

THE EYE THAT LED THE WAY - CHOIROIDAL METASTASES AS INITIAL PRESENTATION OF ADENOCARCINOMA LUNG

Oncology

Dr. L K Rajeev	Associate Professor, DM Medical Oncology, Kidwai Memorial Institute of Oncology
Dr Manjunath S Hiremani*	Senior Resident, DM Medical Oncology, Kidwai Memorial Institute of Oncology *Corresponding Author
Dr. Suma M N	Associate Professor, MD Pathology, Kidwai Memorial Institute of Oncology
Dr. Suresh Babu M. C	Professor and HOD, DM Medical Oncology, Kidwai Memorial Institute of Oncology
Dr Lokesh K. N	Professor, DM Medical Oncology, Kidwai Memorial Institute of Oncology
Dr. Rudresha A. H	Associate Professor, DM Medical Oncology, Kidwai Memorial Institute of Oncology
Dr. Smitha C Saldanha	Associate Professor, DM Medical Oncology, Kidwai Memorial Institute of Oncology
Dr. Giri G V	Associate Professor, DM Medical Oncology, Bangalore Medical College and Research Institute

ABSTRACT

Choroidal metastases are rare ocular manifestations of systemic malignancies, most often arising from breast or lung primaries. Presentation as the initial sign of lung cancer is exceedingly rare. We report the case of a 32-year-old female with no comorbidities, who presented with diminution of vision and was found to have a central choroidal lesion on ocular examination. Metastatic workup revealed a right lower lobe lung mass with nodal and bone metastases. Biopsy confirmed adenocarcinoma (TTF-1, CK7, Napsin positive; CK20 negative). Molecular testing demonstrated an EGFR G719S mutation, and she was treated sequentially with pemetrexed-carboplatin, followed by afatinib with good tolerance at 30 mg daily. The patient also received intravitreal bevacizumab with regression of the ocular lesion and maintained partial systemic response at 10 months follow-up. This case underscores the importance of recognizing ocular metastases as a potential initial presentation of lung cancer. Early diagnosis, molecular profiling, and a multidisciplinary approach are essential to optimize visual function and systemic outcomes.

KEYWORDS

Choroidal Metastases, Adenocarcinoma Lung, G719S mutation, Afatinib

INRODUCTION

As per GLOBOCAN 2022, Lung Cancer is the most common cancer worldwide. According to recent SEER database, most common sites of metastases seen in adenocarcinoma lung is bone, brain, liver, adrenal metastases.[1] Other unusual sites are skin, soft tissue, kidney, bone marrow, muscle. Choroidal metastases from a lung cancer is rare. But it presenting as a initial presentation is even rarer. Choroidal metastasis is the most common intraocular malignancy, with the choroid being particularly vulnerable due to its rich vascular supply.[2] Breast carcinoma is the most frequent primary in women, while lung cancer predominates in men. The reported incidence of ocular metastasis from lung cancer ranges between 2–7%.[3] Given its rarity and nonspecific presentation, a high index of suspicion is required. Early recognition is critical as ophthalmic findings may provide the first clue to an occult primary lung malignancy. Here we present a case report of a female patient with such a presentation.

Case:

History

A 32 year female with complains of diminution of vision of one month history. She was a non smoker and had no past relevant medical history. On ophthalmological evaluation she had best corrected visual acuity finger counting at 2mtrs and 6/6 in left eye. Fundoscopic examination of right eye revealed central yellowish mass lesion, clinically diagnosed to have right eye masquerades syndrome (choroidal metastases) and referred for further evaluation and management.

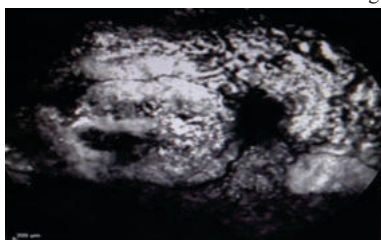


Figure 1: Ophthalmic Evaluation

IR fundus image shows an irregular hyporeflective choroidal lesion with distorted overlying vessels and patchy hyperreflectivity.

On Examination: Vitals stable and head to toe examination was unremarkable.

Systemic Examination: RS : Reduced breath sounds and dullness in right infrascapular area.

