Iraqi Journal of Veterinary Sciences

www.vetmedmosul.com

Ovine pulmonary adenocarcinoma: Pathological, histochemical and immunohistochemical properties

R.M. Alsaidya[1] and S.S. Al-Mahmood[2]

[1]Veterinarian, Private sector, [2]Department of Pathology and Poultry Diseases, College of Veterinary Medicine, University of Mosul, Mosul, Iraq

Article information

Article history:
Received 21 January, 2025
Accepted 26 March, 2025
Published 01 April, 2025

Keywords:
OPV
Immunohistochemistry
Sheep
Retrovirus

Correspondence:
S.S. Al-Mahmood
dr.saevan981@gmail.com

Abstract

Ovine pulmonary adenocarcinoma (OPA) is a viral endemic disease in different geographical areas, including Mosul city, Iraq. We aimed in the current study to observe the gross and microscopic lesions caused by natural infection with OPA, in addition to recording the reactivity of this viral disease in sheep with some tissue markers such as $CD45_{RO}$, P_{53}, Ki_{67}, and VEGFA using immunohistochemical assay. A total of 73 lung tissue samples were collected from sheep that showed clinical signs of OPA; 21 samples only showed gross and microscopic OPA lesions. The samples with pathognomic lesions for OPA were subjected to immunohistochemical assay using tissue markers against $CD45_{RO}$, $P_{53,}$ Ki_{67}, and VEGFA. The result showed gross lesions of edematous lungs, pale to purple, with hard consistency. Microscopically, the neoplastic tissue has two stages: the early stage, with neoplastic cells well defined as either cuboidal or columnar with feathery cytoplasm, while the late stage has neoplastic cells poorly differentiated and usually found as cellular debris in the lumen of affected alveoli and bronchioles. The result of IHC showed a strong positive reaction with $CD45_{RO}$ and P_{53}, a positive reaction with VEGFA, and a negative reaction with Ki_{67}. In conclusion, the lesions of naturally occurring OPA have two major forms, either classic or atypical forms, in addition to the mixed form; all these forms have the same IHC reactivity, where they are strongly positive for $CD45_{RO}$, P_{53}, and VEGFA, while they are negatively stained with Ki_{67}.

DOI: 10.33899/ijvs.2025.156829.4097,

Introduction

Ovine pulmonary adenocarcinoma (OPA) is a contagious viral lung disease of sheep, also known as sheep pulmonary adenomatosis and ovine pulmonary carcinoma (1). OPA was first described in South Africa in the 19th century and was called Jaagsiekte disease, a name derived from the clinical signs of affected sheep, which usually show respiratory disaster and walk behind the flock when moving between pastures (2). Since its first report diagnosed this condition, the disease has been reported worldwide in sheep (3). OPA virus is a double-stranded RNA virus, characterized by primarily causing proliferative tumors in Clara cells and type II pneumocytes (1); in addition to these two cells, the virus's oncogenic transformation extends to other types of cells in the lung tissue (4). The neoplastic lesions are often associated with lung fibrosis due to the huge deposition of collagen fibers in the interstitial tissue between the alveoli (5). In less widespread cases, hyperplasia of the alveoli can be observed, especially in lung cells infected with the retrovirus; these cells are characterized by the presence of neoplastic mitotic figures with the absent or slight deposition of collagen fibers in the interstitial tissue (6). The cancerous growth in the lung is accompanied by a large and dense production of foamy fluids inside the lung tissue, which causes respiratory arrest (7). The latent period between infection and the appearance of clinical signs is relatively long, extending from several months to a year; in many

cases, infection may occur without any clinical signs in infected sheep, allowing the virus to be transmitted and spread in the flock (8). Although pulmonary adenocarcinoma in sheep has been described since the nineteenth century, the method of eradicating this disease is unknown, and the only method that can be used to prevent the spread of the disease and control it is culling herds (1). The most important clinical signs of the disease were the heavy production of foamy fluids from the lungs, which can be easily observed when lifting the animal's hind limbs, which begin to secrete from the nose; it can be described as clear, white, or slightly pink, foamy, and flow from the nose in large quantities (8). Histologically, neoplastic proliferating cells present in the alveoli originated basically from Clara cells, type II pneumocytes, and epithelial cells lining the alveoli, or a mixture of all or some of these cells, characterized with elongated, cubic, or hexagonal cells and containing a slightly eosinophilic cytoplasm, also the nuclei characterized by enlarged size and contain many neoplastic mitotic figures (9). This disease is characterized by a high incidence in sheep in Mosul, especially in the wet months, and its occurrence is often associated with infection with liver flukes; the infected sheep showed signs of losing conductions with drooping heads and foamy nasal discharge (10).

In the current study, we aimed to accurately describe OPV pathological findings and the IHC properties of these neoplastic lesions.

Materials and methods

Ethical approve

This study was proved by the College of Veterinary Medicine, University of Mosul, with a proposal numbered UM.VET.2024.018 dated 20/05/2024.

Samples collection

76 lung samples that showed clinical signs of OPA were collected from different geographical areas in Mosul city from 01/09/2024 till 20/12/2024. The lung samples were collected from sheep, showing the clinical signs of nasal watery discharge with respiratory illness and the gross appearance of OPV lesions. The samples were examined grossly, and the lesions were reported and recorded; a representative sample was collected and immersed in 10% neutral buffered formalin for 72 hours before it could be submitted for histopathological examination (11).

