Frequency of ocular metastases in patients dying of cancer in eye bank populations

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Abstract

Aims—To examine the frequency of intraocular metastases in patients who had died of cancer, in an eye bank and necropsy population sample.

Methods—The first group included 302 cancer cases received from the Wisconsin Eye Bank between 1988 and 1993. In the second group, ocular pathology records at the Wilmer Institute from 1976 to 1980 were analysed for ocular metastases in necropsy subjects dying of cancer. Non-ocular cancer was the cause of death in 741 cases; among these, 510 were attributed to carcinomas.

Results—In the Wisconsin Eye Bank group, three cases (1%) had gross metastases. Out of 255 carcinoma cases, one (0.4%) had gross metastases. In the Wilmer Institute group, gross metastases were observed in 35 (4.7%) cases. Of the 510 patients dying of carcinomas, six (1.2%) had macroscopic metastases. Ocular metastases were detected histopathologically in 93 of 741 (12.6%) of cases.

Conclusion—Even though it is difficult to assess the true frequency of ocular metastases in patients dying of cancer, the answer to this question was attempted by determining the frequency of ocular metastasis in patients who died of cancer and who donated their eyes to the Wisconsin Eye Bank or had postmortem examination at the Johns Hopkins Hospital. Microscopic metastases were found in 12.6% of cases. The frequency of gross metastases has decreased over the past 12 years from 4.7% to 1% (p value=0.005) owing to improved treatment of leukaemia; however, the frequency of macroscopic metastases due to carcinomas has not changed (p value=0.38).

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Horner in 1864¹ and Perl in 1872² were the first to describe metastatic disease in the eye. Since that time, reports of ocular metastases have steadily accumulated.^{3,4} In a clinical study in 1944, Godtfredson⁵ reported that, of 8712 patients with metastatic cancers referred for radiation therapy, six (0.07%) had ocular involvement. In 1967, Albert *et al*⁶ found, by ophthalmoscopic examination, intraocular metastases in five of 213 (2.3%) patients with known metastatic carcinoma.

The rate of ocular metastasis is even higher in postmortem studies since occult microscopic disease can be detected. In a postmortem study

involving 230 patients, Bloch and Gartner⁷ found 23 cases (10%) to have metastases to the globe. In a prospective histopathological study of eyes from 716 subjects who had malignant neoplasms at the time of death, Nelson *et al*³ found ocular metastases in 52 (7.3%). They also observed that of 376 patients, dying of all types of carcinoma, 15 (4.0%) had ocular metastases. Of 512 patients with uveal metastases in the files of the Wills Eye Hospital, Shields *et al*⁸ found that the iris was also involved in 40 (7.8%).

As patients with metastatic malignancies live longer, ocular metastases will be detected more frequently.⁴ Although the prognosis of patients with ocular metastases is poor, if such lesions are detected early enough, they can be treated effectively with radiation therapy to improve vision and help maintain the quality of the patient's life.^{9,10}

Intraocular metastases are the most common malignancy of the eye.^{7,11,12} We examined two groups of postmortem eyes (one by the dissecting microscope and the other histopathologically) to obtain information regarding the frequency of intraocular metastases in patients who have died of cancer.

Materials and methods

The study consisted of two groups. The first group included eyes donated to the Wisconsin Eye Bank. A total of 11 553 pairs of eyes were donated to the Wisconsin Eye Bank between 1988 and 1993. The eye bank accepts all eyes except those from donors who have rabies, hepatitis, encephalitis, HIV, septicaemia, and

Table 1 Frequency of gross ocular metastases in patients dying of cancer from Wisconsin Eye Bank

Primary malignancy	Number of patients examined	Number of ocular metastases
Leukaemia	25	1
Lymphoma	10	0
Multiple myeloma	8	1
Sarcoma	4	0
Bladder	8	0
Brain	6	0
Breast	14	0
Cervical	1	0
Colorectal	23	0
Cutaneous melanoma	2	0
Oesophagus	2	0
Gall bladder	1	0
Gastric	3	0
Head and neck	3	0
Hepatic	5	0
Lung	81	0
Ovary	10	0
Pancreas	12	1
Prostate	28	0
Renal	3	0
Squamous cell	1	0
Unknown primary	4	0
Unspecified cancer	48	0
Total	302	3
Total carcinoma	255	1

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Figure 1 The left eye of a patient with gross metastasis to the choroid. The primary site was prostate ($\times 1.25$).

Jacob-Creutzfeldt disease. The donated eyes of patients who die of leukaemia and lymphomas are not used for corneal transplantation. However, donated eyes of patients who die of other cancers may be used for corneal transplantation, if the patient is younger than 65 and there is no evidence of gross ocular metastasis. Of the total number of eyes received, 1476 were not used for transplant and were submitted to the eye pathology laboratory; 302 of these subjects had died of non-ocular cancers. Formalin fixed eyes were dissected in the horizontal meridian and examined under the dissecting microscope. When evidence of metastasis was found, the eye was processed for light microscopy by standard methods.³ Histological sections were stained with haematoxylin and eosin and examined by light microscopy.

