

## Choroidal metastasis as the sole initial presentation of metastatic lung cancer

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Hematol Oncol Stem Cell Ther 2012; 5(1): 60-65

DOI: 10.5144/1658-3876.2012.60

Choroidal metastasis as an initial presenting feature of metastatic lung cancer is exceedingly rare. External beam radiotherapy (EBRT) is an effective and widely accepted therapeutic modality. However, data addressing the effectiveness of other treatment strategies is limited. We present a patient with choroidal metastases secondary to lung cancer and review the relevant literature. A 25-year-old male presented with deterioration of vision. His evaluation revealed bilateral choroidal metastasis secondary to adenocarcinoma of the lung. Unfortunately, his vision continued to deteriorate despite treatment with EBRT and chemotherapy. Choroidal metastasis as an initial presentation of metastatic lung cancer is exceedingly rare, as only 30 cases have been reported. EBRT and systemic chemotherapy are effective therapeutic modalities. This case report could prove helpful to clinicians faced with a similar exceedingly rare scenario.

Choroidal metastasis as an initial presenting feature of metastatic lung cancer is exceedingly rare.<sup>1</sup> Furthermore, available literature about effective treatment strategies is limited. We present a clinical scenario involving a young male patient with bilateral choroidal metastases from lung cancer, and review the relevant literature in an attempt to highlight the epidemiological features, pathological characters, therapeutic regimens and disease outcomes of this poorly understood disease entity.

### CASE

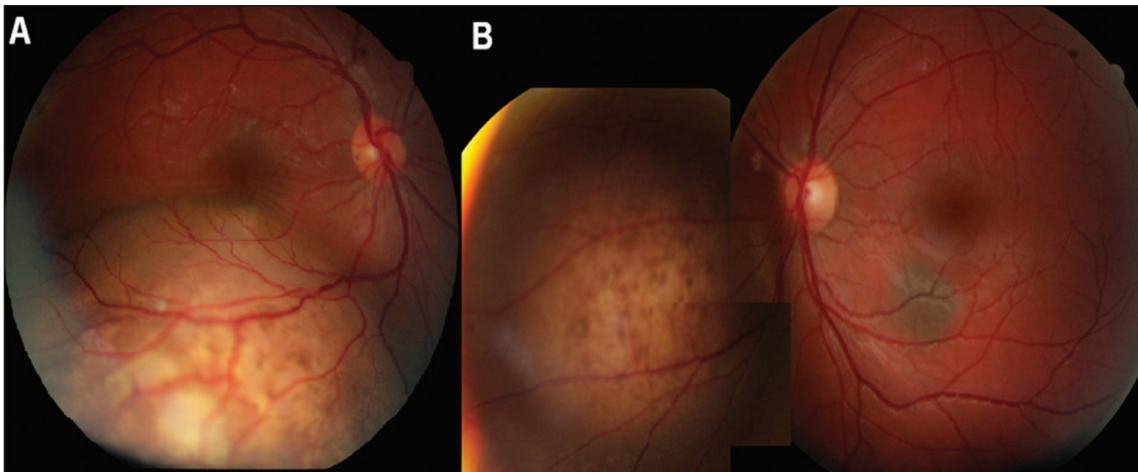
A 25-year-old man presented with decreased vision in the right eye for two weeks. He acknowledged smoking one pack of cigarettes daily for four years. Ophthalmic examination revealed his best corrected visual acuity to be 20/200 in the right eye and 20/20 in the left eye. Results of slit lamp examination were unremarkable. Funduscopic examination of the right eye showed an ill-defined, yellow-white elevated lesion in the choroid more than 10 times the disc diameter, involving the macula and the inferior edge of the fovea with associated serous retinal detachment (**Figure 1A**). Funduscopic examination of his left eye showed an ill-defined, yellow-white elevated lesion in the choroid more than 5 times

the disc diameter in size, nasal to the disc (**Figure 1B**). Fluorescein angiography of his right eye revealed early hypofluorescence and late phase showed hypofluorescence from the surface of his choroidal tumor associated with accumulated sub-retinal fluid. A B-scan ultrasound revealed a dome shaped, elevated choroidal lesion with moderate internal reflectivity.

