

Unilateral exudative retinal detachment as the first manifestation of lung carcinoma

Thamarai **Munirathinam**, **Neoh** Pei Fang

Department of Ophthalmology, Hospital Enche' Besar Hajjah Khalsom, Kluang, Johor Malaysia

Abstract

Background: Exudative retinal detachment without ocular metastasis is extremely rare.

Case presentation: We report a case of sudden onset of painless vision loss in the left eye with relative afferent pupillary defect. Fundus features suggested exudative retinal detachment. Abnormal cutaneous findings and lung findings led to the suspicion of malignancy. Computed tomography of the brain and orbit showed no ocular metastasis; however, imaging of thorax, abdomen and pelvis revealed lung malignancy with distant metastasis. Immunohistochemistry profile of the skin biopsy was suggestive of metastatic adenocarcinoma.

Conclusion: A high index of suspicion, thorough physical examination and prompt intervention can be lifesaving.

Keywords: adenocarcinoma, exudative retinal detachment, lung carcinoma

Correspondence: Dr. Thamarai Munirathinam, MD, Department of Ophthalmology, Hospital Enche' Besar Hajjah Khalsom, KM 5 Jalan Kota Tinggi, 86000 Kluang, Johor, Malaysia.

E-mail: nitaraicz88@gmail.com

Lekang retina secara eksudatif tanpa tanda metasis pada bagian okular sebagai manifestasi awal kanker paru-paru

Abstrak

Latar belakang: Lekang retina secara eksudatif tanpa tanda metasis pada tisu okular adalah amat jarang terjadi.

Kes: Kami melaporkan satu kes kehilangan penglihatan secara tiba-tiba tanpa rasa sakit di mata kiri dengan kehadiran kerosakkan pupil aferen secara relatif (relative afferent pupillary defect). Pemeriksaan fundus menunjukkan lekung retina secara eksudatif. Berdasarkan pemeriksaan dan kehadiran tanda abnormal pada kulit serta hasil dari pemeriksaan paru-paru, kanker merupakan salah satu penyebab utama. Walaubagaimanapun, pengimbasan tomografi otak dan orbit tidak menunjukkan tanda metastasis okular, namun pengimejan toraks, abdomen dan pelvis menunjukkan kehadiran kanker paru-paru dengan metastasis yang jauh. Profil imunohistokimia ke atas biopsi kulit menunjukkan ciri-ciri adenokarsinoma metastatik.

Konklusi: Dengan indeks kecurigaan yang tinggi, pemeriksaan fizikal yang menyeluruh dan intervensi yang cepat boleh menyelamatkan nyawa.

Key words: adenokarsinoma, kelekangan retina secara eksudatif, kanker paru-paru

Introduction

Exudative retinal detachment (ERD) is defined by Ghazi *et al.* as detachment of neurosensory retina from the underlying retinal pigmented epithelium, caused by fluid accumulation in the subretinal space due to leakage from retinal or choroidal vessels in the absence of retinal breaks or traction.¹ Inflammatory, infectious, infiltrative, neoplastic, vascular, and degenerative conditions may be associated with blood-retinal barrier breakdown and the sequential development of ERD. Retinal detachment occurs when the ability of the retinal pigment epithelium to pump the leaking fluid into the choroidal circulation is compromised.