Histological protocol

After tissue fixation, slices of the affected area were collected in thickness not more than 7mm with 1.5*1.5 dimensions; these samples were put in labeled tissue cassettes (Mevid, China, EM01-102-02), later they were submitted to tissue processing started with dehydration with an ascending concentration of ethyl alcohol (Scharlau, Spain, ET00052500), cleared with Xylene (Scharlau, Spain, XI00602500), using hot paraffin wax pellets at 58ºC (Scharlau, Spain, PA01122500) infiltrated using automatic benchtop tissue processor (TP1020, Leica, Germany), embedding using paraffine center (HistoCore Arcadia, Leica, Germany) then left until get solidify (12). Tissue blocks were trimmed at 25µm then sectioned at a thickness of 4±2µm using an automated microtome (HistoCore AUTOCUT, Leica, Germany); paraffine ribbons were floated in the flotation water bath (HistoCore M, Leica, Austria), then stained using Harri's hematoxylin and alcoholic eosins (H&E), later tissue slides stained with Masson's trichrome (MT) and Periodic Acid Schiff reagent (PAS) to explain more histological elements (12).

Immunohistochemical protocol

Primary antibodies were used from Elabscience® as explained in table 1, in brief slides were dewaxed in xylene and rehydrated by descending ethyl alcohol to distilled water, then antigen retrieval using citric buffer solution at pH 6.0 at 60ºC for one hour, then let to be cooled to room temperature, then washed with PBS at 7.4 pH for three times, then anti peroxidase activity applied using 3%H_2O_2 for 15 minutes, then washed with PBS at 7.4 pH for three times, then tissue sections blocked using 5% goat serum and incubate for 30 minutes at 37ºC, then incubated with primary antibody overnight in humidity chamber at 4ºC, then washed with PBS at 7.4 pH for three times, and incubated with secondary antibody sharing the same primary antibody host origin for 45 minutes at 37ºC, later slides washed with PBS at 7.4 pH for two times, and stained with DAB stain prepared freshly for 1 minutes at room temperature (13). Later, tissue slides were dehydrated, cleared, and mounted using DPX (11,12).

Table 1: IHC primary antibodies and material used

Item	Company #
$CD45_{ro}$ polyclonal antibody	E-AB-70024
P53 polyclonal antibody	E-AB-93244
Ki67 polyclonal antibody	AN004340L
VEGFA polyclonal antibody	E-AB-19306
Goat Anti-Rabbit IgG	E-AB-1034
DAB detection kit	E-IR-R101

Results

Gross pathology

The lung was swallowed and wet with a waved surface; these lungs did not collapse during post-mortem examination when the thoracic cavity was exposed. The neoplastic tissue either appeared as small scattered nodules diffused in lung tissue, or these neoplastic areas appeared as diffuse lesions of hard tissue with diffused lobulated nodules on the whole lobe of the lung. These nodules appear slightly elevated from the lung surface and have a solid texture, which appears

white to gray in color and, in some cases, as faint purple, surrounded with purple to red normal lung tissue. In mild cases, the neoplastic areas appeared in the cranioventral parts of the affected lung, while in severe cases, these lesions appeared in all lung lobes; in addition, these neoplastic areas have white to gray to purple hard nodules surrounded by a red, soft zone of normal or emphysematous tissues. In deep cutting to lung tissue, these nodules appeared as white, numerous hard nodules scattered through lung tissues; in severe cases, they coalesce together, which gives these diseases named glandular tissues, and a frothy fluid oozing from lung tissue and with slight pressure these fluids pour from it (Figure 1).

Figure 1: In a natural case of OPA, the lung showed a pale to white color, with a granulated appearance, and easily fragmented in small pieces, with solid consistency.

Histopathology

Histopathological examination of the neoplastic area of affected lungs showed hard tissue growth, which appeared as neoplastic epithelial cells that were either cuboidal or columnar in shape; these neoplastic cells appeared in alveolar walls and in the epithelial lining of bronchioles and bronchi, these neoplastic lesions suffering from intensive hyperplasia which led to compressing to surrounded interstitial tissues lead to fibrosis by collagen fiber deposition. These neoplastic cells were found as papillary or acinar in the alveoli and bronchioles, which significantly replaced the epithelial lining of these two structures with the flat alveolar cell type I, and their nucleus showed few mitotic figures. They appeared at basic locations in both cuboidal and columnar cells. Still, the cytoplasm appeared vacuolated in columnar cells and more eosinophilic clear in cuboidal cells. In some cases, these neoplastic tissues may be found sloughed as cellular debris in the lumen of affected alveoli and bronchioles, which causes the closure of these pathways and is associated with serous exudation. Fibrosis by collagen deposition is mostly seen in the interstitial tissue surrounding these neoplastic structures, while in severe cases, the whole lung tissue appears fibrotic, causing the fibrous tissue surrounding the groups of neoplastic alveoli and their bronchioles. All these lesions are mostly seen with massive infiltration of mononuclear inflammatory cells, especially macrophages and lymphocytes (Figures 2-6). The lung section stained with Masson's trichrome stain showed massive deposition of collagen fiber around the affected alveoli and bronchioles in the interstitial tissues, which makes the neoplastic tissue surrounded as islands between the collagen fibers, in addition to that PAS stain showed the presence of mucin materials and colloid droplet deposition in these neoplastic cells (Figures 7 and 8).

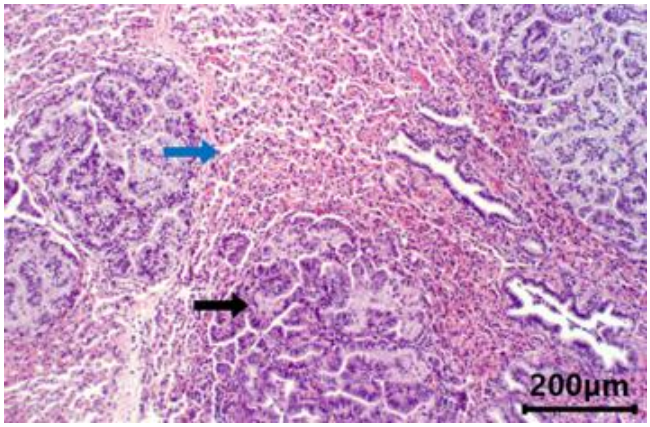

Figure 2: Histopathological section in the lung showed natural lesions of OPA. A neoplastic area in the alveolar structure (black arrow), surrounded by fibrous connective tissue, separates these neoplastic areas as islets (blue arrow). H&E.

