

Study of Ocular Manifestations in Systemic Malignancies

Khochikar Nilima M.¹, Karambelkar VH²

¹Resident, Department of Ophthalmology, Krishna Institute of Medical Sciences Deemed To Be University, Karad, Maharashtra, India; ²Professor & Head of the Department, Department of Ophthalmology, Krishna Institute of Medical Sciences Deemed to be University, Karad-415110, Maharashtra, India.

ABSTRACT

Introduction: Primary ophthalmic tumours are well known, but the eye is a rare site for disseminated malignancy. The eye and orbit can get affected by cancer due to the direct effect of metastatic neoplastic infiltration or compression or by circulating antibodies involving paraneoplastic retinal degeneration.

Aim: The present study aims to objectify the ocular manifestations in systemic malignancies.

Methodology: This cross-sectional study was conducted on patients presenting with systemic malignancies to the out-patient department of Krishna Hospital Karad, Maharashtra, from December 2018 to May 2020.

Result: Ophthalmic manifestations were seen in 21.77% of patients with systemic malignancies.

Conclusion: All patients with systemic malignancies (primary and metastatic) should undergo a thorough ophthalmic examination regularly to prevent visual loss.

Key Words: Ocular manifestations, Systemic malignancies, Metastatic, Visual loss, Ophthalmic, Antibodies

INTRODUCTION

Primary ophthalmic tumours are well known, but the eye is a rare site for disseminated malignancy. The eye and orbit can get affected by cancer due to the direct effect of metastatic neoplastic infiltration or compression or by circulating antibodies involving paraneoplastic retinal degeneration. Hematogenous and direct spread also do account for the ocular manifestations of systemic malignancies.¹

Metastatic tumour to the uvea is the most common form of presentation. The choroid is the most common site for uveal metastasis. Iris and ciliary body metastases are present in 10% of cases. Retina, optic disc, vitreous, and conjunctiva are affected when there is already uveal tract involvement. Choroidal metastases are associated with an unusually large amount of subretinal fluid presenting as complete retinal detachment and or a mass on ocular ultrasound.¹ In cases of space-occupying lesions, papilledema, abducent nerve palsy, nystagmus and optic atrophy are the most common presenting signs.²

Breast and lung carcinomas for women and lung and gastrointestinal (GI) carcinomas for men most commonly metastasize to the eye and orbit. The incidence of metastasis to the eye from breast cancer is around 47%, from lung cancer is around 21%, and that from the GI tract is around 4%. Melanoma, urological malignancies also manifest with ocular metastasis. Most patients presenting with ocular metastases already have a history of treated primary cancer. However, approximately 1/3rd of patients has no history of primary cancer viz. primary adenocarcinoma of the lung, which can present for the first time with ocular metastases in up to 50% of cases.^{1,3,4} Metastasis to the eye and orbit and paraneoplastic disorders represent a very bad prognostic sign. The average survival following a diagnosis of uveal metastases is 7 months.³

As the incidence of malignancy is on the rise in India, it is important to study the ocular manifestation of these nonocular malignancies especially when there is sparse literature on this. The majority of the studies conducted in the past were autopsy studies. Early and prompt diagnosis with appropriate investigations and apt treatment can restore the

Corresponding Author: Karambelkar VH, Professor & Head of the Department, Department of Ophthalmology, Krishna Institute of Medical Sciences Deemed to be University, Karad-415110, Maharashtra, India. ISSN: 2231-2196 (Print) ISSN: 0975-5241 (Online) Received: 05.02.2021 Revised: 08.04.2021 Accepted: 12.05.2021 Published: 11.10.2021

vision and improve the quality of life in these unfortunate patients. Therefore, this research was conducted to study the occurrence and clinical features of ocular manifestations in systemic malignancies.

METHODOLOGY:

This cross-sectional study was conducted on patients presenting with systemic malignancies to the out-patient department of Krishna Hospital Karad, Maharashtra, from December 2018 to May 2020. According to a study "ocular-metastases",⁵ the proportion of ocular manifestations in systemic malignancies is 10%. Therefore, by using formula – N=4PQ/L,² where P=10%, Q= 100-P (90%), L=4%, at 95% confidence interval, the sample size comes up to 225. Patients with primary ophthalmic tumours and malignancies arising from radiation were excluded. Data entry was done in Microsoft excel 2019 and imported to SPSS version 21.0 for data analysis. The p-values were considered statistically significant if and when p > 0.05. The ethical clearance has been given and by protocol number 0236/2018-2019).