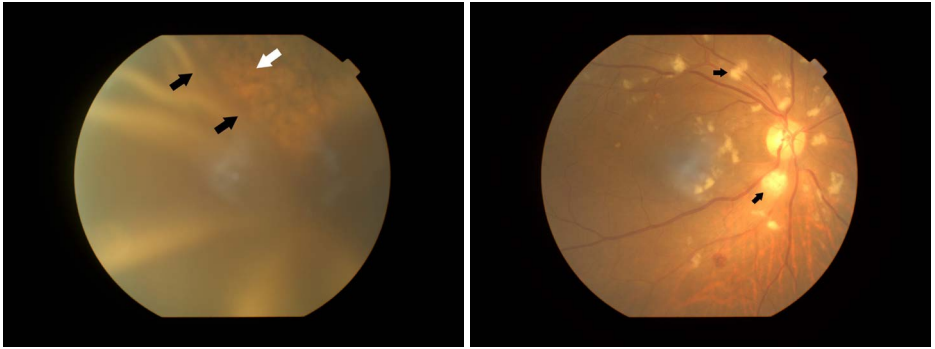


Fig. 1. (Left) Fundus photograph of the right eye shows scattered cotton wool spots (black arrows). (Right) Fundus photograph of the left eye shows near total retinal detachment (black arrows), with minimal flat retina associated with pigmentary changes superiorly (white arrow).

Case report

A 66-year-old man, former smoker with underlying type 2 diabetes mellitus, hypertension, and dyslipidaemia presented with sudden onset of painless decrease of vision associated with floaters in his left eye for 6 months. He had intermittent palpitation associated with dizziness. He had been unwell with constitutional symptoms such as loss of appetite and weight. Best-corrected visual acuity in the left eye was hand movement with presence of relative afferent pupillary defect; best-corrected visual acuity in the right eye was 6/12. Bilateral anterior segment examination and intraocular pressure were normal. Fundoscopy of the left eye (Fig. 1, left) revealed near total ERD with minimal flat retina superiorly. There was no retinal break at the peripheral retina on three-mirror examination and scleral indentation of the left eye. Shifting fluid sign was present in the left eye during the examination. Tobacco dust was not present in the affected eye. The patient also denied any history of high myopia, ocular trauma, previous ocular surgeries, or barricade laser done. Fundoscopy of the right eye (Fig. 1, right) showed multiple cotton wool spots at all four retinal quadrants. There was no associated intraocular inflammation such as anterior chamber cells or vitritis. Upon general examination, the patient was pale and showed sinus tachycardia. Multiple indurated skin lesions with central ulceration were seen on the scalp, neck, and chest (Fig. 2). There was reduced breath sound in the upper zone of the right lung.

Full blood count and peripheral blood film indicated severe normochromic normocytic anaemia with reticulocytosis. No blast cells were seen. Serum albumin level was low (30 g/L), indicating hypoalbuminemia of chronic illness,



Fig. 2. Well-defined, indurated lesions (black arrow) with central ulceration (white arrow).

which may lead to ERD. Raised levels of C-reactive protein (58 mg/L) and lactate dehydrogenase (322 U/L) were found, which are associated with advanced lung carcinoma. Carcinoembryonic antigen (CEA), an important marker for malignant tumours, including non-small cell lung carcinoma, was 174 U/ml. High levels of urea (37.4 mmol/L) and creatinine (484 μ mol/L) indicated acute or chronic renal failure in keeping with the advanced metastasis. There were no bacteria or fungi detected on blood and urine culture. Other tests including screening for tuberculosis, syphilis, hepatitis B and C, human immunodeficiency virus, toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus screening were negative.

Contrast-enhanced computed tomography of the thorax, abdomen and pelvis revealed right, upper lobe, contrast-enhancing mass measuring 7.5 x 7.0 x 5.5 cm with right pleural effusion (Fig. 3). Multiple mediastinal nodal, bone, peritoneal, and adrenal metastasis were present. There was no evidence of choroidal mass, orbital, or brain metastases.

Skin biopsy was reported to be most likely metastatic adenocarcinoma based on the immunohistochemistry profile of the tumour cells tested positive for EMA, Ber-EP4, CEA, cytokeratin 7 (CK7), and P63, with absence of transformation zone from the native adnexal structures. Infiltrative neoplastic epithelioid cells featured moderate to severe nuclear polymorphism.