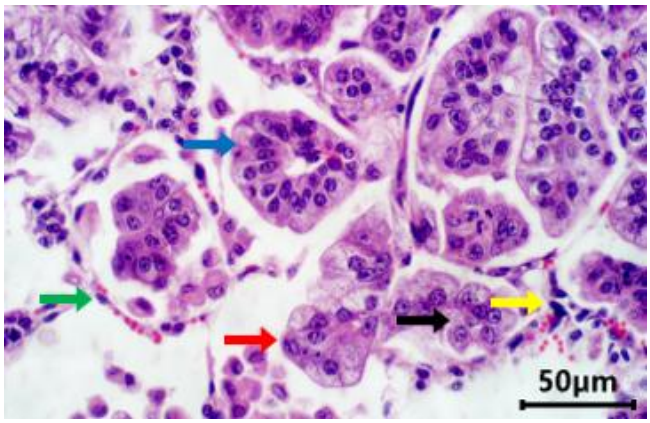

Figure 3: Histopathological section in the lung showed natural lesions of OPA. Showed the neoplastic cells in the early stage of neoplastic transformation where the cells appeared as cuboidal (black arrow) or columnar (blue arrow) in the alveolar structure, with few infiltrations of lymphocytes (yellow arrow), the cell nucleus where have few mitotic figures (red arrow) while other cells showed normal nucleus (green arrow). H&E.

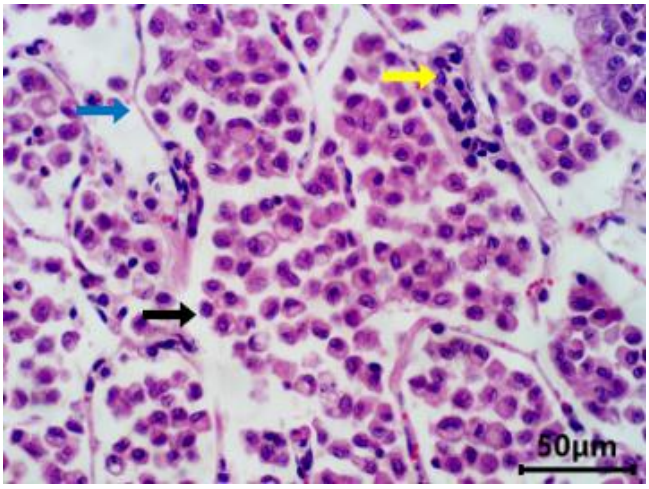

Figure 4: Histopathological section in the lung showed natural lesions of OPA. Showed the neoplastic cells in the final transformation stage (black arrow), where they sloughed in the space of the alveolar basement membrane (blue arrow), these neoplastic cells with infiltration of lymphocytes (yellow arrow). H&E.

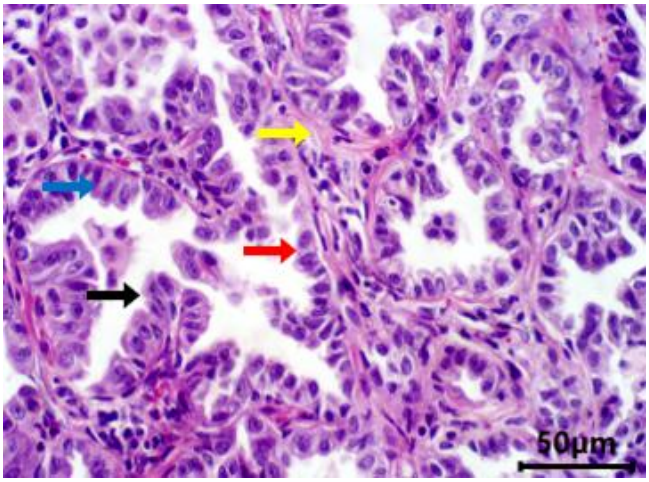

Figure 5: Histopathological section in the lung showed natural lesions of OPA. Showed figure-like projection of neoplastic cells (black arrow), which are either columnar (blue arrow) or cuboidal cells (red arrow) with deposition of collagen fibers (yellow arrow) between these affected alveoli. H&E.

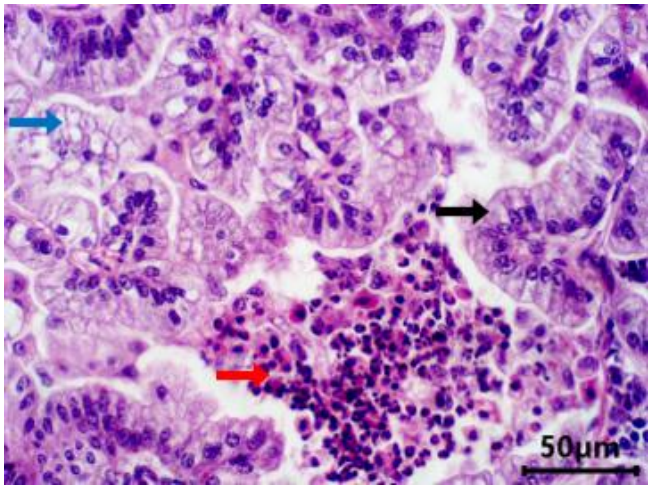

Figure 6: Histopathological section in the lung showed natural lesions of OPA. Showed the neoplastic transformation mainly in alveolar cell type II, known as Clara cells (black arrow), which is mainly characterized by the presence of vacuolar structure in the cytoplasm (blue arrow) with infiltration of multinucleated inflammatory cells (red arrow) as an indicator for secondary bacterial infection. H&E.

