

Choroidal Metastasis: Clinical Aspects at A Referral Ocular Oncology Center

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Abstract

Purpose: To report clinical aspects of choroidal metastasis at an ocular oncology referral center

Methods: We reviewed the records of all patients with choroidal metastasis referred to an ocular oncology referral center over a 10-year period retrospectively. The study was performed to identify and analyze clinical presentations and features of patients with choroidal metastasis.

Results: A total of 113 choroidal metastases were diagnosed in 60 eyes of 48 consecutive patients. There were 17 male (35.4%) and 31 female (64.6%) patients with a mean age of 54.5 years (median: 42; range, 29- 82 years) at the time of choroidal metastasis diagnosis. The median and mean numbers of choroidal metastasis were one and three tumors in each eye respectively. The primary cancer location was found to be the breast in 18 patients (37.5%), lung in 11 (22.9%), lymphoproliferative system in three (6.3%), thyroid in three (6.3%), gastrointestinal tract in three (6.3%), prostate in two (4.2%), brain in one (2.1%) and unknown primary in seven (14.5%). The most common primary cancer was the breast in females and lung in males. The main ocular symptoms of choroidal metastasis at diagnosis were blurred vision in 42 patients followed by pain in five patients. The choroidal metastasis was unilateral in 36 patients (75%) and bilateral in 12 patients (25%).

Conclusion: The clinical features and primary sites of choroidal metastasis in Iranian patients were similar to those of published reports in this regard. One out of every seven patients had no known primary cancer at the time of choroidal metastasis presentation.

Keywords: Choroidal Metastasis, Intraocular Tumors, Cancer

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Introduction

Metastatic carcinoma to the eye is the most frequent intraocular malignancy which has been recognized since 1872, when Perls reported the first case of these tumors.¹ Although any part of the eye may be involved, it is well known in the ophthalmology literature that the choroid is by far the most common site for metastatic lesion to the eye.²⁻⁵ In case of disseminated cancer, uveal metastases could be the first presenting site of the disease and the ophthalmologist might be the first physician to detect this type of cancer.^{2,6-10}

A large autopsy study revealed that ocular metastasis occurs in 9.3% of patients dying of cancer.¹¹ Albert et al¹² in their experience of 213 patients with known systemic cancer found that 2% of cases had choroidal metastasis. More extensive clinical studies showed that choroidal metastasis occurs predominantly in patients in whom systemic metastasis involve more than one organ system.¹³

Although the most common primary sites of metastasis are breast in women and lung in men,¹⁴⁻¹⁶ Shields et al¹⁷ in their experience with a large group of patients with uveal metastases, noted that 34% of patients had no previous history of cancer. In spite of comprehensive systemic evaluation by medical and ocular oncologists, in approximately half of them, the primary site of cancer remained undiagnosed and 45% of those patients died of diffuse metastatic disease. In an era of increasing life expectancy of patients with cancer, it is not surprising that the number of uveal metastases will increase steadily.¹⁸ Some authors have indicated the higher incidence of specific types of cancer and their clinical presentations in different countries.¹⁹

We report the first series of the ophthalmic clinical aspects of metastatic tumors to the choroid in Iranian patients from one of the major ocular oncology centers.

Methods

We retrospectively analyzed the charts of all patients from the ocular oncology service at Rassoul Akram Hospital of Iran University of Medical Sciences with the clinical diagnosis of metastatic tumors to the choroid between April 2002 and April 2012. Patients with a choroidal

metastatic tumor were enrolled in this study for further analysis. The diagnosis of choroidal metastasis was based on fundus examination findings and results of non-invasive modalities.

The data collected included the patients' age at the time of choroidal metastasis diagnosis, gender, the person who first realized presence of the disease (ophthalmologist, medical oncologist or themselves), past medical history, laterality (unilateral or bilateral), involved eye(s), and symptoms (e.g. blurred vision, pain, visual field defect, floater and flashes). A detailed ophthalmic examination including the best corrected visual acuity (BCVA), intraocular pressure (IOP) measurement and slit-lamp and fundus examination was performed. A comprehensive evaluation was done for all patients to rule out other possible metastatic foci in the other parts of the globe and orbit.