Investigation

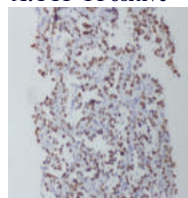
PET CT : Figure 1



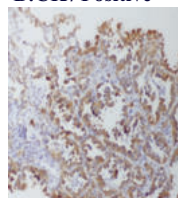
Right Lung Lower Lobe mass: 3.8x4.6x4.1 cm occluding segmental bronchi, abutting adjacent pleura. B/L Mediastinal, hilar, subcarinal lymph nodes. Enhancing lesion posterior chamber of eye. Right adrenal gland lesion. Vertebral and left acetabular metastases.

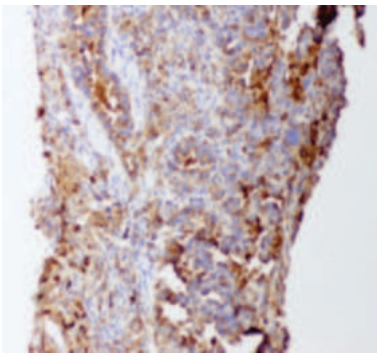
Biopsy of the Lung Lesion: Figure 2 A/B/C

A:TTF-1 Positive



B:CK7 Positive



C:NAPSIN Positive

BIOPSY OF LUNG LESION: TTF-1 +, CK7+, NAPSIN +
DIAGNOSIS: ADENOCARCINOMA OF LUNG.

Treatment History

She was started with Pemetrexed + Carboplatin + Zolendronic acid, awaiting molecular panel report. She had severe ocular inflammation post starting chemotherapy and was treated with topical and systemic steroids after ophthalmologic opinion. RT opinion was sought, but was not contemplated as patient was not symptomatic for primary disease. With repeated ocular inflammation with chemotherapy, she was started on Afatinib 40mg based on molecular studies report.

NGS Report:

Gene	Variant	Frequency	RefSeq	Protein	Effect	Pathogenicity	Frequency
EGFR	G719S (G>T)	100%	Exon 19	Val231Leu	Missense	Pathogenic	100%
TP53	G152A (G>T)	100%	Exon 8	Val157Glu	Missense	Pathogenic	100%

Figure 3: EGFR G719S Mutation, TP53 Mutation

But as she had dermatological toxicity with AFATINIB 40mg, the dose was changed to 30mg OD. Patient tolerated 30mg dose, with reassessment showing partial response after 10months of therapy. Meanwhile she also received Intravitreal Avastin (1.25mg) for ocular metastases third dose recently.

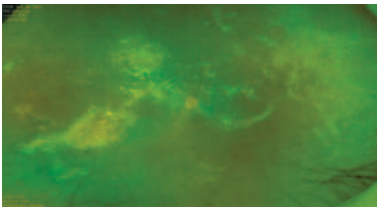


Figure 4: Recent Fundoscopy Showed Decrease in Size of Choroidal Lesion.

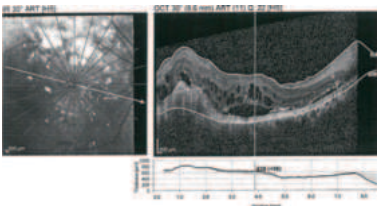


Figure 5: Recent Oct Showing Regression in Fluid and Lesion.

DISCUSSION

Most common intraocular malignancy is uveal metastasis. Most often metastases involve the posterior part of the eye due to rich vascular supply within the uvea. Within Uvea, choroid is most commonly involved site followed by iris and ciliary body.[4] Primary source of choroidal metastases is Breast (Females) followed by Lung (Males). Less commonly involved sites being Kidney, GI tract, Prostate, Skin (melanoma). Reports of CM as the first manifestation of lung cancer are rare, making the published cases clinically significant.[5]

Most reported cases involve middle-aged to elderly patients (40–80 years). However, even very young patients have also been described as

in our case.[6] Both genders are affected, though adenocarcinoma predominates in women and smoking history is common in men. The initial symptom across studies is visual impairment (blurring, diminished acuity, or painless loss of vision). Examination typically reveals yellow-white, elevated choroidal lesions with or without serous retinal detachment. Unilateral, unifocal involvement is more frequent in lung cancer compared to breast cancer, which often presents with bilateral/multifocal disease. All case reports highlight the importance of ophthalmic evaluation (fundoscopy, OCT, fluorescein angiography, ultrasonography) in detecting CM. Systemic work-up (CT, PET-CT, or biopsy) confirms lung origin.