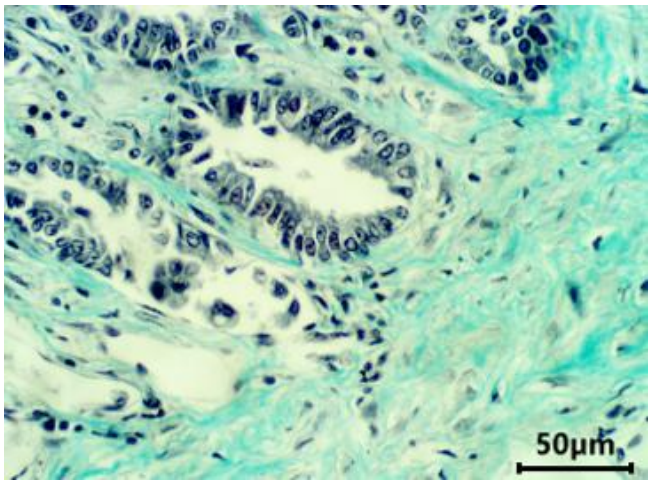

Figure 7: Histopathological section in the lung showed natural lesions of OPA. Showed deposition of green collagen fibers around the neoplastic alveoli (black arrow) and deposition of the same green collagen fibers around groups of these alveoli (red arrow), giving these lesions the shape of islands. Mason's trichrome.

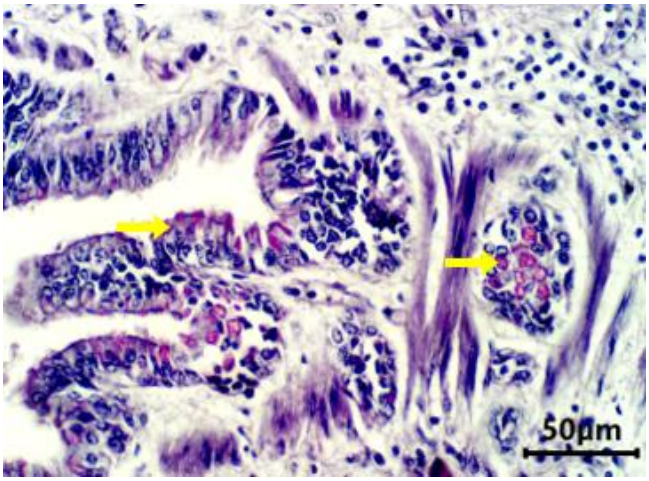

Figure 8: Histopathological section in the lung showed natural lesions of OPA. Showed the presence of surfactant material inside vacuoles in neoplastic Clara cells (yellow arrow). PAS.

Immunohistochemistry

IHC examination of the neoplastic area of affected lungs showed a strong positive reaction with CD45ro in the activated neoplastic T cells that are present in these lesions, in which this T cell appeared with large cytoplasm positive for CD45ro and the nucleus has few mitotic figures; these cells were recorded in the final stage of neoplastic alveoli (Figure 9). The neoplastic cells were negatively reacted with Ki67 antibodies; on the other hand, the lymphocytes present within the alveolar wall stained weakly positive with Ki67, which appeared as golden-brown patches in the cytoplasm of these cells (Figure 10).

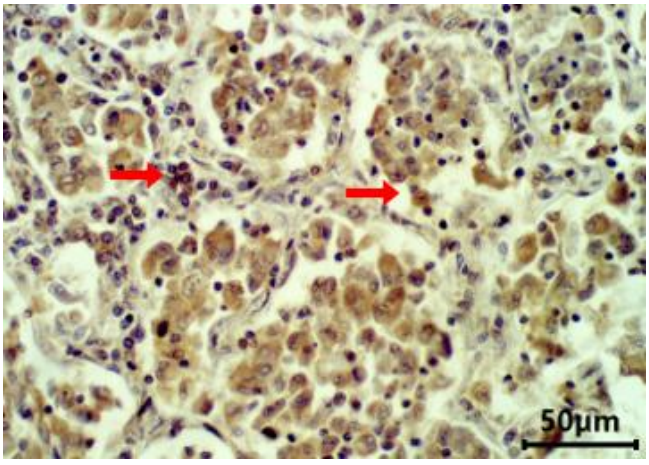

Figure 9: Histopathological section with IHC staining in the lung showed natural lesions of OPA. A strong positive reaction appeared, with golden-brown batches inside poorly differentiated neoplastic cells (red arrow) in the affected alveoli. CD45ro.

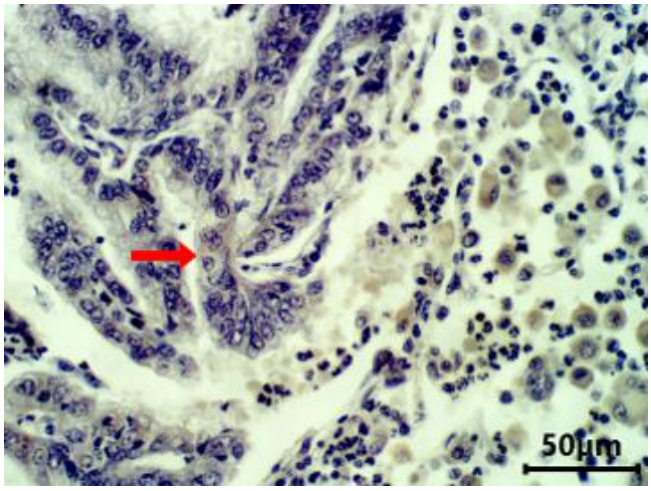

Figure 10: Histopathological section with IHC staining in the lung showed natural lesions of OPA. The negative reaction to Ki67 antibodies in the nucleus neoplastic cells (red arrow) was observed. Ki67.

The neoplastic cells were found to strongly and positively react with P53 antibodies. These cells were found especially in the walls of alveoli and bronchioles, which appeared as cuboidal or columnar cells with golden-brown cytoplasm, and the nucleus have few to moderate mitotic figures (Figure 11). Also, the epithelial cells lining the blood vessels within the neoplastic areas were stained positively with VEGF antibodies; these cells appeared as flat cells with positive cytoplasm with golden-brown granules (Figure 12).

