

Choroidal metastasis from lung adenocarcinoma: a rare case report

C. PORRELLO¹, R. GULLO¹, C.M. GAGLIARDO¹, A. VAGLICA¹,
M. PALAZZOLO¹, F. GIANGREGORIO¹, D. IADICOLA², G. PROFITA²,
F. LO FASO³, G. TOMASELLO⁴, F. CARINI^{4*}, G. COCORULLO^{2*}

SUMMARY: Choroidal metastasis from lung adenocarcinoma: a rare case report.

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The choroid is the most common site for intraocular metastatic di-

sease. Orbital metastasis as metastatic site of lung adenocarcinoma is very rare and in literature a very exiguous number of cases is present. This is a case report of a woman with history of lung adenocarcinoma and, after surgery, detection of a choroidal mass described as lung metastasis, responding to Gefinitib therapy. However a biopsy was not performed. After two years there was a great dimension decrement of the lung metastasis but she is still suffering from recurrent pleural effusion, with pleural thickenings biopsied and diagnosed as recurrences of disease.

KEY WORDS: Lung metastasis - Choroidal metastasis - Lung adenocarcinoma - Orbital biopsy.

Introduction

The choroid is the most common site for intraocular metastatic disease (1).

Ocular metastases are generally symptomatic. The most common ocular symptoms at diagnosis include blurred vision (70%), flashes and floaters (12%), and less, commonly pain (7%) (2, 3).

Ocular pain carries a broad differential diagnosis from dry eye to corneal abrasion, orbital pseudotumor, lacrimal gland malignancy, and many others. The combination of ocular pain with an intraocular mass narrows the differential to entities including scleritis, inflammatory retinal/choroidal mass with

uveitis, hemorrhagic choroidal detachment, secondary glaucoma with retinal detachment from underlying retinal or choroidal tumor, choroidal melanoma with tumor necrosis, choroidal metastasis, and others.

With regard to choroidal metastasis, low-grade ocular discomfort (pain) without glaucoma or visible necrosis has been recorded as a presenting symptom in 7% of cases overall, but increases to 13% in eyes with metastatic lung cancer. The cause for metastasis-related pain is speculated to be related to tumor invasion, particularly within the sclera (4).

About late-stage lung adenocarcinoma, a current analysis provides a better understanding of the metastatic sites including bone (39%), brain (25%), liver (16%), and adrenal glands (13%).

Orbital metastasis as metastatic site of lung adenocarcinoma is very rare and in literature a very exiguous number of cases is present (5).

In this case report we want to add our Thoracic Surgical Centre's experience of a choroidal mass described as lung metastasis.

¹ Department of Thoracic Surgery, Azienda Ospedaliera Universitaria "Paolo Giaccone di Palermo", Palermo, Italy

² Department of General and Emergency Surgery, Azienda Ospedaliera Universitaria "Paolo Giaccone di Palermo", Palermo, Italy

³ Unit of General and Mininvasive Thoracic Surgery, "Azienda Ospedaliera Marche Nord", Italy

⁴ Department of Experimental Biomedicine and Clinical Neuroscience, Section of Anatomy, (BIONEC), University of Palermo, Palermo, Italy

* The Authors G. Cocorullo and F. Carini contributed equally to this article

Corresponding author: Calogero Porrello, e-mail: calogero.porrello@gmail.com

Case report

The patient was a 56-year-old nonsmoker Caucasian woman with history of lung adenocarcinoma and presenting a choroidal mass described as metastasis from the lung. She did not present other comorbidities.

In April 2016, after instrumental detection of 3 omolateral nodules among the right lower and medium right lung lobes, TC guided biopsy pointed out a non-mucinous ALK negative adenocarcinoma, so that in May 2016 she went under major thoracic surgery and a bilobectomy was performed. After serial MRI studies, no cerebral metastasis was found. At post-operative tissue diagnosis, 3 nodular growths of cm 4,5x2,3x2,2; cm 3x3x2 e cm 1,6x1,5x1,3 were described as non mucinous adenocarcinoma (for the first one) and lepidic adenocarcinoma (for the second ones) (pTNM: T4N1; stage IIIA).

After surgery, only one cycle of chemotherapy with cisplatin was administered because of marrow toxicity.

In April 2017, because of eye symptoms as blurred vision and feeling of foreign body at the right eye, during an eye counseling a bulbar ultrasonography Etg showed a domed lesion in the upper temporal right sector, with a longitudinal and transversal diameter respectively of mm 8.38-2.17, not interesting macular area. At the A-scan test there was an high reflectivity. This provided a presumptive diagnoses of choroidal metastasis, as secondary to the lung cancer.