Survival after choroidal metastases in lung primary ranges from 0.5 months to 19months.[7] Thus associated with poor prognosis and indicating aggressive nature of disease. Treatment is palliative, as these suggest hematogenous spread of cancer. Aim being to improve quality of life and to restore or preserve vision. Various modalities that can be used for vision preservation are transpupillary therapy, photodynamic therapy, orbital irradiation, chemotherapy, targeted therapy etc. In our case patient was treated with targeted therapy for uncommon G719S mutation. Other similar case reports with their treatment is given below.

Study	No	Mutation	Targeted Therapy	Outcome
Inoue et al. (2010)[8]	1	EGFR (un-specified)	Gefitinib	Improved of vision at 3mon & tumor regression.
Chen et al. (2011)[9]	1	EGFR (un-specified)	Erlotinib → Docetaxel	Visual acuity improved after 2 month.
Shimomura et al. (2013)[10]	1	EGFR exon 19 deletion	Gefitinib	Vision Stabilized for 2 years.
Yang et al. (2014)[11]	4	EGFR (1/4 patients)	Chemo (non-targeted)/ Gefitinib	Died at 3 months after diagnosis of CM.
Maskell et al. (2017)[12]	1	EGFR (not detailed)	Gefitinib	CM controlled 3 weeks, then systemic progression.
Cui et al. (2017)[13]	1	ALK (EML4-ALK)	Crizotinib → 2nd-gen ALK	Initial response, then progression at 16 months.
Rao & Gragoudas (2015)[14]	1	ALK (EML4-ALK)	Crizotinib (3rd line)	CM & brain metastases after 6 months of crizotinib.
Lu et al. (2015)[15]	1	ROS1 rearranged	Crizotinib (2nd line)	Improvement in vision after 3 weeks of crizotinib.
Okuma et al. (2015)[16]	1	ALK (EML4-ALK)	Alectinib	Complete vision recovery in 2 weeks.
Funazo et al. (2017)[17]	1	ALK (EML4-ALK)	Alectinib	Good general and ocular response.

CONCLUSION

Choroidal metastases from lung being rare, it being as a initial presentation is even rarer. As most common ocular malignancy being metastatic deposits, high index of suspicion is a must and any lesion per se to be taken as metastatic disease and evaluated for the primary. Multidisciplinary approach and care should form cornerstone of management. Increased awareness of this rare presentation can help with prompt recognition and appropriate management for optimizing patient outcomes.

Management is primarily palliative, with external beam radiotherapy providing excellent local control and vision preservation, while systemic chemotherapy and, more recently, targeted therapies and immunotherapy offer extended survival in molecularly defined subsets. Despite these advances, prognosis remains guarded, as ocular involvement usually reflects disseminated disease.

REFERENCES

- Li J, Zhu H, Sun L, Xu W, Wang X. Prognostic value of site-specific metastases in lung cancer: A population based study. J Cancer. 2019 Jun 2;10(14):3079-3086. doi: 10.7150/jca.30463. PMID: 31289577; PMCID: PMC6603375.
- Arepalli S, Kaliki S, Shields CL. Choroidal metastases: origin, features, and therapy. Indian J Ophthalmol. 2015 Feb;63(2):122-7. doi: 10.4103/0301-4738.154380. PMID: 25827542; PMCID: PMC4399120.
- Migaou A, Ben Saad A, Joobeur S, Ben Abdeljelil N, Zina S, Cheikh Mhammed S,

