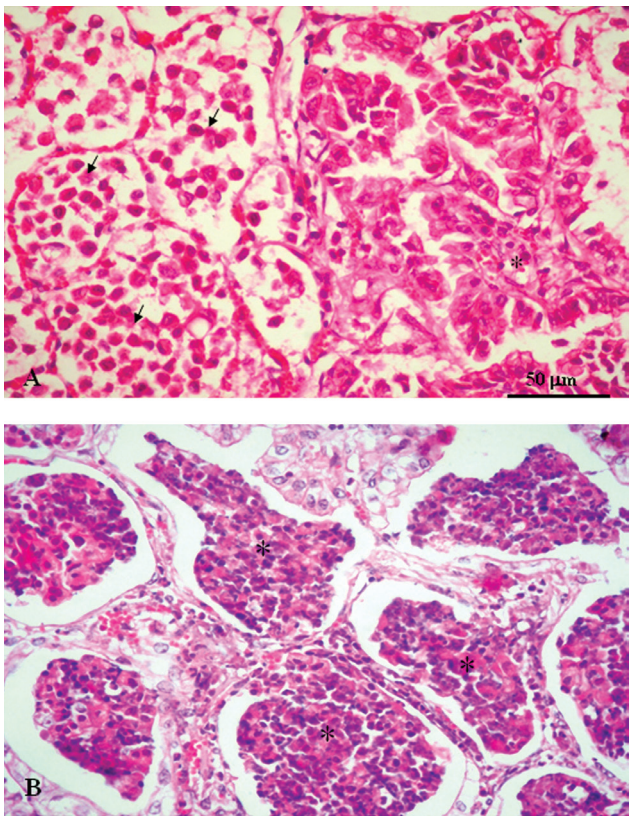

Figure 4. A) Lung with OPA showing epithelial growths (asterisk) and desquamated alveolar macrophages in air spaces (arrows). B) Lung with OPA showing massive desquamated alveolar macrophages in air spaces (asterisks).

for the disease and it causes significant economic losses. This current report describes OPA in an Egyptian sheep farm. In which, clinical and histopathological pictures of the disease were described. These characteristic features still an efficient tool for diagnosis of the disease.

Four dead and five sick young adult sheep (6-12 months) were presented to the Department of Pathology, Faculty of Veterinary Medicine, Assiut University, Assiut, Egypt from Al-Hawatka sheep farm in Assiut Governorate. Dead animals were thin and had mucosal nasal discharges. Sick animals showed symptoms of respiratory distress and flow of copious amounts of mucoid fluid from their nostrils. All animals were subjected for necropsy. At necropsy, tissue specimens were taken from lungs, mediastinal lymph nodes, liver, heart, kidneys and brain and kept in 10% neutral buffered formalin for histopathological examination. After 48h of fixation in neutral buffered formalin, specimens were routinely processed for histopathological examination, sectioned at 4 µm and stained with hematoxylin and eosin (HE) (Bancroft and Stevens 1990). Stained sections were examined under a light microscopy and photographed using a digital camera.

The owner of the sheep farm stated that the presented dead animals died after six weeks of respiratory distress. During which, they showed difficulty to breathe especially at herding and flow of copious mucoid fluid from the nostrils. They also showed marked loss of their body weight. The owner added that those animals did not respond to antibiotics and other kind of treatments. At necropsy, all animals showed enlarged lungs with presence of multiple hard grayish areas and accumulation of mucoid fluid in the pleural cavity. Sectioning of the lungs revealed solid and grey nodules that exuded frothy fluid. No apparent lesions were observed in mediastinal lymph nodes, liver, heart, kidneys and brain (Data not shown). Histopathological examination of HE-stained tissue sections from all dead and slaughtered animals revealed many non-encapsulated neoplastic foci originating from the alveolar epithelial lining (Figure 1B). First, alveolar epithelial lining appeared transformed into cuboidal and co-

lumnar cells, and then threw into papillary and acinar forms that filled alveolar spaces as well as expanded into adjacent tissue (Figure 2A, B). Proliferated cells appeared supported by loose connective tissue containing some fibroblasts and small blood vessels (Fig. 3A). Tumor cells showed more or less cytoplasmic vacuolation (Figure 3B). There were no growths emanating from bronchiolar epithelial lining. Around neoplastic growths, there was large number of swollen macrophages in alveolar spaces (Figure 4A). These macrophages appeared large and ruffled and in some cases, they clustered with some neoplastic cells in the alveolar spaces (Figure 4B).