The anatomical locations of the metastatic lesion(s) at fundus (macula, superior, nasal, inferior or temporal) as well as the number of the metastatic foci at each eye were recorded. Further evaluation for the evidence of subretinal fluid and rubeosis iridis was carried out. In case of multifocal lesions in an eye the largest metastatic lesion was considered as the reference lesion to determine anteroposterior location (macula, between macula and equator, between equator and ora serrata), the largest basal dimension and thickness as well as the color and shape of the tumor.

Furthermore, information regarding the site of primary cancer, time lag between the diagnosis of choroidal metastasis and the date of primary cancer detection as well as past medical or surgical treatments for the management of the disease were collected.

Results

From April 2002 until April 2012 a total of 60 eyes of 48 patients were found to have choroidal metastasis. There were 17 male patients (35.4%) and the mean age at presentation of choroidal metastasis was 54.5 years (median: 42; range, 29-82 years). Unilateral disease was evident in 36 patients (75%). The right eye was involved in 31 eyes (51.7%).

Among 48 patients with choroidal metastasis, at the time of ocular presentation, 38 patients (79.1 %) had a positive history for primary cancer, and 10 patients (20.9%) reported no history of known cancer. Following the comprehensive systemic evaluation by medical oncologist, the primary site of cancer was detected in only 3 (30%) of 10 patients. Those three patients (two men and one woman) were found to have carcinoid tumor of the lung. So, the primary cancer location was found to be the breast in 18 patients (37.5%), lung in 11 (22.9%), lymphoproliferative system in three (6.3%), thyroid in three (6.3%), gastrointestinal tract in three (6.3%), prostate in two (4.2%), brain in one (2.1%) and unknown primary in seven (14.5%) (Figure 1). Of the 36 patients with unilateral involvement the primary site of cancer was breast, lung and unknown primary cancer in 14 patients (38.9%), five patients (13.9%), and nine patients (25%) accordingly. Bilateral choroidal metastasis involvement was found in 12 patients (25%) and was from primary cancer of breast in four patients (33.3%), lung in three (25%), lymphoproliferative system in two (16.7%) and others in three (25%) of them.

The most common primary cancer site for the 31 female patients was breast in 18 (58.1%) followed by lung in six (19.4%), thyroid in three (9.7%), gastrointestinal tract in one (3.2%), lymphoproliferative in one (3.2%) and unknown in two (6.4%) of cases (Table 2). The primary cancer site evaluation for the 17 male patients revealed lung cancer in five (29.4%), gastrointestinal tract in two (11.8%), prostate in two (11.8%), lymphoproliferative in two (11.8%), brain in one (5.9%) and unknown in five (29.4%) of

them. In spite of complete systemic work-up and FNAB in some cases, no known primary site was detected in 29.4% (5/17) and 6.4% (2/31) of male and female patients respectively (Table 1).

The mean interval time between the primary cancer diagnosis and choroidal metastatic tumor diagnosis in 38 patients with a known primary source, was found to be 22 months. In subgroup analysis, it was 60 months for brain, 49.5 months for prostate, 16.4 months for lung, 15 months for thyroid, 10.1 months for breast and 1.2 months for gastrointestinal tract cancer.

At choroidal metastasis diagnosis, the most common ophthalmic symptoms were blurred vision in 42 patients (87.5%), pain in five (10.4%), visual field defect in three (6.2%), flashes and floater in two (4.2%). Some of the patients presented the disease with more than one symptom and one patient with breast cancer was asymptomatic at the time of presentation.

Figure 2 summarizes the BCVA in the involved eye at the time of clinical diagnosis. Of the total of 48 cases, 30 patients (63%) had unifocal and 18 patients (37%) had multifocal choroidal metastases. The median number of choroidal metastasis per eye was one and the mean was three and maximum number of choroidal lesions in an eye was 10.

The topographic distribution of metastatic choroidal tumors has been illustrated in figure 3. The anteroposterior location of the epicenter of the mass was posterior to the equator in 49 eyes (81.7%) (Figure 4).

The mean basal diameter of the largest metastatic focus was 8.5 mm and the mean thickness was 4.2 mm.