In May 2017 molecular test was performed to research EGFR mutations in 18-19-20-21 exons, using as methodic DNA genomic extraction and real-time PCR: it accessed the mutation p.L858R (c.2573T>G) in the 21 exon. For that reason, Gefitinib therapy (anti-EGFR) was administered and is still representing her therapy.

Periodic successive eye counselings taked place. Just the first one showed a great decrease of metastasis' dimensions: longitudinal and transversal diameter respectively of mm 2.63- 2.17, compatible as anti-EGFR therapy response. At the last one (March 2018), after correction, visual acuity was 10/10 in both right and left eyes. Intraocular pressure and anterior segment findings were normal in each eye. There were no inflammation signs. Lesion's dimen-

sions were the same (2.63-2.17 mm) so that, although the dimension decrement, no indication to interrupt therapy was given and, after a discussion with ophthalmologists and oncologists an invasive biopsy wasn't performed because of metastasis' size and the high risk of complications, which would further affect his potential vision.

As of May 2018, she is still suffering from recurrent pleural effusion, with pleural thickenings biopsied and diagnosed as recurrence of disease. She is also continuing the therapy with Gefitinib. Future eye and routine controls have been already programmed.

Discussion

Orbital metastases of cancer are rare and comprise about 3-7% of orbital lesions and about 10% of orbital tumors. They most commonly originate from primary lesions of the breast (39-48%), prostate and skin (melanoma) (12%), lung (8%), and kidney (7-11%) in whites. It is probable that, with the increasing number of lung cancer's cases, the number of patients with an orbital metastasis will increase too (6).

In literature a very exiguous number of case reports about this topic is present. Therefore, orbital metastasis or symptoms as the initial presentation of lung adenocarcinoma are even more uncommon, so that can induce in misdiagnosis (7), either as an orbital primary tumor or benign lesion.

Searching on Pubmed, Medline and others, we found only a few number of case reports similar to ours. The symptoms are comparable. In one of Liangchao Sun et al. (8) a response to chemotherapy (two cycles of pemetrexed and cisplatin) and palliative radiotherapy is reported. As regards our patient, we could not value a possible benefit of chemotherapy because of a bone marrow toxicity after the first cycle. On the contrary we can suppose a modest response to EGFR-inhibitors.

This one could be a useful remark for scientific community: are lung adenocarcinoma orbital metastasis good-responders to chemotherapy? Should be this a sign of good prognosis? Already, this remains unclear and needs further studies to be clarified.

Another point to analyze could be performing or

not an orbital fine needle aspiration biopsy (FNAB), which is cytological, and/or a core biopsy or an open invasive biopsy as a useful supplement or an alternative to obtain an adequate tissue sample for histological diagnosis, which reached a diagnostic accuracy of 94% in some reports (9). The choice of a biopsy procedure had been fully weighted for the cost/benefit ratio (10, 11). Ophthalmologists, both in the first case report and in our case, denied to execute it for its high risk of complications (damage to the eye globe, optic nerve, vessels, and even the needle-track tumor seeding simultaneously) (12). A possible doubt is: could we make diagnosis of metastasis without a certain tissue diagnosis? (13-15). The response to the biologic therapy in our case has been considered as first criterion to attribute the mass to the lung adenocarcinoma. But could it be sufficient? In the last two ophthalmological controls, although the substantial initial reduction of mass longitudinal diameter after treatment, its dimensions were not totally regressed. According to these data it could seem a diagnosis' mistake occurred or that, for this patient and/or the orbital lesion this kind of treatment could be inadequate. Furthermore in the thoracic surgery management a possible orbital invasive biopsy, followed by tissue diagnosis and molecular testing, could help physicians in a correct and certain diagnosis and to administer an adequate specific-target therapy.

Through tissue diagnosis, to make differential diagnosis from a distant metastasis or from a primary orbital tumor, could have a central role before surgery to determine the cTNM and so the anatomical operability: in the first case M1b (TNM 2018) -

stage IV while in the second one M0 and so, respectively, inoperable and operable tumor.

Conclusion

A case of diffuse choroidal metastasis from lung adenocarcinoma with blurred vision and feeling of foreign body, previously unrecognized, emphasizes the importance of knowing that eye disorders should be possible early symptoms of metastatic choroidal-orbital tumors. Thus, with the increasing number of lung cancer's cases, a large index of suspicion is essential when an orbital lesion appears in a patient with history of lung adenocarcinoma. For this reason, the clinical history should never be undervalued. Imaging studies (ocular Etg and OCT) are essential to characterize the orbital metastases for obtaining the provisional diagnosis. Therefore, as regarding the diagnostic algorithm of the choroidal mass and lung adenocarcinoma surgical management, focusing on the role of choroidal mass biopsy is necessary: the choice of a biopsy procedure should be fully weighed for the cost/benefit ratio but applied whereas possible. About their efficacy in orbital metastases, novel drugs, especially the EGFR-inhibitors, need further and stronger evidence.