RESULTS

This cross-sectional study including 225 participants with systemic malignancies yielded the following results.

Baseline characteristics: The mean age of patients in the study population was 52.32 ± 20.26 years. The majority of 113 (50.2%) patients were in the age group of 51-75 years. Ophthalmic manifestations were seen in 49 patients (21.77%) of which, 31(63%) were males and 18(37%) were females.



Figure 1: Primary malignancies in which ophthalmic manifestations were seen.

The primary malignancies in which ophthalmic manifestations were seen are depicted in Figure 1. The most common primary malignancy was Head and Neck malignancy (28.57%), followed by breast (24.48%), genitourinary tract (20.40%), hematopoietic (10.20%), lung (8.16%), bone (4.08%), skin and endometrium (2.04%). Table 1 shows the list of ophthalmic manifestations in the patients.

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Primary Malignancy	Ophthalmic manifestations	Number	Percentage	Age (Mean± SD) in Years
Carcinoma Breast (n=12)	Choroidal Mets	3	6.12	72 ± 8.60
	LR Palsy	2	4.08	62.5 ± 6.09
	Ptosis	2	4.08	53 ± 3
	Proptosis	4	8.16	74.75 ± 4.60
	CAR in both eyes	1	2.04	56 ± 0.0
Carcinoma of Lung (n=4)	Ptosis	1	2.04	76 ± 0.0
	LR Palsy	2	4.08	70.5 ± 7.5
	CAR	1	2.04	77 ± 0.0
Haemopoietic Malignancy	Sub-hyaloid Hemorrhage	5	10.2	10.17 ± 22.47
Genito-urinary malignancy (n	=11)			
Ca. Urinary Bladder	Choroidal Mets	2	4.1	17±0.0
Ca. Prostate	Proptosis	5	10.20	70 ± 5.18
	LR Palsy	1	2.04	69 ± 0.0
	Ptosis	1	2.04	72 ± 0.0
RCC	Choroidal Mets	1	2.04	67 ± 0.0
Wilm's Tumour	Subconjunctival Hemorrhage	1	2.04	9 ± 0.0
Bone Cancer (n=2)				
Ca. Osteogenic Sarcoma	Sub-hyaloid Hemorrhage	1	2.04	28 ± 0.0
Ca. Mandibular Sarcoma	Sub hyaloid Hemorrhage	1	2.04	26 ± 0.0

Table 1: Primary malignancies and ophthalmic manifestations in patients (N=49)

Primary Malignancy	Ophthalmic manifestations	Number	Percentage	Age (Mean± SD) in Years		
Pleomorphic adenoma of lacri- mal gland	Exposure keratopathy, ptosis, left sided temporal pallor of disc	1	2.04	25±0.0		
Head and Neck Malignancies (n=14)						
Ca. Larynx	LR Palsy	3	6.1	74.67 ± 15.20		
	Ptosis	2	4.1	60 ± 0.0		
Ca. Maxilla	Proptosis	4	8.2	56 ± 23.61		
Ca. Ethmoid	Proptosis	1	2.04	47 ± 0.0		
Temporal Lobe Glioblastoma	LR Palsy	1	2.04	38 ± 0.0		
Astrocytoma Left Temporal Lobe	Papilledema	1	2.04	41 ± 0.0		
Left Parietal lobe astrocytoma	Papilledema	1	2.04	33 ± 0.0		
Left Temporal lobe astrocytoma	Optic atrophy	1	2.04	55±0.0		

Table 1: (Continued)

The different primary malignancies have different tissues of preference in the eye. The details are depicted in Table 2. More cases in the intraocular group 28 (57.14%) as com-

pared to adnexa group 21(42.86%) respectively. There was no significant difference among any of the study variables (malignancies) with ocular manifestation (p>0.05).