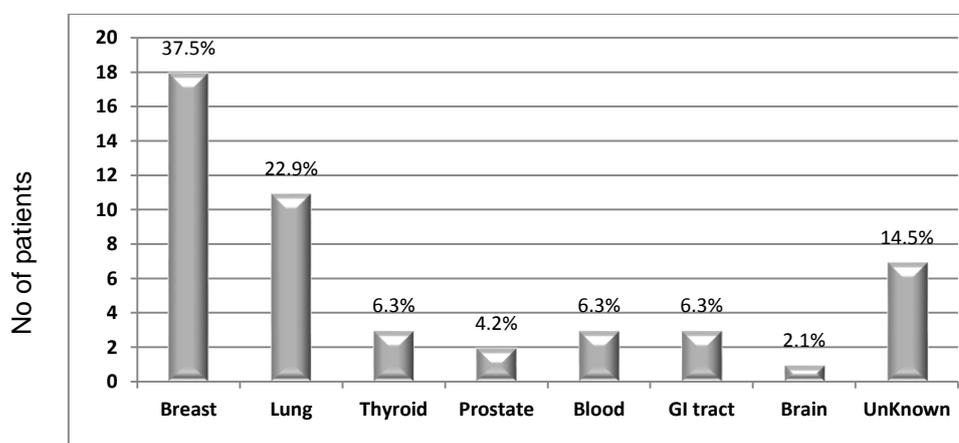


Figure 1. Location of primary cancer in 48 patients with choroidal metastasis

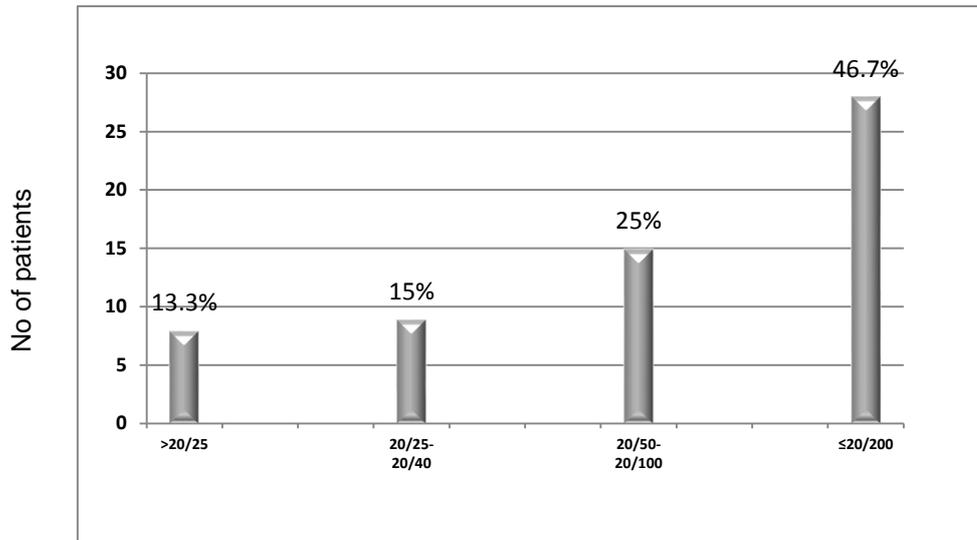


Figure 2. Visual acuity at the time of diagnosis of choroidal metastasis in 60 eyes