- Rouatbi N, Fahem N. Choroidal metastasis as the initial presentation of lung adenocarcinoma: A case report. *Respir Med Case Rep.* 2020 Jan 3;29:100992. doi: 10.1016/j.rmcr.2019.100992. PMID: 31956477; PMCID: PMC6957837.
4. Shields CL, Kalafatis NE, Gad M, Sen M, Laiton A, Silva AMV, Agrawal K, Lally SE, Shields JA. Metastatic tumours to the eye. Review of metastasis to the iris, ciliary body, choroid, retina, optic disc, vitreous, and/or lens capsule. *Eye (Lond).* 2023 Apr;37(5):809-814. doi: 10.1038/s41433-022-02015-4. Epub 2022 Mar 19. PMID: 35306540; PMCID: PMC10050009.
 5. Abed R, Alhroub W, Asbeh YA, Rabee A, Bannoura S, Madia A. A rare presentation of primary lung adenocarcinoma mimicking bilateral interstitial infiltration: A case report and literature review. *Int J Surg Case Rep.* 2025 Feb;127:110899. doi: 10.1016/j.ijscr.2025.110899. Epub 2025 Jan 15. PMID: 39823974; PMCID: PMC11786693.
 6. Shields, Carol & Acaba-Berrocal, Luis & Selzer, Evan & Mayro, Eileen & Newman, Jennifer & Malik, Kunal & Welch, R. & Shields, Jerry. (2018). UVEAL METASTASIS BASED ON PATIENT AGE IN 1,111 PATIENTS: Comparison of Clinical Features and Outcomes Per Age Category. *Retina.* 40. 1. 10.1097/IAE.0000000000002364.
 7. Das SK, Sahoo TK, Parija S, Majumdar SKD, Parida DK. Choroidal Metastasis as Initial Presentation in Adenocarcinoma of Lung: A Case Report. *J Clin Diagn Res.* 2017 Mar;11(3):XD04-XD06. doi: 10.7860/JCDR/2017/22533.9446. Epub 2017 Mar 1. PMID: 28511491; PMCID: PMC5427417.
 8. Inoue, M., Watanabe, Y., Yamane, S., Kobayashi, S., Arakawa, A., Tsukahara, T., Kaneko, T., Kadonosono, K., 2010. Choroidal metastasis with adenocarcinoma of the lung treated with gefitinib. *Eur. J. Ophthalmol.* 20, 963–965.
 9. Chen, C.J., McCoy, A.N., Brahmer, J., Handa, J.T., 2011. Emerging treatments for choroidal metastases. *Surv. Ophthalmol.* 56, 511–521. <https://doi.org/10.1016/j.survophthal.2011.05.001>.
 10. Shimomura, I., Tada, Y., Miura, G., Suzuki, T., Matsumura, T., Tsushima, K., Terada, J., Kurimoto, R., Sakaida, E., Sekine, I., Takiguchi, Y., Yamamoto, S., Tatsumi, K., 2013. Choroidal metastasis of non-small cell lung cancer that responded to gefitinib. *Case Rep. Ophthalmol. Med.* 2013, 213124. <https://doi.org/10.1155/2013/213124>.
 11. Yang, C.-J., Tsai, Y.-M., Tsai, M.-J., Chang, H.-L., Huang, M.-S., 2014. The effect of chemotherapy with cisplatin and pemetrexed for choroidal metastasis of non-squamous cell carcinoma. *Canc. Chemother. Pharmacol.* 73, 199–205. <https://doi.org/10.1007/s00280-013-2341-4>.
 12. Maskell, D., Geropantas, K., Kouroupis, M., Glenn, A., Ajithkumar, T., 2017. Treatment of choice for patients with EGFR mutation-positive non-small cell lung carcinoma presenting with choroidal metastases: radiotherapy or TKIs? *Can. J. Ophthalmol. J. Can. Ophtalmol.* 52, e22–e25. <https://doi.org/10.1016/j.jcjo.2016.09.010>.
 13. Cui, Z.-H., Zhang, Y., Liang, L.-L., Li, Z.-H., Abramova, I., Hao, Q., 2017. Development of a new choroidal metastasis in resistance to crizotinib therapy in anaplastic lymphoma kinase-rearranged non-small cell lung cancer. *Int. J. Ophthalmol.* 10, 310–314. <https://doi.org/10.18240/ijo.2017.02.21>.
 14. Rao, R.C., Gragoudas, E.S., 2015. Choroidal metastases from EML4-ALK-positive non small-cell lung adenocarcinoma. *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.* 33, e112–114. <https://doi.org/10.1200/JCO.2013.50.2740>.
 15. Lu, S., Azada, M.C., Ou, S.-H.I., 2015. Choroidal metastasis response to crizotinib in a ROS1-rearranged NSCLC patient. *Lung Cancer Amst. Neth.* 87, 207–209. <https://doi.org/10.1016/j.lungcan.2014.12.011>.
 16. Okuma, Y., Tanaka, Y., Kamei, T., Hosomi, Y., Okamura, T., 2015. Alectinib for choroidal metastasis in a patient with crizotinib-resistant ALK rearranged positive non-small cell lung cancer. *OncoTargets Ther.* 8, 1321–1325. <https://doi.org/10.2147/OTT.S83179>.
 17. Funazo, T., Morita, K., Ikegami, N., Konishi, C., Nakao, S., Ariyasu, R., Taki, M., Nakagawa, K., Hwang, M.H., Yoshimura, C., Wakayama, T., Nishizaka, Y., 2017. Successful treatment with alectinib for choroidal metastasis in anaplastic lymphoma kinase rearranged non-small cell lung cancer. *Intern. Med.* 56, 2317–2320. <https://doi.org/10.2169/internalmedicine.8488-16>.