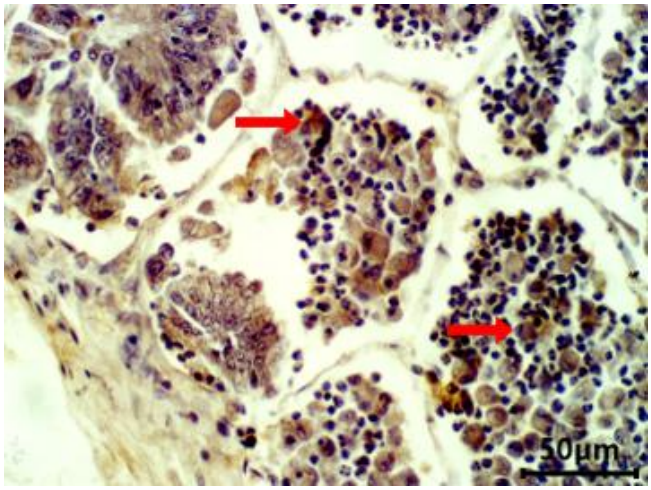

Figure 11: Histopathological section with IHC staining in the lung showed natural lesions of OPA. A strong positive reaction appeared as cytoplasmic golden-brown batches in the columnar neoplastic cells in the walls of affected alveoli (red arrow) and the poorly differentiated neoplastic cells in the lumen of alveoli (blue arrow). P53.

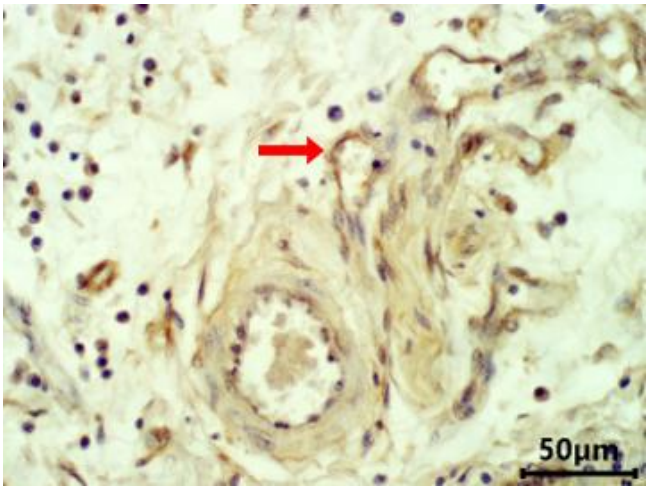

Figure 12: Histopathological section with IHC staining in the lung showed natural lesions of OPA. A strong positive reaction appeared as cytoplasmic golden-brown granules in the epithelial cells of new blood vessels (red arrow). VEGF.

Discussion

The result of the current study indicated the presence of OPV natural cases in Mosul city and Iraq; these natural cases were recorded yearly in the autumn and winter seasons (14-17). The statistical study showed that this neoplastic disease in sheep increases in incidence during wet conditions since it is an aerosol-transmitted virus, and the increase in humidity and cold weather will help increase the occurrence (18).

The current study describes the classical and pathognomic of gross and microscopic lesions caused by natural infection with neoplastic retrovirus in sheep that causes ovine pulmonary adenocarcinomas. The gross lesions were described previously as pale to purple areas of neoplastic tissue present mainly in the cranioventral lobe of the lung, and in severe cases, it includes all lobes of the lungs; these areas were firm in cut and having areas filled with necrotic tissues, also these areas characterized by slightly elevated above the lung surface with red color zone of demarcation, in addition to pinpoint hemorrhages areas may be recorded (19-29).

In contrast, the current study explains the microscopic lesions in detail, where the main characteristic neoplastic transformation was recorded in the formation of cuboidal or columnar neoplastic cells present in the walls of alveoli and bronchioles, in addition to poorly differentiated neoplastic cells that present in the final stage of this cancer development associated with necrotic area and infiltration of lymphocytes with scattered multinucleated inflammatory cells as response to secondary bacterial infection, with wide distribution of collagen fibers in two characteristic form, the first one as wide collagen bundles that separate the neoplastic area as islets, the second one as fine collagen fibers deposition around the walls of neoplastic alveoli, also the neoplastic transformation of alveolar cell type II which know as Clara cells to produce an abundant proteinous materials that present as positive to PAS stain appeared as vacuoles inside these cells stained as bright pink in color (30-37).

CD45 protein is also known as protein tyrosine phosphate receptor C (PTPRC), an enzyme that is encoded by PTPRC gen; this enzyme has an important role in innate immunity regulation by activating T lymphocytes during neoplastic transformations caused by a viral infection, in addition, this gen has an important role in cell growth cycle specially during mitotic phase and in oncogenic cell transformation were its activated to suppressing the neoplastic transformation of cells (38-40).

Ki67 is a nuclear protein considered a tissue marker for proliferating cells that is expressed in the nucleus of cells during the interphase of cell division; this protein is expressed by the MKi67 gene that is present in the surface location of chromosomes; the function of this gene related to synthesis of rRNA which is expressed in high rate in cells with high proliferation rate, in OPA infection the neoplastic cells did not have interphase of cell cycle since they are in neoplastic mode proliferation, which considered as the landmark for Ki67 in sheep infection with JSRV (41-44).

VEGF is a cytoplasmic tissue marker produced to enhance angiogenesis, especially in cases of high need for oxygen supply, especially during inflammation, healing, and asthma. It is a member of platelet-derived growth factors, important for the vasculogenic of embryos to develop the circulatory system and for new blood vessel formation in a process termed angiogenesis; this protein can stimulate the stem and endothelial cells within the walls of blood vessels or surroundings areas to proliferate and migrate to produce new blood vessels; also these factors were produced by neoplastic cells to increase the blood supply to enhance the growth of virus and their infected cells (45-47).