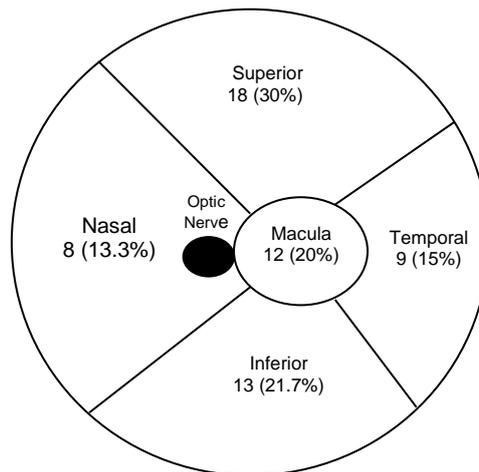


Figure 3. Radial distribution of largest choroidal metastasis in 60 eyes

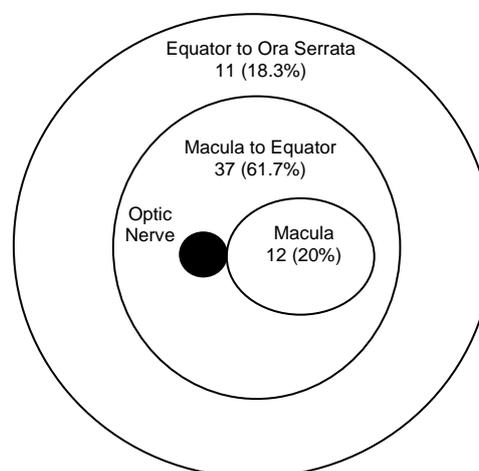


Figure 4. Antro-posterior distribution of largest choroidal metastasis in 60 eyes

Table 1. Choroidal metastases related to site of primary cancer in 60 eyes of 48 patients

	Prostate	Thyroid	Lung	Breast	GI	Unknown	LP	Brain
Eyes(n=60)								
OD (n=31)	1	1	7	13	2	4	2	1
OS (n=29)	1	2	7	9	2	4	3	1
Patient (n=48)	2	3	8	18	3	10	3	1
Age (years)	68.5	52.7	43.5	45.8	62.3	50.8	57	55
Sex								
Male(n=17)	2	0	3	0	2	7	2	1
Female(n=31)	0	3	5	18	1	3	1	0
Laterality								
Unilateral(n=36)	2	3	5	14	2	9	1	0
Bilateral(n=12)	0	0	3	4	1	1	2	1
Time Before Eye Problem								
Diagnosis(Months)	49.5	15	16.4	10.1	1.2	-	5	60
Type								
Single (n=32)	1	3	5	12	2	8	1	0
Multiple (n=16)	1	0	3	6	1	2	2	1
Referred From								
Ophthalmologist	1	1	4	10	1	8	-	1
Oncologist	-	-	1	1	-	-	-	-
Self	1	2	3	6	2	2	3	-
Symptoms								
None	-	-	-	1	-	-	-	-
Blurred vision	2	3	7	15	3	8	3	1
Flashes, Floaters	-	-	-	1	-	1	-	-
Pain	-	-	1	2	1	1	-	-
Visual field defect	-	1	1	1	-	-	-	-
*No. of metastasis	1.5	1	3.1	2.1	2.7	1.5	4.3	8
*Size of Choroidal metastasis(mm)								
*Base	13	5	10.6	8.4	12.2	9.5	6.3	3
*Thickness	5.5	2.2	3.6	2.5	3.8	3.4	2.7	1.5
Color								
Yellow to white	1	1	5	9	1	3	2	1
Brown/gray	-	-	-	1	-	1	-	-
Creamy	1	2	3	8	2	6	1	-
Subretinal fluid	-	1	5	16	4	7	1	1
Retinal Hemorrhage	-	-	1	-	-	1	-	-

GI: Gastrointestinal tract, LP: Lymphoproliferative, *: Mean

Table 2. Primary site for choroidal metastases in rank order by gender

Female	Male
Breast	Lung
Lung	Unknown
Thyroid	Gastrointestinal
Unknown	Prostate
Gastrointestinal	Lymphoproliferative

Discussion

Our study showed that in Iranian patients with choroidal metastasis the general clinical and ocular findings as well as the primary sites of metastasis were similar to that of other published reports in this regard. Several authors^{2,20} have indicated that the choroid as part of the uvea is the most common site for metastatic lesions to the eye. It is speculated that the high vascular content of the choroidal

tissue may be the cause of involvement of this layer by metastatic disease.^{4,17,21,22} Published data from various centers have pointed out that breast cancer in women and lung cancer in men are the most common primary cancers to metastasize to the uveal tract¹⁴⁻¹⁶ and this is consistent with our results.