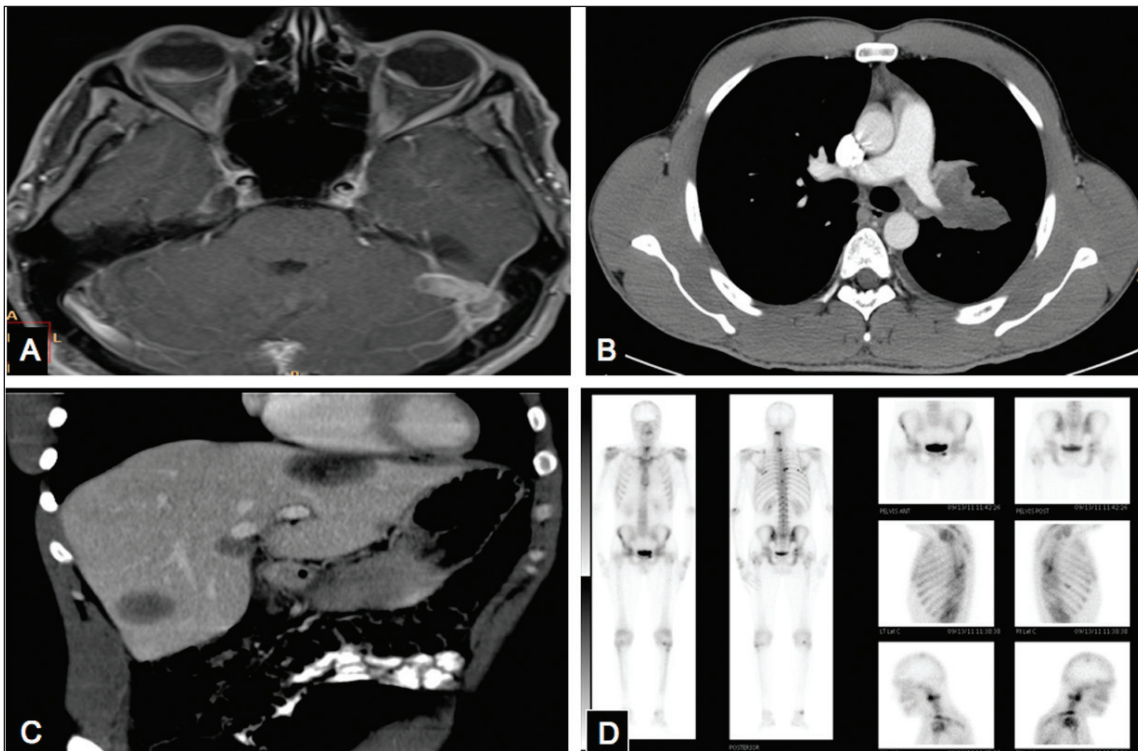
The remaining physical examination was normal except for two hard subcutaneous nodules on his chest. In a search for a primary malignancy, imaging studies were done, which showed a left lung hilar mass, multiple liver metastasis, and widespread bone metastasis (**Figure 2**).

A CT-guided lung biopsy as well as biopsy of the skin nodules was performed. The tumor showed proliferation of groups of cells within a markedly desmoplastic stroma (**Figure 3A**). The cells contained intra-cytoplasmic vacuoles that stained positive with mucicarmine stain (**Figure 3B**) consistent with adenocarcinoma. Immunohistochemistry positivity for TTF-1 antibody was demonstrated (**Figure 3C**). Occasional tumor cells were positive for cytokeratin 5/6 and P63. The overall features were consistent with moderately differentiated adenocarcinoma of lung origin.

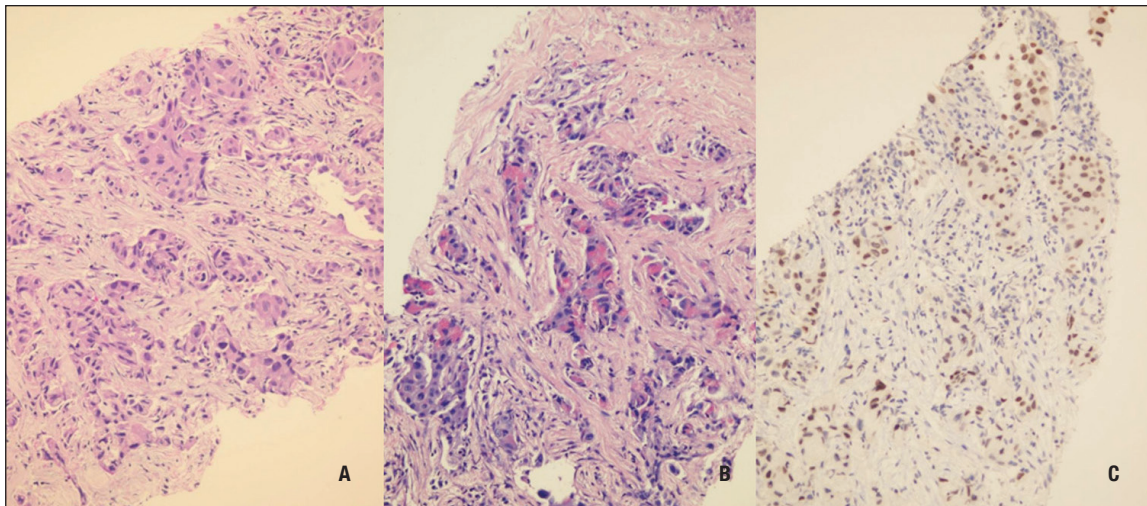
The patient was started on chemotherapy with cisplatin and docetaxel, and EBRT to both orbits.