Table 2: Different malignancies and tissue of preference

Malignancy	Intraocular Manifestation		Manifestati	p-value	
	Number	Percentage	Number	Percentage	
CA. Breast (n=12)	6	12.24	6	12.24	0.48
CA. Lung (n=4)	3	6.12	1	2.04	0.57
Haemopoietic Malignancy (n=5)	5	10.20	0	0.00	0.10
Bone Cancer (n=2)	2	4.08	0	0.00	0.46
Ocular Adnexa (n=1)	0	0.00	1	2.04	-
Genito-Urinary Tract (n=11)	5	10.20	6	12.24	0.23
Head and Neck Cancer (n=14)	7	14.29	7	14.29	0.32
Total	28	57.14	21	42.86	

Various malignancies affect different structures in the eye. Ca. the breast had ocular manifestation in the posterior segment (8.16%), adnexa (8.16%) and CNS manifestation (8.16%), but no manifestation in the anterior segment. Ca. Lung had ocular manifestation in the posterior segment (2.04%) and CNS manifestation (6.12%), but no manifestations in the anterior segment and adnexa. Haemopoietic malignancies (10.20%) and Bone cancers (2.04%) had ocular manifestation only in the posterior segment. The genitourinary tract had ocular manifestations in the anterior segment (6.12%), adnexa (10.20%) and CNS manifestations (4.08%). Head neck cancers manifested in the adnexa (10.20%) and had CNS manifestations (18.37).

DISCUSSION

This observational study was conducted on 225 patients. Ocular manifestations were seen in 49 (21.77%) patients. The mean age of these patients was 54.2 ± 22.39 years, of which 61% were males and 39% were females. Ocular metastasis is often detected late because the patients may not have any visual symptoms or the systemic symptoms may be too severe.⁵ Even in our study the majority of our patients, i.e., 41% presented within 6 months to two years of being diagnosed with malignancy. Around 37% presented later than two years. **Shah et al.**, in their study of 187 patients with uveal metastasis from lung cancer reported that the mean age at presentation was 62 years. The mean interval between the diagnoses of lung cancer and uveal metastases was around 2.5 years.⁶

In our study, most of the ocular metastasis was from head and neck malignancy (28.57%), followed by breast (24.48%), genitourinary tract (20.40%), hematopoietic (10.20%), lung (8.16%), bone (4.08%), skin and endometrium (2.04%).

Among the head and neck cancers like Ca larynx presented with LR palsy (6.1%) and ptosis (4.1%), Ca Maxilla presented with proptosis (8.2%), Ca Ethmoid also presented with proptosis (2.04%), Temporal Lobe Glioblastoma presented with LR Palsy (2.04%), astrocytoma of the temporal lobe (R) and left parietal lobe astrocytoma presented with Papilledema (2.04% each), and left temporal lobe astrocytoma presented with optic atrophy (2.04%). Similar to our study, Yan and Gao in their retrospective study of 35 males and 11 females with a mean age of 47 years, also reported head and neck cancers (nasopharyngeal carcinoma, 30.34%) as the most common malignancy with ocular manifestations. Other head and neck cancers were medullary thyroid carcinoma (2.17%) and lacrimal gland carcinoma (2.17%). The most common ocular presentations were abnormal eye position (65.22%), followed by proptosis (63.04%), increased orbital pressure (54.35%), diplopia (54.35%), and decreased ocular motility (52.17%).7

The incidence of ocular metastasis with primary breast cancer ranges between 5 and 30%.^{8,9} In our study it was 24.48%. The most common ocular manifestation in breast carcinoma was proptosis, followed by choroidal METS, Lateral rectus palsy, ptosis, and retinopathy. Kreusel et al. reported intraocular metastasis in 4.6% of patients with breast cancer with the choroid being the most common site.9 Supriya and Lokesh reported a case of Exudative Retinal Detachment in a 38-year-old female with adenocarcinoma of the breast. It was characterized by the collection of sub-retinal fluid with no retinal breaks or traction. ¹⁰ Madanagopalan et al. reported a rare case of CRVO in a case of breast carcinoma where the retina showed extensive haemorrhages and dilated retinal veins. ¹¹ Francone et al. ¹² and Maliepaard et al. ¹³ reported cases where ocular metastases were the primary presentation of breast cancer.