Shield et al in an excellent survey of 520 eyes of 420 patients with uveal metastases¹⁷

showed that, similar to other studies,^{14-16,23} the choroid is the most common site of uveal involvement by metastatic disease, representing 88% of metastatic foci. They reported patients with uveal metastases who either evaluated with known cancer and known systemic metastatic disease or for a second opinion and further evaluation. They reported that at the time of ocular diagnosis 34% of cases had no history of cancer. The primary site of metastasis was not discovered in 17% of the patients in spite of the comprehensive systemic evaluation. In a similar result, we were unable to find the origin of choroidal metastasis in 14.5% (7/48) of our cases. In our study, the distribution of the unknown primary sites of the gender based cancer rate at the last visit was 29.4% (5/17) and in 6.4% (2/31) in male and female patients respectively which is comparable with that of in Shields' cases (29% and 12%). Interestingly in patients who suffered a choroidal metastasis with no history of cancer, the lung was the most common eventual primary cancer site. Metastasizing breast cancer accounts for 39% to 49% of all uveal metastases.²⁴ Our data showed that breast cancer was the underlying primary tumor in 37.5% of the cases. Similar to prior studies,¹⁷ bilateral involvement at presentation was evident in one quarter of our patients.

Stephens⁵ and Shields¹⁷ found that the blurred vision was the most common presenting symptom. From our results, except for six patients (12.5%) with normal visual acuity (VA), decreased VA was evident in the rest of the patients. Although it has been reported^{5,17} that ocular pain in patients with choroidal metastasis might be related to inflammation, elevated IOP, scleral invasion, or tumor necrosis, we could not find a definite cause in the five patients with ocular pain at the presentation time. One of the important characteristics of metastatic lesions is presence of multiple foci in the fundus. It has been recognized that approximately 20% of patients with uveal metastasis have multifocal involvement in one eye.²⁵ However the rate of multifocal presentation has been reported in as much as high as 54% in some reports.²⁶ Our result revealed that 18 patients (37%) had multiple foci of choroidal metastasis in one eye.

It is well known that choroidal metastasis usually appears as a creamy-yellow color mass at the posterior pole when viewed through the ophthalmoscope.^{17,27} Our data showed that 96% of choroidal metastases were judged to be yellow and/or creamy. Somehow pigmented choroidal metastases from breast and unknown primary sources were present in two cases. Brown-colored metastatic tumors are usually secondary to metastatic melanoma from both cutaneous and contralateral choroidal sources; however, very large tumors originating in the breast, lung, and gastrointestinal tract occasionally assumed a light brown color.²⁸ The presence of 81.7% of metastatic lesions posterior to the equator in our patients is compatible with the reported results by Freedman and Shields.^{17,29}

It has been recognized that breast and lung are the primary sites for most metastatic tumors to the choroid in females and males respectively.^{14-17,29} In our study the most common tumor source in female was breast whereas in the male patients, unknown primary tumor and lung cancer had similar prevalence. This may have been reflected due to small number of our cases or perhaps because of selection bias in excessive enrollment of patients with unknown primary source of metastasis. We are considering repeating those tests previously performed to assess the metastatic status of cases with undetermined sources of metastasis.

There are some limitations in our study. Since our department is one of the referral centers for ocular oncology services in the university, selection bias may be present in our study. Another limitation is the small number of patient population. In spite of these limitations, we believe that the results of our study from a practical standpoint reflect the conditions as seen by the general ophthalmologist or retina specialist.

Conclusion

We herein reported the first case series of choroidal metastasis in Iranian patients. We have described the presenting ocular features of these patients and showed that there is no significant difference in clinical presentations of our patients with those of other reports.