**Figure 1.** A) Right eye fundus examination showed a yellow-white elevated lesion in the choroid, inferiorly located involving the macula with associated serious retinal detachment. B) Left eye funduscopy revealed a choroidal metastasis at the nasal edge of the optic disc.



**Figure 2.** A) Orbit MRI axial, T1 WI's post contrast image showing soft tissue nodular lesions in the posterior parts of the eye globes mainly at the right side, demonstrating homogeneous contrast enhancement. B) Enhanced CT scan of the chest; mediastinal window shows left hilar soft tissue mass encasing the left main pulmonary artery. C) CT scan through the liver shows multiple hypodense liver lesions represent metastases. D) Bone scan demonstrates multiple active bone lesions represent metastases.



**Figure 3.** Microscopic examination of the biopsy from lung mass. A) Sheets of tumor cells with acidophilic cytoplasm are seen (Hematoxylin and eosin,  $\times 20$ ). B) Mucicarmine stain highlighted intra-cytoplasmic mucin ( $\times 20$ ). C) Positive nuclear staining with TTF-1 ( $\times 20$ ).

Unfortunately, the patient continued to experience rapid deterioration of vision in the right eye (visual acuity dropped from 20/200 to counting fingers at 1 meter) and the left eye (visual acuity dropped from 20/20 to 20/200). Funduscopic examination showed a right total serous retinal detachment (RD) and left nasal and inferior serous RD involving the macula. He received EBRT as 30 Gy/10 Fx over two weeks to both orbits via a pair of parallel-opposed beams. Following completion of radiotherapy, follow-up ophthalmic evaluation (clinical and ultrasonic) showed stability in the size of choroidal lesions in both eyes but no regression of serous RD. Systemic steroids and posterior sub-tenon steroid injections were applied as treatment for serous retinal detachment. Following the second cycle of chemotherapy, imaging studies revealed significant progression of lung mass and liver lesions.

## DISCUSSION

The choroid is a rare site of involvement by metastatic carcinomas. Godtfredsen<sup>2</sup> reported only six patients (0.07%) in a survey that included 8712 patients with malignancy. Furthermore, choroidal involvement typically occurs late in the course of metastatic cancer.<sup>3</sup> Following breast neoplasm, lung cancer is the second most common cancer to metastasize to the choroid.<sup>1</sup> Postmortem examination of donated eyes of patients with carcinomas showed a 6.1% frequency of eye involvement in patients dying of lung cancer; however, only 2.7% of all lung cancer patients in that series had gross metastasis while the remaining had only microscopic metastasis.<sup>4</sup> This finding suggests that most pa-

tients die when the choroidal metastasis is at a microscopic stage and before developing visual symptoms, which explains the rarity of this site of metastasis as a presenting feature.

Characteristics of the 30 reported cases and their metastatic lung cancer are outlined in **Table 1**. At 25 years, our patient is the youngest reported case of choroidal metastases secondary to lung cancer. Nineteen patients (61 %) had accompanying retinal detachment at their initial ophthalmologic evaluation. Most patients had multi-organ metastasis, with the brain, liver and bone as the most common metastatic sites. Choroidal metastasis can be distinguished from primary choroidal melanoma by clinical characteristics; typical choroidal metastasis is more often of a plateau-shape than dome-shape; is yellow-white or mottled in color and associated with subretinal fluid and retinal detachment. FFA characterized by mottled hyperfluorescence in early stage while leakage in late stages and B-scan ultrasonography usually shows moderate reflectivity. Usually no biopsy is needed unless extensive staging work up has failed to reveal the primary or other metastatic sites.<sup>5</sup>