The incidence of ocular metastasis with primary lung cancer is reported to be 0.2% to 7%.^{6,14} In our study it was 8.16%. Similar to our study, **Yan and Gao** reported an incidence of that 8.6%.⁷ In a review of 950 uveal metastases by **Shields** et al. the incidence of ocular metastasis with primary in the lung was reported in 21% cases.¹⁵ The most common ocular manifestations seen in our study were LR Palsy, Ptosis, and Carcinoma Associated with Retinopathy (CAR). They are more common in men. Contradictory to our study, **Shah** et al. reported that choroid was the commonest involvement (88%), followed by iris (10%) and ciliary body (2%).⁶ Hoang et al. and Hernández-Da Mota et al. reported ocular metastasis as first presentation in older male patients due to metastatic lung adenocarcinoma.^{16,17} Many case studies are reported where the first clinical presentation was ocular in case of primary in lung. ^{18,19}

Ocular manifestations in haematological malignancies are well documented now. In our study, sub-hyaloid haemorrhage (10.2%) was the only ocular manifestation that was seen in such malignancies. Similar to our findings, Koshy et al. reported a prevalence of 10.4% for sub hyaloid haemorrhages in patients of acute/chronic leukaemia.²⁰

Carcinoma of the Genito-urinary tract can also present with ocular metastasis. In our study, Ca Prostate presented with proptosis (10.20%), LR Palsy and ptosis (2.04% each), Ca Urinary Bladder presented with Choroidal Mets (4.1%), and RCC presented with Choroidal Mets (2.04%) too. Uluocak et al. reported a metastatic orbital cancer secondary to prostatic adenocarcinoma in a 73-year-old man presenting with a history of ipsilateral visual loss and one-sided proptosis, periorbital swelling, and pain. ²¹ Lefresne et al. also reported an 81-year-old man with poorly differentiated carcinoma prostate who presented with pain, proptosis, and blindness.²² Pompeu et al. reported two cases where one patient presented with a mass in the eye and another with an ulcerated lesion on the inferior tarsal conjunctiva both of whom had primary RCC. ²³ Hart et al. reported a 70-year-old man with persistent lateral rectus mass and orbital haemorrhage after retrobulbar anaesthesia. On biopsy, the lesion was found to be metastatic RCC. ²⁴ Patil et al. reported a case of a 43-year-old male with sudden onset of binocular diplopia on lateral gazes. The patient showed features of ipsilateral one-and-a-half syndrome and investigations further revealed primary RCC. 25 Mitsui et al. reported a case of a 43-year-old bladder cancer patient, 17 months post radical cystectomy with a choroidal disorder and multiple nodules in the abdomen and head. On biopsy, it was revealed as a metastasis from the bladder cancer. ²⁶ In another case report by Wiltshire et al. an 88-year-old man presented with acute loss of vision due to choroidal metastasis. A diagnosis of primary urothelial carcinoma of the bladder was later made.27 Therefore, it is necessary that in an older male with visual and urinary symptoms, the genitourinary system should be evaluated as a potential primary site.

In our study, a case of Osteogenic Sarcoma and Mandibular Sarcoma presented with Sub hyaloid Hemorrhage (2.04% each). Very few case reports are published in this area. Agarwal A. reported a case of orbital metastasis presenting as proptosis in osteosarcoma.²⁸ Rajabi et al. reported a case of a 55-year-old male known case of scapular bone osteosarcoma presenting with pain, decreased vision, proptosis, conjunctival injection, and chemosis.²⁹

Other systemic malignancies that can present as ocular metastasis are the Gastrointestinal tract³⁰ and skin. ³¹ In our study a patient presented with ocular symptoms like ptosis, exposure keratopathy, and optic atrophy whose primary was squamous cell Carcinoma of the lid. We found no ocular manifestation in Gastrointestinal malignancies.

CONCLUSION

Ophthalmic manifestations were seen in 21.77% of patients with systemic malignancies. So, to conclude, the authors believe that all patients with systemic malignancies (primary and metastatic) should undergo a thorough ophthalmic examination regularly in a time framed manner to diagnose asymptomatic patients with ocular involvement at the earliest and prevent visual loss.

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