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Case Report

A Case Report on Choroidal Metastases from Adenocarcinoma of Lung – Tip of the Iceberg!

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Abstract

Adenocarcinoma is a type of non small cell lung cancer (NSCLC), constituting about 40 to 50% of the total cases of lung cancer. It is more common in non-smokers and women. It usually starts in the periphery of the lung and is a slow growing lesion, leading to prolonged latency prior to diagnosis. As a result, these patients are often diagnosed at an advanced stage with metastatic disease. It commonly metastasizes to the bones, liver, brain and rarely to the eye. The choroid is the most common ocular site for metastatic disease, due to its abundant vascular supply. The most common primary tumor that leads to choroidal metastases (CM) is lung cancer in males and breast cancer in females. Gastrointestinal tract, pancreas, prostate, kidney, skin melanoma, other rare primary sources. Lung cancer accounts for 20 to 39% choroidal metastasis. Choroidal metastases may be the presenting sign of systemic malignancy, and this is particularly true for metastatic lung carcinoma. We present a 44 years old patient who presented to our hospital due to visual impairment and chronic cough and on evaluation was found to have disseminated adenocarcinoma of lung with bilateral, multiple choroidal metastasis.

Keywords: Lung Cancer; Choroid; Primary; Metastases; Dissemination

Introduction

Lung cancer is the commonest primary, causing intraocular metastasis in males. Adenocarcinoma of lung tends to present late with widespread metastases. The choroid is the most common site of intraocular metastases, due to its abundant blood supply. Shah., *et al*. analyzed uveal metastases from lung cancer in 194 patients with 374 tumors and found that choroid was the most common site of intraocular metastases (88%) and that choroidal metastases tend to be unifocal (77%) and unilateral (82%) [1]. Choroidal metastases in lung cancer is usually present when multiple other organs are affected. We report a case of 44-year-old male, non-smoker who presented with visual impairment due to multiple and bilateral choroidal metastases from a silent primary and on evaluation was ultimately found to harbor adenocarcinoma of the lung.

Case Report

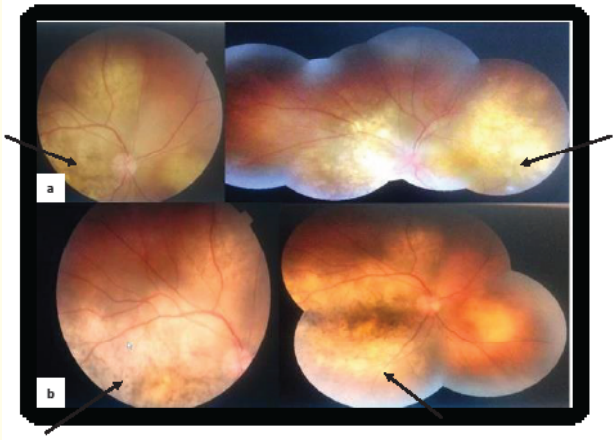
A 44 years old gentleman, farmer by occupation, was admitted to Tata Main Hospital (TMH) with history of cough productive of sputum for 5 months prior to hospitalization. The sputum was whitish in color, scanty in amount without postural variation and hemoptysis. It was associated with decreased appetite and weight loss of approximately 4 to 5 kilograms. There was history of intermittent fever without rigors for 1 month. His vision had decreased gradually over past 3 months and he had initially difficulty in seeing distant objects.

However, his vision had rapidly deteriorated in the last 15 days and he was able to perceive only hand movements close to his eyes. He could not read book print and newspaper. He had difficulty in walking and carrying out activities of daily living due to visual impairment which brought him to our hospital. There was no history of double vision, headache, restricted eye movements, seizure and altered sensorium. He did not consume alcohol and tobacco in any form. He did not have history of any significant medical ailment in the past.

On admission, he was lean, coherent, did not have pallor, icterus, pedal edema, and cyanosis. A hard, discrete, non-tender, left supra-

clavicular lymph node was palpable. His was afebrile, with pulse rate of 106/minute, blood pressure 110/70 mm Hg, and respiratory rate of 18/ minute with accessories mildly working.

Examination of respiratory system revealed centrally placed trachea, inspiratory crepitations in the left interscapular and infrascapular regions. Examination of the cardiovascular and gastrointestinal systems were normal. He was oriented in time, place and person. His visual acuity was 4/60 in right eye and 6/60 in the left eye. Pupils were normal sized. Light reflex was sluggish in both eyes. Extra ocular movements were normal and painless. Examination of the anterior segment of the eyes was normal. Results of his slit lamp examination were unremarkable. His intra-ocular pressure was also normal. Fundi examination revealed early papilledema with retinal odema and yellow-white lesions (deposits) in all quadrants of the choroid in both eyes (Figures 1a-1d).