Conclusion

We conclude that the lesions of naturally occurring OPA have two major forms, either classic or atypical forms in addition to the mixed form; all these forms have the same IHC reactive where they strongly positive to CD45ro, P53, and VEGF, while they are negatively stained with Ki67.

Acknowledgment

The authors thank the College of Veterinary Medicine, University of Mosul, for supporting the current study.

Conflict of interest

None.

References

1. Abd Abass F, Khudhair YI. Clinical, molecular, and pathological investigations of ovine pulmonary adenocarcinoma in the middle of Iraq. Open Vet J. 2022;12(2):264-72. DOI: 10.5455/ovj.2022.v12.i2.15
2. York DF, Querat G. A History of Ovine Pulmonary Adenocarcinoma (Jaagsiekte) and Experiments Leading to the Deduction of the JSRV Nucleotide Sequence. In: Fan H, editor. Jaagsiekte Sheep Retrovirus and Lung Cancer. Current Topics in Microbiology and Immunology. Germany: Springer; 2003. 1–23 pp. DOI: 10.1007/978-3-642-55638-8_1
3. Dykes JR, M'Fadyean J. Lung disease in sheep, caused by the Strongylus rufescens. J Comp Pathol Therap. 1888;1:139-46. DOI: 10.1016/s0368-1742(88)80043-2
4. Al-Husseiny S, Jassim A, Mansour KA, kshash QH. Phylogenetic analysis of Jaagsiekte sheep retrovirus (JSRV) in Iraqi Awassi sheep. Iraqi J Vet Sci. 2020;34(2):351–5. DOI: 10.33899/ijvs.2019.126172.1255
5. Amini F, Mostafa-Tehrani A. A five-year survey (2002-2007) on ovine pulmonary adenomatosis in a mixed-breed sheep flock. Bulg J Vet Med. 2013;16(2). [available at]
6. Armezzani A, Varela M, Spencer TE, Palmarini M, Arnaud F. "Menage a trois": the evolutionary interplay between JSRV, enJSRVs and domestic sheep. Viruses. 2014;6(12):4926-45. DOI: 10.3390/v6124926
7. De las Heras M, Ortín A, Salvatori D, de Villareal MP, Cousens C, Ferrer LM, Cebrián LM, de Jalón JA, Gonzalez L, Sharp JM. A PCR technique for the detection of Jaagsiekte sheep retrovirus in the blood suitable for the screening of ovine pulmonary adenocarcinoma in field conditions. Res Vet Sci. 2005;79(3):259-64. DOI: 10.1016/j.rvsc.2005.02.003
8. Salvatori D. Studies on the Pathogenesis and Epidemiology of Ovine Pulmonary Adenomatosis (OPA) [Ph.D. dissertation]. UK: University of Edinburgh; 2005. 11-15 p.
9. Mishra S, Kumar P, Dar JA, George N, Singh V, Singh R. Differential immunohistochemical expression of JSRV capsid antigen and tumour biomarkers in classical and atypical OPA: a comparative study. Biol Rhythm Res. 2021;52(6):946-56. DOI: 10.1080/09291016.2019.1610857
10. Al-Ajeli RR, Al-Qadhi AS, Al-Mahmood SS, Alkattan LM. Pathological study of neoplasms surgically excised from animals attended the veterinary teaching hospital. Iraqi J Vet Sci. 2021;35(1):9-14. DOI: 10.33899/ijvs.2019.126188.1260
11. Al-Mahmood SS, Farhan AM, Daoud ZS, Hamed OS. Pathological study of liver lesions in cattle slaughtered at Kirkuk province abattoir. Iraqi J Vet Sci. 2017;31(1):7-16. DOI: 10.33899/ijvs.2017.126713
12. Al-Mahmood SS. Improving light microscopic detection of collagen by trichrome stain modification. Iraqi J Vet Sci. 2020;34(2):473-481. DOI: 10.33899/ijvs.2020.126176.1256
13. Al-Jameel WH, Al-Sabaawy HB, Abed FM, Al-Mahmood SS. Immunohistochemical expression of proliferation markers in canine osteosarcoma. Iraqi J Vet Sci. 2022;36(4):1097-1102. DOI: 10.33899/ijvs.2022.133138.2177
14. Mansour KA, Al-Husseiny SH, Kshash QH, Jassim A. Clinical-histopathological and molecular study of ovine pulmonary adenocarcinoma in Awassi sheep in Al-Qadisiyah Province, Iraq. Vet World. 2019;12(3):454-458. DOI: 10.14202/vetworld.2019.454-458
15. Jassim A, Al-Husseiny SH, Mansour KA, Kshash QH. First molecular diagnosis of ovine pulmonary adenocarcinoma in Awassi sheep in Iraq. Al Qadisiyah J Vet Med Sci. 2017;16(1):105-10. DOI: 10.29079/vol16iss1art46
16. Abass FA, Khudhair YI. Clinical, molecular, and pathological investigations of ovine pulmonary adenocarcinoma in the middle of Iraq. Open Vet J. 2022;12(2):264-272. DOI: 10.5455/OVJ.2022.v12.i2.15