Optical coherence tomography, ultrasound B-scan, and positron-emission

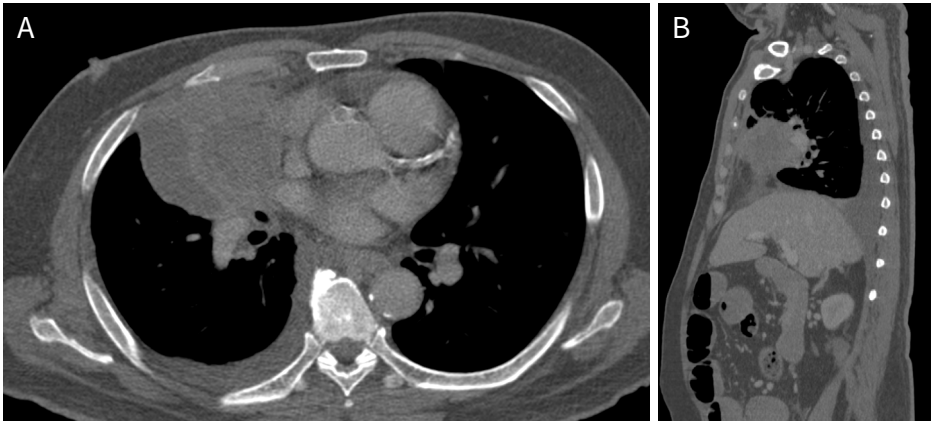


Fig. 3. (A) Axial section of contrast-enhanced computed tomography (CECT) of the thorax. (B) Sagittal section of CECT of the thorax shows enhancing mass (white arrow) with hyperdense centre arising from the anterior segment of right upper lobe.

tomography scan were not available at our health care centre, and the patient refused to be referred to tertiary centres for further workup. Thus, these investigations were not performed. He was diagnosed with ERD in the left eye secondary to metastatic lung adenocarcinoma. The patient died due to the illness 2 months later after refusing treatment and defaulting follow-up.

Discussion

Lung carcinoma is the second most frequently diagnosed cancer after breast cancer in women and prostate cancer in men.² It is common among men aged 55.1 ± 11.2 years and in former or active smokers. The most common histologic types are adenocarcinoma followed by squamous and small-cell carcinoma.³

Metastatic lung adenocarcinoma to the eye is very rare. The eye and orbit may be affected by cancer either directly, due to metastatic infiltration by neoplastic cells or compression, or indirectly from circulating antibodies associated with paraneoplastic retinal degeneration.

Our literature search showed that approximately 50 cases have been reported worldwide with ERD as the first symptom of lung carcinoma metastasis to the eyeball.³ However, only three cases of ERD as the first symptom of lung carcinoma without concomitant ocular metastasis have been reported worldwide.⁴⁻⁵ Thus, we report another case of ERD as the first manifestation of malignancy.

ERD develops when fluid collects in the subretinal space. There are numerous theories regarding the disruption of the integrity of blood-retinal barrier attributed by inflammatory, infectious, infiltrative, neoplastic, vascular, and degenerative

conditions and the sequential development of ERD.⁶ Retinal vessel occlusion by tumour cells could lead to retinal ischemia, and increases the permeability of the vascular endothelium and subretinal fluid leakage. Other changes, such as hypercoagulability and hypoalbuminemia, may result in formation of thrombus within small retinal vessels.⁷

The detection of scattered cotton wool spots (CWS) in the right fundus indicates an ischemic retina.⁸ It has been reported that CWS indicates blockage of a retinal arteriole caused by abnormalities in the vascular endothelium, abnormal erythrocytes, or emboli. The axoplasmic debris accumulates at the junction of healthy and anoxic retinas. In this case, the patient's blood pressure was within the normal range. There were no diabetic retinopathy changes noted in the right eye. Coagulation profile was within the normal range and there were no other retinal changes present to suggest hypercoagulable state. This should alert the ophthalmologist to arrange an extensive examination as it is usually a serious sign of vascular damage.

Cutaneous metastases from the lungs are rare but must be ruled out in patients with suspicious skin lesions, history of lung carcinoma, or tobacco exposure, as presented in our patient. The most common sites for cutaneous metastases are the scalp, head, neck, and chest, with the most common histological diagnosis being adenocarcinoma.⁹ The percentage of patients with lung cancer that develop cutaneous metastases ranges from 1% to 12%, with an overall incidence of 5.3% for all cancers. Mean survival time from diagnosis of lung carcinoma is 10.3 months; for diagnosis of skin metastasis it is 4.9 months.¹⁰ The prognosis for patients having lung cancer with skin metastasis is thus very poor.