Figures 1a and b: Collated images of fundi of both eyes showing bilateral choroidal metastases.

Motor system examination revealed normal tone and power. The deep tendon reflexes were normally elicitable and plantar were flexors. There was no sensory deficit. Neck was soft.

His hemoglobin was 11.1 gm/dl, total WBC count 14,800 cu mm with 63% neutrophils, 20% lymphocytes, 13% eosinophils, and 4% basophils, MCV 74.6fl and platelet count 2.25 lakhs/cu mm. His liver function tests revealed total bilirubin 0.48 mg/dl, direct fraction 0.36 mg/dl, indirect fraction 0.12 mg/l, Alanine transaminase (ALT) 25 U/L, Aspartate transaminase (AST) 83.6 U/L, Alkaline phosphatase (ALP) 633.6 U/L, gamma glutamyl transferase (GGT) 84.8 U/L, total serum proteins 6.03 g/dl, serum albumin 2.31 g/dl and globulin 3.72 g/dl, prothrombin time (PT) 19 sec, control 11sec, and PT (INR) 0.99. Renal function tests showed blood urea 38.2 mg/dl and serum creatinine 1.1 mg/dl. Serum iron was 22.9 mcg/dl, and serum ferritin was 367.8 ng/ml. His chest radiograph showed non-homogenous opacity in the mid and lower zones of the left lung (Figure 2) while the chest x-ray done elsewhere one week after the onset of cough was normal. Ultrasound of his whole abdomen showed mild hepatomegaly with no focal lesions. Contrast enhanced computerized tomography (CECT) of chest revealed large soft tissue density mass lesion involving left lingula and lower lobe of left lung with patchy lesions in the adjoining lung and an enlarged 1cm lymph node in the pretracheal region.

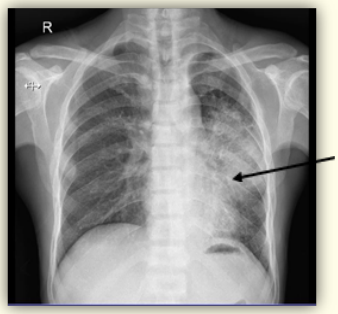
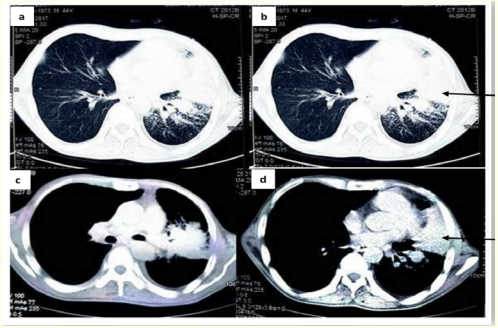
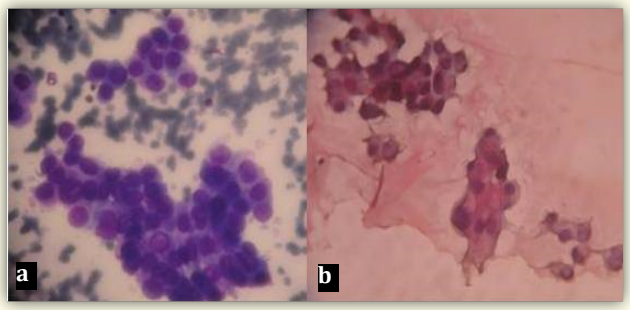


Figure 2: Chest x ray showing non-homogenous opacity left mid zone.

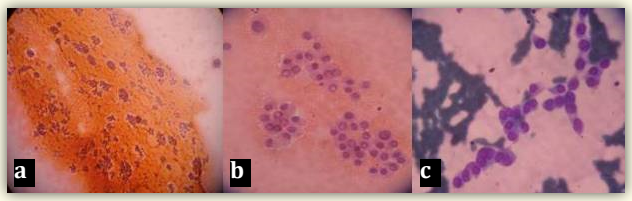
Also, osteolytic lesions were found in multiple ribs, scapula and head of the humerus with focal rib expansion and adjoining soft tissue mass in the ribs on the right (Figures 3a-3d). Fine Needle Aspiration Cytology (FNAC) of left supraclavicular lymph node showed features suggestive of metastatic non-small cell lung cancer (NSCLC) - adenocarcinoma (Figures 4a and 4b). CT guided FNAC of the left lung mass was also suggestive of adenocarcinoma of the lung (Figures 5a-5d).



Figures 3a-d: CECT thorax showing opacity involving the lingual and lower lobe of the left lung.