17. Al-Mahmood SS, Mohammed AM, Al-Sabaawy HB, Farhan AM. Pathological lesions of acute sodium chloride toxicity in common carp: Case report. Iraqi J Vet Sci. 2021;35(3):417-419. DOI: 10.33899/ijvs.2020.126917.1417
18. Quintas H, Pires I, Garcês A, Prada J, Silva F, Alegria N. The Diagnostic Challenges of Ovine Pulmonary Adenocarcinoma. Ruminants. 2021;1(1):58-71. DOI: 10.3390/ruminants1010005
19. Sharp JM, DeMartini JC. Natural history of JSRV in sheep. Curr Top Microbiol Immunol. 2003;275:55–79. DOI: 10.1007/978-3-642-55638-8_3
20. Palmarini M, Sharp JM, de las Heras M, Fan H. Jaagsiekte sheep retrovirus is necessary and sufficient to induce a contagious lung cancer in sheep. J Virol. 1999;73:6964–6972. DOI: 10.1128/JVI.73.8.6964-6972.1999
21. De Las Heras M, Borobia M, Ortin A. Neoplasia-Associated Wasting Diseases with Economic Relevance in the Sheep Industry. Animals. 2021;11:381. DOI: 10.3390/ani11020381
22. Wilson DG. Tumors of the Respiratory Tract. In: Meuten DJ, editor. Tumors in Domestic Animals. 5th ed. USA: John Wiley & Sons Inc.; 2017. 467–498 pp.
23. DeMartini J. Retroviral Oncogenesis in an ovine model of lung cancer; Proceedings of the 55th Annual Meeting of the American College of Veterinary Pathologists & 39th Annual Meeting of the American Society of Clinical Pathology; Middleton, WI, USA. 13 November 2004; Middleton, WI, USA: International Veterinary Information Service; 2004.
24. De las Heras M, Gonzalez L, Sharp JM. Pathology of ovine pulmonary adenocarcinoma. Curr Top Microbiol Immunol. 2003;275:25–54. DOI: 10.1007/978-3-642-55638-8_2
25. Griffiths DJ, Martineau HM, Cousens C. Pathology and pathogenesis of ovine pulmonary adenocarcinoma. J Comp Pathol. 2010;142:260–283. DOI: 10.1016/j.jcpa.2009.12.013
26. Hudachek SF, Kraft SL, Thamm DH, Bielefeldt-Ohmann H, DeMartini JC, Miller AD, Dernell WS. Lung tumor development and spontaneous regression in lambs coinfected with Jaagsiekte sheep retrovirus and ovine lentivirus. Vet Pathol. 2010;47:148–162. DOI: 10.1177/0300985809352787
27. Uzal FA, Delhon G, Murcia PR, De las Heras M, Luján L, Fernandez Miyakawa ME, Morris WE, Gonzalez MJ. Ovine pulmonary adenomatosis in Patagonia, Argentina. Vet Res Commun. 2004;28:159–170. DOI: 10.1023/B:VERC.0000012110.49600.12
28. Garcia-Goti M, Gonzalez L, Cousens C, Cortabarria N, Extramiana AB, Minguijon E, Ortín A, De las Heras M, Sharp JM. Sheep pulmonary adenomatosis: Characterization of two pathological forms associated with Jaagsiekte retrovirus. J Comp Pathol. 2000;122:55–65. DOI: 10.1053/jcpa.1999.0344
29. Toma C, Bâlteanu VA., Tripon S, Trifa A, Rema A, Amorim I, Pop RM, Popa R, Catoi C, Taulescu M. Exogenous Jaagsiekte Sheep Retrovirus type 2 (exJSRV2) related to ovine pulmonary adenocarcinoma (OPA) in Romania: Prevalence, anatomical forms, pathological description, immunophenotyping and virus identification. BMC Vet Res. 2020;16:296. DOI: 10.1186/s12917-020-02521-1
30. Borobia M, De las Heras M, Ramos JJ, Ferrer LM, Lacasta D, De Martino A, Fernández A, Loste A, Marteles D, Ortín A. Jaagsiekte sheep retrovirus can reach Peyer's patches and mesenteric lymph nodes of lambs nursed by infected mothers. Vet Pathol. 2016;53(6):1172-9. DOI: 10.1177/0300985816641993
31. Caporale M, Centorame P, Giovannini A, Sacchini F, Di Ventura M, De las Heras M, Palmarini M. Infection of lung epithelial cells and induction of pulmonary adenocarcinoma is not the most common outcome of naturally occurring JSRV infection during the commercial lifespan of sheep. Virol. 2005;338(1):144-53. DOI: 10.1016/j.virol.2005.05.018
32. De las Heras M, De Martino A, Borobia M, Ortín A, Álvarez R, Borderías L, Giménez-Más JA. Solitary tumours associated with Jaagsiekte retrovirus in sheep are heterogeneous and contain cells expressing markers identifying progenitor cells in lung repair. J CompPathol. 2014;150(2-3):138-47. DOI: 10.1016/j.jcpa.2013.09.001
33. De Las Heras M, Gonzalez LG, Sharp JM. Pathology of ovine pulmonary adenocarcinoma. Curr Top Microbiol Immunol. 2003;275:25–54. DOI: 10.1007/978-3-642-55638-8_2