Acknowledgements and credits

None to declare.

Conflict of interest

The Authors declare that they have no conflicts of interest.

We obtained the informed consent to this case report.

References

1. Hua R, Li W, et al. Failure of ocular photodynamic therapy for secondary choroidal metastasis: a case report and literature review. *Oncotarget*. 2017 Oct 16;8(55):95030-95035.
2. Singh N, Kulkarni P, et al. Choroidal metastasis as a presenting manifestation of lung cancer: a report of 3 cases and systematic review of the literature. *Medicine (Baltimore)*. 2012 Jul;91(4):179-94.
3. Shields CL, Shields JA, et al. Survey of 520 eyes with uveal metastases. *Ophthalmology*. 1997;104:1265-1276.
4. Shah SU, Mashayekhi A, et al. Uveal metastasis from lung cancer: clinical features, treatment, and outcome in 194 patients. *Ophthalmology*. 2014;121:352-357.
5. Hess KR, Varadhachary GR, Taylor SH, et al. Metastatic patterns in adenocarcinoma. *Cancer*. 2006;106(7):1624-1633.
6. Ahmad SM, Esmali B. Metastatic tumors of the orbit and ocular adnexa. *Curr Opin Ophthalmol*. 2007;18(5):405-413. (Bonavolonta G, Strianese D, Grassi P, et al. An analysis of 2,480 space-occupying lesions of the orbit from 1976 to 2011. *Ophthal Plast Reconstr Surg*. 2013;29(2):79-86.
7. Cocorullo G, Scerrino G, Melfa G, Raspanti C, Rotolo G, Mannino V, Richiusa P, Cabibi D, Giannone AG, Porrello C, Gulotta G. Non-functioning parathyroid cystic tumour: malignant or not? Report of a case. *G Chir*. 2017 Sep-Oct;38(5):243-249.
8. Liangchao Sun, Yali Qi, Xindong Sun, Jinming Yu, Xue Meng. Orbital metastasis as the initial presentation of lung adenocarcinoma: a case report. *OncoTargets and Therapy*. 2016:9.
9. Gong Y, Sneige N, Guo M, Hicks ME, Moran CA. Transthoracic fine-needle aspiration vs concurrent core needle biopsy in diagnosis of intrathoracic lesions: a retrospective comparison

- of diagnostic accuracy. *Am J Clin Pathol.* 2006;125(3):438-444.
10. Iadicola D, De Marco P, Bonventre S, Grutta EM, Barletta G, Licari L, Gulotta G. Bowel wall thickening: inquire or not inquire? Our guidelines. *G Chir.* 2018 Jan-Feb;39(1):41-44.
 11. Melfa G, Porello C, Cocorullo G, Raspanti C, Rotolo G, Attard A, Gullo R, Bonventre S, Gulotta G, Scerrino G. Surgeon volume and hospital volume in endocrine neck surgery: how many procedures are needed for reaching a safety level and acceptable costs? A systematic narrative review. *G Chir.* 2018 Jan-Feb;39(1):5-11.
 12. Yarovoy AA, Bulgakova ES, Shatskikh AV, Uzunyan DG, Kleyankina SS, Golubeva OV. CORE needle biopsy of orbital tumors. *Graefes Arch Clin Exp Ophthalmol.* 2013;251(8):2057-2061.
 13. Porrello C, Gullo R, Vaglica A, Scerrino G, Giuseppe S, Licari L, Raspanti C, Gulotta E, Gulotta G, Cocorullo G. Retrospective Analysis of 29 Patients with Multiple Pulmonary Metastases from Colorectal Carcinoma Resected by a 1318-nm Laser. *Am Surg.* 2018 Mar 1;84(3):460-462.
 14. Salamone G, Licari L, Guercio G, Comelli A, Mangiapane M, Falco N, Tutino R, Bagarella N, Campanella S, Porrello C, Gullo R, Cocorullo G, Gulotta G. Vacuum-Assisted Wound Closure with Mesh-Mediated Fascial Traction Achieves Better Outcomes than Vacuum-Assisted Wound Closure Alone: A Comparative Study. *World J Surg.* 2018 Jun;42(6):1679-1686.
 15. Porrello C, Gullo R, Vaglica A, Scerrino G, Salamone G, Licari L, Raspanti C, Gulotta E, Gulotta G, Cocorullo G. Pulmonary Laser Metastasectomy by 1318-nm Neodymium-Doped Yttrium-Aluminum Garnet Laser: A Retrospective Study About Laser Metastasectomy of the Lung. *Surg Innov.* 2018 Apr;25(2):142-148.
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