EBRT is effective in treating and palliating patients with asymptomatic and symptomatic choroidal metastases. Doses in the range of 3000 to 4000 cGy delivered via conventional fractionation are well tolerated and result in visual stabilization or improvement in up to 85% of cases.<sup>6-10</sup> A unilateral radiation portal is appropriate in patients presenting with unilateral choroidal metastasis.<sup>11</sup> However, it should be noted that patients included in these studies had a diagnosis of



**Table 1.** Characteristics of 30 reported cases with lung cancer and choroidal metastases.

Author/Journal	Age (years)/ Gender	Laterality	Histology	Metastatic sites	Treatment	Choroidal response/ survival
Singh et al. J Med Case Reports. 2010 Jun 19;4:185.	50/M	Right	ADC	Not clear	CTX	CR/Not clear
Inoue et al. Eur J Ophthalmol. 2010 Sep-Oct;20(5):963-5.	68/F	Bilateral	ADC	Not clear	Gefitinib	PR/Not clear
George et al. J Thorac Oncol. 2009 May;4(5):661-2.	42/F	Right	LCC	Cervical LN, lung	CTX and Bev	CR/AWD after 7 cycles
John et al. J Thorac Oncol. 2010 Aug;5(8):1289.	56/M	Bilateral	SCLC	Liver	None	Not clear
Lakhanpal et al. Ann Ophthalmol. 1982 Sep;14(9):864-6.	38/F	Right	ADC	Brain, bone	EBRT and CTX	PR after EBRT/DWD after 7 months
Cury Júnior et al. Arq Bras Oftalmol. 2008 Mar-Apr;71(2):291-4.	65/F	Left	Not clear	Pleura	Not clear	Not clear
Kostrzewski et al. Pol Merkuriusz Lekarski. 2011 Sep;31(183):171-4.	61/F	Bilateral	NSCLC	Not clear	CTX	CR/Not clear
Herrag et al. Ann Thorac Surg. 2010 Mar;89(3):1013-4; author reply 1014.	55/M	Right	ADC	Liver, bone	CTX and EBRT	PR/Not clear
Kaur et al. Am J Ophthalmol. 2007 Feb;143(2):369-70.	51/F	Right	ADC	No other sites	CTX and EBRT, enucleation	PD/DWD after 7 months
Mauget-Fayssse et al. Acta Ophthalmol Scand. 2006 Aug;84(4):552-4.	66/M	Right	ADC	Bone, pleura	CTX and PDT	PR/Not clear
Shields et al. Retina. 2005 Apr-May;25(3):367-70	57/F	Left	NSCLC	Liver, pleura	Enucleation	PD/DWD after 11 months
Shields et al. Ophthalmic Surg Lasers. 2002 Jul-Aug;33(4):323-5.	75/F	Left	NSCLC	Brain	CTX and WBRT	CR/Alive and FOP after >18 months
Matsuda et al. Nihon Kokyuki Gakkai Zasshi. 2004 May;42(5):410-4.	51/F	Not clear	ADC	Not clear	CTX and EBRT	Not clear/DWD after 6 months
Yamada et al. Nihon Kokyuki Gakkai Zasshi. 2003 May;41(5):370-5.	69/M	Right	ADC	No other sites	Not clear	Not clear
Hasturk et al. Lung Cancer. 2001 Apr;32(1):95-101.	51/M	Left	LCC	Liver, bone	CTX	Not clear/DWD after 4 months
Leys. Retina. 2000;20(2):216-7.	62/M	Left	SCLC	Bone	CTX	PR/ND
Egusa et al. Nihon Kyobu Shikkan Gakkai Zasshi. 1996 Jan;34(1):121-5.	68/M	Left	ASC	No other sites	Enucleation	Lt blindness/Alive WOD at 7 months
Takano et al. Nihon Kyobu Shikkan Gakkai Zasshi. 1995 Jun;33(6):674-7.	72/F	Bilateral	SCC	Kidney	CTX	PR/Not clear
Marchini et al. Stereotact Funct Neurosurg. 1995;64 Suppl 1:67-71.	48/M	Left	ADC	No other sites	Gamma knife	PR/Alive and FOP after 9 months
O'Connell et al. Clin Oncol (R Coll Radiol). 1990 May;2(3):177-9.	71/M	Right	SCC	No other sites	EBRT, enucleation	PD/Alive WOD at 4 years
Simsek et al. Med Oncol. 2008;25(4):400-2.	45/M	Left	NSCLC	Adrenal, porta-hepatis LN	CTX and EBRT	Not clear/DWD at 6 months
Asteriou et al. World J Surg Oncol. 2010 Jan 8;8:2.	46/M	Left	SCC	Bone, brain, Adrenal	CTX and EBRT	Not clear
	45/M	Left	NSCLC	Base of skull	CTX	PR/DWD at 8 months
Evans et al. Thorax. 1971 Jul;26(4):472-5.	54/M	Right	SCC	Liver, Brain	Enucleation only	Not clear/DWD at 3 months
	53/F	Right	NSCLC	Not clear	CTX	PR/DWD at 5 months