Since its occurrence in South Africa in the 19th century, OPA has become a common disease of sheep in most geographical areas of the world (Murgia et al 2011). In the current report, the disease was described in 9 young adult sheep in Assiut governorate in Upper Egypt. Affected animals showed signs of respiratory distress and release of abundant amount of mucoid fluid from their nostrils. It was reported that accumulation of mucoid fluid within the respiratory tract is a pathognomonic symptom of OPA-affected sheep (Palmarini and Fan 2001, Cousens et al 2009, Griffiths et al 2010). Sectioning of lungs of affected animals revealed presence of solid and grey nodules that exuded frothy fluid. Similarly, Palmarini and Fan (2001) reported that lungs of sheep with OPA appeared enlarged with presence of grayish firm masses in the cranio-ventral portion of the organ. No apparent lesions were noticed in the extrathoracic and intrathoracic organs in examined sheep. In contrast, Minguijón et al (2013) reported extrathoracic and intrathoracic metastasis of OPA in sheep. Extrathoracic metastasis were found in the liver, kidneys, skeletal muscles, digestive system, spleen, skin and adrenal glands while intrathoracic metastasis occurred in chest wall, regional lymph nodes, diaphragm and heart. The prominent histopathological finding of OPA in the current report was transformation of alveolar epithelial lining into well-differentiated cuboidal and columnar cells forming non-encapsulated neoplastic foci in the lungs. Transformed cells formed papillary and acinar growths to the inside of the alveoli which sometimes completely occupied the alveolar spaces. These findings are in parallel with the classical structure of OPA as observed in previous reports (Palmarini and Fan 2001, Oda and Youssef 2011). Inconsistent with our findings which returned the origin of neoplastic cells to the alveolar epithelial lining, Griffiths et al (2010) reported that neoplastic transformation in OPA involved both alveolar and bronchiolar secretory epithelial cell, i.e. type II pneumocytes and Clara cells. Recently, Murgia et al (2011) reported that the source of neoplastic cells in OPA is the proliferating type 2 pneumocytes (lung alveolar proliferating cells, LAPCs) and not the bronchioalveolar stem cells, mature post-mitotic type 2 pneumocytes, or proliferating or non-proliferating Clara cells. In this context, it was reported that young sheep had abundant LAPCs and exhibited higher susceptibility to experimental JSRV infection. In contrast, healthy adult sheep had a relatively low number of LAPCs and were resistant to experimental OPA induction (Murgia et al 2011). Likewise in most reported cases, proliferated cells were seen to be supported by loose connective tissue containing some fibroblasts and small blood vessels. Wootton et al (2006) observed nodules of loose mesenchymal tissue admixed with tumor as a part of the fibrovascular core in some cases of OPA. In addition, infiltration of macrophages into alveolar spaces around growths was a further common feature of OPA in the most examined cases. Similarly, Summers et al (2005) reported that the influx of macrophages was the predominant local immune response in ovine pulmonary adenocarcinoma. The authors attributed the lack of an effective immune response in OPA to the local surfactant protein which suppressed the activity of the invading macrophages (Summers et al 2005).

The current report described the clinical and histopathological features of OPA in an Egyptian sheep farm. In which, release of copious amount of mucoid fluid from the nostrils and transformation of alveolar epithelial lining into well-differentiated cuboidal and columnar cells are, respectively, pathognomonic clinical and histology features for OPA.

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