Figures 4a and 4b: FNAC of supraclavicular lumph node.
a- Microphotograph shows few irregular clusters of highly pleomorphic cells [PAPX400]
b- Smear shows three dimensional clusters of cells [MGGX400]



Figures 5a-c: FNAC of lung mass.
a-Acinar and small groups of cells with anisocytosis amidst a hemorrhagic background. [PAPX100]
b-Moderately cellular smear shows acinar pattern of cells [PAPX100]
c-Smear shows cords of pleomorphic cells with irregular nuclei, scanty cytoplasm.[MGGX400]

He refused to undergo CT scan of brain due to financial constraints. Patient left the hospital against medical advice and was advised to consult oncologist for further management.

Discussion

Here, we report a case of bilateral choroidal metastasis of disseminated lung cancer, histologically adenocarcinoma. Lung cancer is one of the commonest cancers and cause of cancer related deaths all over the world [2]. It accounts for 12.7 per cent of all new cancer cases and 18.2 per cent of cancer related deaths worldwide. In India, it is the commonest and most lethal cancer among males and constitutes 10.9 % of all cancer cases and 13 % of all cancer related deaths [3]. The incidence and pattern of lung cancer differs as per geographic region and ethnicity and largely reflect the prevalence and pattern of smoking [4].

Histologically about 80 to 85% of the lung cancers are non-small cell lung cancer while the remaining 10% to 15% are small cell lung cancer (SCLC). Non-small cell carcinomas include adenocarcinoma, squamous cell carcinoma, and large cell carcinoma [4]. Adenocarcinoma is the most common type of NSCLC and accounts for 40 to 50% of these tumors [5-7]. Most cases are associated with smoking; however, among people who have smoked fewer than 100 cigarettes in their lifetimes ("never-smokers") and non-smokers as in our case, adenocarcinoma is the most common form of lung cancer, probably due to an activating mutation of the epidermal growth factor receptor (EGFR) pathway or echinoderm microtubule associated protein and anaplastic lymphoma kinase (EML4-ALK) gene translocation [5]. It is commonly seen in females and usually seen peripherally in the lungs, as opposed to small cell lung cancer and squamous cell lung cancer, which tend to be more centrally located, originate and involve the main conducting airways [7]. In the Western countries and most of the Asian countries, there is a changing trend in the histological types, with adenocarcinoma surpassing squamous cell carcinoma. Most of the previous Indian studies have described squamous cell carcinoma as the commonest histology, however, some recent studies from two major centers have shown a changing pattern in India too [2].

Our patient was young and was never a smoker. His first chest x-ray was normal and patient came to our hospital not for cough, but for visual impairment. The x-ray chest done in our hospital revealed left non-homogenous opacity, initially raising the possibility of pulmonary tuberculosis, which is far more common in our country. The raised ALP levels could be due to the involvement of the liver by granulomatous hepatitis, while the visual impairment could have been due to choroidal tubercles caused by hematogenous dissemination. The other possibility was sarcoidosis, which is a multisystem disorder and can present with chronic cough, dyspnoea, night sweats and weight loss. Pulmonary lesions can vary from nodules, ground-glass opacities, alveolar opacities, fibrosis and mediastinal lymphadenopathy. Raised alkaline phosphatase levels reflect space-occupying hepatic granulomas and occur in 23% of patients. Choroidal granulomas may be found in the eye in addition to uveitis. Possibility of carcinoma lung was thought of, when a hard-supraclavicular lymph node was detected during the subsequent examination, leading to further battery of investigations as described above and the final diagnosis of adenocarcinoma of lung. He already had widespread metastasis to the bones, liver, eyes (choroid), and probably brain on presentation to TMH.

Early signs and symptoms of lung adenocarcinoma that may be

overlooked include fatigue, shortness of breath, mild cough or weight loss. As the symptoms are often vague, it being a slow growing tumor, and often occurs in people not expected to develop such as young people and non- smokers, the diagnosis is often delayed for many weeks to months. Thus, due to the prolonged latency, these patients are often diagnosed at an advanced stage with metastatic disease and a median survival duration of 6 - 10 months [5,7]. The overall frequency of ocular metastasis in patients dying of cancer is approximately 16%, and of lung cancer rises to about 40% [8]. In approximately one fourth of the cases, involvement of the eye may be the presenting feature of the carcinoma [8].

Metastatic tumors are the most common intraocular malignancies in adult population of whom 50% to 70% are women [9]. The choroid layer is the most common ophthalmic site for the metastatic disease, but they can also involve the ciliary body, iris, retina, optic nerve, and in some cases the vitreous. Ocular metastasis occurs in 2 - 9% of all malignancies [5]. In a review of 520 patients presenting with 950 metastases to the uvea, the choroid was involved in 88% of cases [10]. 80% of patients present with a single tumor in one eye and 20% have multiple tumors, bilateral tumors, or both [8,11]. Breast and lung are the most common primary locations of metastasizing cancer [10] and represent more than two-thirds of the cases. The most common primary for ocular metastasis is lung cancer in men accounting for 40 to 60% of the cases, as was in our case; while in female subjects primary tumor is the breast cancer in 70 to 80 % of the cases. Other rare causes reported in the literature include carcinoma of pancreas, gastrointestinal system, kidney prostate, skin melanoma etc. The incidence of symptomatic ocular lung metastasis is between 1% and 7% [9].