سرطانه الخلية الغدية الرئوية في الأغنام: دراسة مرضية، كيمياء نسجية وكيمياء مناعية نسجية

رحمة محمدعلي السيدية[1] و سيڤان سعد المحمود[2]

[1]طبيب بيطري، قطاع خاص، [2]فرع الأمراض وأمراض الدواجن، كلية الطب البيطري، جامعة الموصل، الموصل، العراق

الخلاصة

تعد سرطانه الخلية الغدية الرئوية في الأغنام من الأمراض الفيروسية المستوطنة في مناطق جغرافية مختلفة من العالم بما في ذلك مدينة الموصل والعراق. هدفنا في الدراسة الحالية إلى تسجيل الآفات العيانية والمجهرية الناجمة عن العدوى الطبيعية بسرطانه الخلية الغدية الرئوية في الأغنام، فضلا عن التعرف على تفاعلية هذا المرض الفيروسي الورمي في الأغنام مع بعض المعلمات النسجية والتي شملت $CD45_{RO}$ و P_{53} و Ki_{67} و VEGFA باستخدام كيمياء النسيج المناعي. تم الحصول على ٧٣ عينة من أنسجة الرئة من الأغنام التي أظهرت علامات سريرية تدل على الإصابة بسرطانه الخلية الغدية الرئوية في الأغنام، إذ أظهرت ٢١ عينة فقط الآفات العيانية والمجهرية لسرطانه الخلية الغدية الرئوية في الأغنام. خضعت العينات التي تحتوي على آفات مرضية مؤكدة لسرطانه الخلية الغدية الرئوية في الأغنام لكيمياء النسيج المناعي باستخدام المعلمات النسجية $CD45_{RO}$ و P_{53} و Ki_{67} و VEGFA. أظهرت نتائج الدراسة الحالية أن الآفات العيانية كانت عبارة عن رئة متورمتين، ذات لون شاحب أو أرجواني، مع ملمس صلب. مجهريا، لوحظ أن الأنسجة السرطانية توزعت على مرحلتين، في المرحلة المبكرة كانت الخلايا السرطانية أما مكعبة أو عمودية الشكل ومتميزة بهيولي رغوي، بينما المرحلة المتأخرة كانت الخلايا السرطانية قليلة التمايز ووجدت منسلخة ومتجمعة بشكل أنقاض خلوية في تجويف الحويصلات والقصبات الهوائية المصابة. أظهرت نتائج كيمياء النسيج المناعي تفاعلا موجبا قوياً مع كل من المعلم النسجي $CD45_{RO}$ والمعلم النسجي P_{53}، وتفاعلا إيجابيا معتدل مع المعلم النسجي VEGFA، وتفاعلا سلبيا مع المعلم النسجي Ki67. نستنتج أن الآفات الطبيعية لسرطانه الخلية الغدية الرئوية في الأغنام ذات شكلين رئيسين، والتي أما كانت ضمن الشكل النمطي أو الشكل الغير نمطي فضلا عن الشكل المختلط للنوعين السابقين، كما أن جميع الأنواع السابقة لسرطانه الخلية الغدية الرئوية كانت موجبة مع المعلمات النسجية $CD45_{RO}$ و P_{53} و VEGFA، بينما كانت ذات تفاعل سلبي مع المعلم النسجي Ki_{67}.

34. Al-Abdaly YZ, Alfathi MY, Al-Mahmood SS. Comparison of Azithromycin Toxicity in Chickens and Quails. Iranian J Vet Med. 2023;17(4):321-331. DOI: 10.32598/ijvm.17.4.1005354
35. González L, Juste RA, Cuervo LA, Idigoras I, De Ocariz CS. Pathological and epidemiological aspects of the coexistence of maedi-visna and sheep pulmonary adenomatosis. Res Vet Sci. 1993;54(2):140-6. DOI: 10.1016/0034-5288(93)90049-l
36. Lee AM, Wolfe A, Cassidy JP, McV. Messam LL, Moriarty JP, O'Neill R, Fahy C, Connaghan E, Cousens C, Dagleish MP, McElroy MC. First confirmation by PCR of Jaagsiekte sheep retrovirus in Ireland and prevalence of ovine pulmonary adenocarcinoma in adult sheep at slaughter. Irish Vet J. 2017;70:1-2. DOI: 10.1186/s13620-017-0111-z
37. Martineau HM, Cousens C, Imlach S, Dagleish MP, Griffiths DJ. Jaagsiekte sheep retrovirus infects multiple cell types in the ovine lung. J Virol. 2011;85(7):3341-55. DOI: 10.1128/jvi.02481-10
38. Hermiston ML, Xu Z, Weiss A. CD45: a critical regulator of signaling thresholds in immune cells. Ann Rev Immunol. 2003;21(1):107-37. DOI: 10.1146/annurev.immunol.21.120601.140946
39. Holmes N. CD45: all is not yet crystal clear. Immunol. 2006;117(2):145-55. DOI: 10.1111/j.1365-2567.2005.02265.x
40. Arendt CW, Ostergaard HL. Identification of the CD45-associated 116-kDa and 80-kDa proteins as the α-and β-subunits of α-glucosidase II. J Biol Chem. 1997;272(20):13117-25. DOI: 10.1074/jbc.272.20.13117
41. Liu SL, Miller AD. Oncogenic transformation by the jaagsiekte sheep retrovirus envelope protein. Oncogene. 2007;26(6):789-801. DOI: 10.1038/sj.onc.1209850
42. Maeda N, Palmarini M, Murgia C, Fan H. Direct transformation of rodent fibroblasts by jaagsiekte sheep retrovirus DNA. Proc Nat Acad Sci. 2001;98(8):4449-54. DOI: 10.1073/pnas.071547598
43. Matiasek LA, Platt SR, Adams V, Scase TJ, Keys D, Miller J, Adamo F, Long S, Matiasek K. Ki-67 and vascular endothelial growth factor expression in intracranial meningiomas in dogs. J Vet Intern Med. 2009;23(1):146-51. DOI: 10.1111/j.1939-1676.2008.0235.x
44. McGee-Estrada K, Fan H. Comparison of LTR enhancer elements in sheep betaretroviruses: insights into the basis for tissue-specific expression. Virus Genes. 2007;35:303-12. DOI: 10.1007/s11262-007-0079-y
45. Palmer BF, Clegg DJ. Oxygen sensing and metabolic homeostasis. Mol Cell Endocrinol. 2014;397(1-2):51-8. DOI: 10.1016/j.mce.2014.08.001
46. Cousens C, Meehan J, Collie D, Wright S, Chang Z, Todd H, Moore J, Grant L, Daniel CR, Tennant P, Ritchie A. Tracking ovine pulmonary adenocarcinoma development using an experimental jaagsiekte sheep retrovirus infection model. Genes. 2024;15(8):1019. DOI: 10.3390/genes15081019
47. Griffiths DJ, Martineau HM, Cousens C. pathology and pathogenesis of ovine pulmonary adenocarcinoma. J Comp Pathol. 2010;142(4):260-283. DOI: 10.1016/j.jcpa.2009.12.013