**Table 1** (cont.). Characteristics of 30 reported cases with lung cancer and choroidal metastases.

Author/Journal	Age (years)/ Gender	Laterality	Histology	Metastatic sites	Treatment	Choroidal response/ survival
Tazi et al. Rev Med Interne. 2006 Sep;27(9):699-701.	28/M	Not clear	ADC	Bone, liver, LN	CTX	CR/Not clear
Kreiger et al. Arch Ophthalmol. 1969 Aug;82(2):209-13.	57/M	Bilateral	Not clear	Liver, bone, kidney, adrenal, others	None	Not clear/DWD shortly after diagnosis
Battikh et al. Rev Pneumol Clin. 2004 Dec;60(6 Pt 1):353-6.	52/M	Not clear	ADC	Not clear	CTX	CR/Not clear
Ascaso et al. Ann Thorac Surg. 2009 Sep;88(3):1013-5.	42/F	Bilateral	ADC	Bone, brain, meninges	CTX	Not clear
Manor et al. Br J Ophthalmol. 1978 Feb;62(2):122-9.	44/M	Bilateral	SCLC	Liver, adrenal, kidney, brain, others	CTX and EBRT	PD after CTX, PR after EBRT/DWD at 5 months

ADC: adenocarcinoma; LCC: large cell carcinoma; SCLC: small cell lung cancer; NSCLC: non-small cell lung cancer; ASC: adenosquamous carcinoma; SCC: squamous cell carcinoma; LN: lymph nodes; CTX: chemotherapy; Bev: bevacizumab; EBRT: external beam radiotherapy; PDT: photodynamic therapy; WBRT: whole brain radiotherapy; CR: complete response; PR: partial response; AWD: alive with disease; PD: progressive disease; DWD: died with disease; FOP: free of progression; WOD: without disease.

metastatic breast cancer and only a few presented with choroidal involvement secondary to a lung neoplasm.

The effectiveness of chemotherapy as a single modality in treating choroidal metastasis is not widely reported; however, a study in patients with breast cancer and choroidal metastasis concluded that systemic chemotherapy is as effective as radiotherapy as all six patients treated with systemic chemotherapy alone who showed regression of their choroidal metastasis.<sup>12</sup> Additionally, of the 30 reported cases we reviewed, 14 patients were treated with chemotherapy without additional EBRT; notably, 6 of the 14 patients had complete resolution, and an additional 4 patients had partial regression of the choroidal metastasis.

Although the available level of evidence supporting chemotherapy as a single modality in treating choroidal metastasis is limited, it can be a reasonable alternative when EBRT is not readily available. Among our reviewed cases, all patients who received EBRT had also received chemotherapy, either concurrently or sequentially. Unfortunately, due to the paucity of data, it was difficult to derive firm conclusions about how these two modalities should best be integrated.

Choroidal metastasis is usually associated with widespread multi-organ metastases, and carries an ex-

tremely poor prognosis with survival counted in few months. In the extremely rare event when the choroid is the only metastatic site, enucleation of the affected eye may carry the advantages of confirming the pathological diagnosis, palliating intractable pain and most importantly, offering a chance for long-term survival. O'Connell et al<sup>13</sup> reported a patient who remained alive and free of recurrence 4 years following eye enucleation.

Choroidal metastasis as an initial presentation of metastatic lung cancer is exceedingly rare. EBRT and systemic chemotherapy are effective treatment options associated with clinical and objective visual responses. This case report could prove helpful to clinicians faced with similar, however exceedingly rare scenario.

**Acknowledgment**

*We are grateful to Alice Haddadin and Lubna Al-Useily from the King Hussein Cancer Center Medical Library for assistance.*

**Conflict of interest**

*All authors have no conflict of interest to declare.*

**Consent**

*An informed consent was obtained from the patient.*

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