Perls reported the first case of choroidal metastasis in 1872 [8]. Tumor cell emboli invade the network of posterior short ciliary arteries and then settle in the choroid. Metastatic choroidal lesions typically involve the posterior pole, probably because of the relatively greater blood flow to that area [10,11]. The choroid provides a vascular avenue for tumor emboli to sequester and allows an environment receptive to growth [12]. The characteristic metastatic lesions to the choroid from lung are generally plateau or dome shaped and are often associated with retinal detachment [10]. They are golden yellow to yellowish-white, round to oval lesions. The presence of serous retinal detachment and multiple choroidal lesions is more suggestive of metastases [13].

Our patient had extensive, diffuse choroidal metastasis in both eyes with retinal serous edema and disc edema. The methods used for assessing choroidal lesions, include ultrasonography, fundus auto fluorescence (FAF), fluorescein angiography (FAG) and fine needle aspiration biopsy (FNAB).

To date, only two series, describing 13 and 90 patients, respectively, with predominantly choroidal metastasis from lung cancer, have been published [10,11]. Shields., *et al*. reported that in 56% of patients with intraocular lung cancer metastasis, the primary tumor was detected after the diagnosis of intraocular metastasis [11].

These patients commonly present with blurred vision due to sub retinal fluid. Stephens and Shields reviewed 70 cases of choroidal metastasis and found that blurred vision was the presenting symptom in 80% of patients, pain was noted in 14%, photopia in 13%, red eye and floaters in 7% and visual field defects in 3% [10,14]. However, 9 - 11% of patients present with no symptoms and lesions may be found on routine ocular examination [8].

The differential diagnosis of choroidal metastases includes choroidal melanoma, hemangioma, granuloma, osteoma, and sclerochoroidal calcification [12]. Diagnosis can be difficult in cases without a history of a primary malignancy, and especially in those cases where primary is not detectable even on investigation [8]. However, distinct features on ophthalmoscopy and various imaging modalities distinguish choroidal metastases from other choroidal tumors.

Presence of choroidal metastasis (CM) indicates widespread dissemination of the primary. As they become apparent late in the course of malignancy, their presence is a poor prognostic sign for the long-term survival.

The major determinants of survival after the diagnosis of choroidal metastasis are patient status, primary tumor type and local tumor invasion at the time of diagnosis [12]. The median survival from lung cancer after the discovery of choroidal metastasis is reported to be 3.3 months (range 0.5 to 19 months). Shah., *et al*. reported mean survival time following diagnosis of ocular metastases from lung primary was 12 months [1].

The treatment modalities for carcinoma lung depend upon on the staging of the tumor, patient's functional status and associated comorbid conditions and include surgery, chemotherapy and radiation. Common treatment options for symptomatic bilateral and multifocal choroidal metastases with residual vision include systemic chemotherapy (for chemo-sensitive primary tumors). Regression of choroi-

dal metastasis from lung carcinoma after systemic chemotherapy has been noted [15-17]. In a study of 4 patients with choroidal metastasis treated with systemic chemotherapy alone, tumor regression occurred in 3 patients [15,17]. For patients with solitary metastasis, treatment includes radiotherapy (brachytherapy, External Beam Radio Therapy (EBRT) and plaque radiotherapy), proton beam radiotherapy (PBR) and new methods like photodynamic therapy, transpupillary thermotherapy, gamma knife radiosurgery (GKR) and intravitreal injections of bevacizumab and ranibizumab. Enucleation is done for blind, painful eye.

Conclusion

Metastatic tumors to the choroid are the most common intraocular malignancies. In males, the most common primary site is the lung followed by the gastrointestinal tract, prostate, kidney, skin melanoma and unknown primary. Sometimes, choroidal metastases may be the presenting feature with the primary lurking in the dark. Thus, the presence of CM should make one evaluate extensively for the primary at the above-mentioned sites.

Conversely, CM may also go undetected when they remain asymptomatic. It is diagnostically challenging to distinguish a metastatic lesion from a primary ocular neoplasm and other space occupying lesions. Hence, an interdisciplinary approach to these patients is essential to detect tumor progression and metastatic spread early, in order to provide curative treatment options. The above case is published in view of its rarity, and to emphasize the importance of meticulous clinical examination.

Conflict of Interest

None.

Source of Funding

Nil.

Consent

Written informed consent was obtained from our patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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