The use of immunohistochemical markers is a useful method for ascertaining the site of origin in cases of adenocarcinoma. Cytokeratin 7 (CK-7) has a sensitivity and specificity of 93.8% and 50.0% in primary lung adenocarcinoma and 100% and 25.0% in metastatic lung adenocarcinoma.¹¹ In this case, the most useful immunohistochemical marker for diagnosis was CK-7, which is specific to primary lung adenocarcinoma. It has also been reported that, in cases of poorly differentiated adenocarcinoma, a decreased expression of Napsin A and TTF-1 was seen and a proportion of these tumours have been shown to be P63-positive as demonstrated in our case.

The choice of treatment varies depending on the underlying diseases, size, and location of lesion, number of satellite lesions, and the extent of the neoplasm. Treatment options include chemotherapy, immunotherapy, hormonal therapy, and radiotherapy. Gamma globulin, plasmapheresis, and interleukin-2 receptor blockade with a specific monoclonal antibody comprise the proposed first-line treatment in cases of ERD without ocular metastasis.

Conclusion

Our case report highlights a lung carcinoma that harbours behind an exudative retinal detachment. Malignancy should be suspected in atypical presentations of retinal detachment without obvious retinal tear. A thorough systemic evaluation, diagnostic imaging, and laboratory and immunohistochemistry tests are important to guide the ophthalmologist in identifying the primary site of neoplasia, as prompt intervention may be lifesaving.

Declarations

Consent for publication

Informed consent was obtained from the patient for the publication of the data and images contained in this case report.

Competing interests

None to declare.

Funding

None to declare.

Acknowledgements

None to declare.

References

1. Ghazi NG, Green WR: Pathology and pathogenesis of retinal detachment. *Eye*. 2002;16:411–421.
2. de Groot PM, Wu CC, Carter BW, et al. The epidemiology of lung cancer. *Transl Lung Cancer Res*. 2018;7:220–33.
3. Singh N, Kulkarni P, Aggarwal AN, et al. Choroidal metastasis as a presenting manifestation of lung cancer: a report of 3 cases and systematic review of the literature. *Medicine*. 2012;91:179–94.
4. Modrzejewska A, Krzystolik K, Lubiński W, Modrzejewska M. Spontaneous unilateral exudative retinal detachment as the first manifestation of lung cancer. *Klinika Oczna*. 2018;10;85–8.
5. Zarzecki M, Saeed E, Mariak Z, Konopińska J. Recurrent monocular exudative retinal detachment as the first manifestation of squamous cell lung cancer: A case report. *Medicine*. 2021;100(11).
6. Amer R, Nalcı H, Yalçındağ N. Exudative retinal detachment. *Surv Ophthalmol*. 2017 Nov-Dec;62(6):723-769.
7. Chinta S, Rani PK, Manusani U. Bilateral Exudative Retinal Detachment as a Presenting Sign of Acute Lymphoblastic Leukemia. *Middle East Afr J Ophthalmol*. 2012;19(4):410–412.

8. Schmidt D. The mystery of cotton wool spots: a review of recent and historical descriptions. *Eur J Med Res.* 2008;13:231-266.
9. Kamble R, Kumar L, Kochupillai V, et al. Cutaneous metastases of lung cancer. *Postgrad Med J.* 1995;71:741-743.
10. Terashima T, Kanazawa M. Lung Cancer with Skin Metastasis. *Chest.* 1994;106:1448-50.
11. Gurda GT, Zhang L, Wang, Y, et al. Utility of five commonly used immunohistochemical markers TTF-1, Napsin A, CK7, CK5/6 and P63 in primary and metastatic adenocarcinoma and squamous cell carcinoma of the lung: a retrospective study of 246 fine needle aspiration cases. *Clin Transl Med.* 2015 Apr 21;4:16.