References

1. Perls M. Carcinose capillarembolie det choriodea. *Virchows Arch Pathol Anat* 1872;56:445-8.
2. Singh AD, Damato BE, Pe'er J, Murphree AL, Perry J. *Clinical ophthalmic oncology: SciELO Spain*; 2009.
3. Ryan SJ, Schachat AP, Wilkinson CP, Hinton DR, Saddy SVR, Wiedemann P. *Retina*. St. Louis, Mosby;2006;812-8.
4. Ferry AP, Font RL. Carcinoma metastatic to the eye and orbit: I. A clinicopathologic study of 227 cases. *Arch Ophthalmol* 1974;92(4):276-86.
5. Stephens RF, Shields JA. Diagnosis and management of cancer metastatic to the uvea: a study of 70 cases. *Ophthalmology* 1979;86(7):1336-49.
6. Asteriou C, Konstantinou D, Kleontas A, Paliouras D, Samanidis G, Papadopoulou F, et al. Blurred vision due to choroidal metastasis as the first manifestation of lung cancer: a case report. *World J Surg Oncol* 2010;8:2.
7. Melo DH, Pierre Filho Pde T, Gomes PR, Holanda AG, Amadei LP. [Choroidal metastasis of gastric adenocarcinoma as a first sign of systemic disease recurrence: case report]. *Arq Bras Oftalmol* 2010;73(5):467-8.
8. Elliott D, Salehi-Had H, Plous OZ. Adenocarcinoma of the esophagus presenting as choroidal metastasis. *Dis Esophagus* 2011;24(2):E16-8.
9. John SS, Horo S, Braganza AD, Kuriakose T. Bilateral choroidal metastasis from carcinoma of the submandibular gland. *Indian J Ophthalmol* 2008;56(1):75-6.
10. John VJ, Jacobson MS, Grossniklaus HE. Bilateral choroidal metastasis as the presenting sign of small cell lung carcinoma. *J Thorac Oncol* 2010;5(8):1289.
11. Nelson CC, Hertzberg BS, Klintworth GK. A histopathologic study of 716 unselected eyes in patients with cancer at the time of death. *Am J Ophthalmology* 1983;95(6):788-93.
12. Albert DM, Rubenstein RA, Scheie HG. Tumor metastasis to the eye: I. Incidence in 213 adult patients with generalized malignancy. *Am J Ophthalmol* 1967;63(4):723-6.
13. Wiegel T, Kreusel KM, Bornfeld N, Bottke D, Stange M, Foerster MH, et al. Frequency of asymptomatic choroidal metastasis in patients with disseminated breast cancer: results of a prospective screening programme. *Br J Ophthalmol* 1998;82(10):1159-61.
14. Shields JA. Metastatic tumors to the uvea. *Int Ophthalmol Clin* 1993;33(3):155-61.
15. De Potter P. Ocular manifestations of cancer. *Curr Opin Ophthalmol* 1998;9(6):100-4.
16. Kaushik S, Arya SK. Choroidal metastasis from an occult primary. *J Postgrad Med* 2003;49(3):268-71.
17. Shields CL, Shields JA, Gross NE, Schwartz GP, Lally SE. Survey of 520 eyes with uveal metastases. *Ophthalmology* 1997;104(8):1265-76.
18. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev* 2010;19(8):1893-907.
19. Lee J, Lee S, Sohn J, Yoon YH. Clinical features of uveal metastases in Korean patients. *Retina* 2003;23(4):491-4.
20. Wharam J, Schachat AP. Choroidal metastasis. In: Ryan SJ (ed). *Retina*. St. Louis, Mosby;2006;812-8.
21. Bloch RS, Gartner S. The incidence of ocular metastatic carcinoma. *Arch Ophthalmol* 1971;85(6):673-5.
22. Jensen OA. Metastatic tumours of the eye and orbit. A histopathological analysis of a Danish series. *Acta Pathol Microbiol Scand Suppl* 1970;212:Suppl 212:201+.
23. Camarillo C, Sanchez Ronco I, Encinas JL. [Choroidal metastases]. *Anales Sis San Navarra [online]*. 2008;31(Suppl 3):127-34.
24. Demirci H, Shields CL, Chao AN, Shields JA. Uveal metastasis from breast cancer in 264 patients. *Am J Ophthalmol* 2003;136(2):264-71.
25. Munteanu M, Giuri S, Rosca C, Boruga O, Cretu O. Multifocal choroidal metastases from thyroid carcinoma: a case report. *Chirurgia (Bucur)* 2013;108(2):268-72.
26. Soysal HG. Metastatic tumors of the uvea in 38 eyes. *Can J Ophthalmol* 2007;42(6):832-5.
27. Shields JA, Shields CL. *Intraocular tumors: a text and atlas*: Philadelphia: WB Saunders; 1992.
28. De Potter P, Shields JA, Shields CL, Yannuzzi LA, Fisher YE, Rao VM. Unusual MRI findings in metastatic carcinoma to the choroid and optic nerve: a case report. *Int Ophthalmol* 1992;16(1):39-44.
29. Freedman MI, Folk JC. Metastatic tumors to the eye and orbit: patient survival and clinical characteristics. *Arch Ophthalmol* 1987;105(9):1215-9.