In the second group, ocular pathology records at the Wilmer Eye Institute from 1976 to 1980 were analysed for cancer as the cause of death and for intraocular metastases. A total of 741 subjects died of cancer and their eyes were obtained at necropsy performed at the Johns Hopkins Hospital or from the Maryland Eye Bank. Eyes were examined by transillumination, macroscopically, and microscopically at the Wilmer Institute.

Table 2 Frequency of gross ocular metastases in patients dying of cancer from Johns Hopkins Hospital

Primary malignancy	Number of patients examined	Number with ocular metastases (%)
Leukaemia	115	16 (13.0)
Lymphoma	60	4 (6.7)
Multiple myeloma	31	7 (22.6)
Sarcoma	25	1 (4.0)
Carcinoma	510	7 (1.4)
Lung	147	4 (2.7)
Breast	36	0
Oropharynx	21	1 (4.8)
Ovarian	16	1 (6.3)
Pancreas	28	1 (3.6)
Other	262	0
Total	741	35 (4.7)

Results

The results from the Wisconsin Eye Bank group are summarised in Table 1. Of 302 subjects three (1.0%) had gross abnormalities and intraocular metastases were proved by histological sections. The causes of death were chronic leukaemia, multiple myeloma, or pancreatic carcinoma (Fig 1).

In the group from the Wilmer Institute, a total of 741 cases were found in which cancer was the cause of death. Of these, macroscopic metastases were observed in 35 (4.7%) cases (Table 2). Gross metastasis was found in seven of 510 (1.4%) patients dying of carcinoma; 15 of 115 (13.0%) subjects with leukaemia, and four of 60 (6.7%) with lymphoma.

Microscopic metastasis was observed in 93 (12.6%) of the 741 subjects. Ocular involvement was observed in 40 of 115 (34.8%) patients dying with various types of leukaemia and in 14 of 60 (23.3%) patients with lymphoma. The frequency of ocular involvement with various types of sarcoma as the primary tumour was four of 25 (16%) (Table 3).

In 510 subjects dying of carcinoma, 25 (5.1%) had microscopic metastases. Nine of 147 (6.1%) and three of 36 (8.3%) subjects with lung and breast carcinoma, respectively, had ocular involvement (Figs 2 and 3). No ocular metastases were described in cases of colorectal cancer (Table 4).

Discussion

In the present study, microscopic metastasis was found in 93 of 741 (12.6%) of patients dying of all cancers. In a postmortem examination of 230 patients who died of systemic carcinoma, Block and Gartner⁷ reported 23 cases (10%) with metastases to the globe. In another postmortem histopathological study from 1973 to 1982, Nelson and coworkers³ performed ocular examinations on at least one eye from each body with a malignant neoplasm and undergoing necropsy at Duke University Medical Center. They found that 52 of 716 (7.3%) subjects had intraocular metastases. Additionally, Ferry and Font¹¹ reported that out of 227 carcinoma cases metastatic to the eye or orbit in the Registry of Ophthalmic Pathology at the Armed Forces Institute of Pathology, 196 were metastatic to the globe (Table 5).

In the present study, ocular metastases were present in 25 of 510 (5.1%) patients dying of carcinoma. Additionally, ocular metastases were found in nine of 147 (6.1%) patients dying of lung cancer and three of 36 (8.3%) patients dying of breast cancer. Bloch and

Table 3 Frequency of ocular metastasis in patients dying of cancer by histopathological study from the Johns Hopkins Hospital

Cancer	Number of patients examined	Number with ocular metastasis (%)
Leukaemia	115	40 (34.8)
Lymphoma	60	14 (23.3)
Multiple myeloma	31	9 (29.0)
Sarcoma	25	4 (16.0)
Carcinoma	510	26 (5.1)
Total	741	93 (12.6)

Figure 2 Histological section of the right eye showing a prominent focus of metastatic carcinoma involving the choroid (haematoxylin and eosin X2.25).

Gartner⁷ found ocular metastases in 23 of 230 (10%) patients dying of carcinomas. Ocular metastases were observed in three of 53 (5.7%) lung cancer patients and 19 of 52 (36.5%) breast cancer patients. Nelson and coworkers³ detected ocular metastases in 15 of 376 (4.0%) patients dying of carcinomas. In their study, ocular metastases were present in six of 89 (6.7%) patients with lung carcinoma and 81 of 196 (41.3%) patients with breast carcinoma. In the study by Ferry and Font¹¹ 62 of 196 (31.6%) metastases to the eye were due to lung cancer and 81 of 196 (41.3%) were due to breast cancer.

In the Wilmer group, the frequency of gross ocular metastases in patients dying of carcinomas was 1.1% compared with 0.4% in the Wisconsin group. No statistical difference was detected between these two values (p=0.38). In the Wilmer group, gross metastases were seen in nine of 147 lung

Figure 3 Histological section of the right eye showing a prominent focus of metastatic carcinoma involving the choroid (haematoxylin and eosin X30).

Table 4 Frequency of ocular metastases in patients dying of carcinomas by histopathological study from the Wilmer Institute

Primary tumour	Number of patients examined	Number with ocular metastases (%)
Lung	147	9 (6.1)
Colorectal	43	0
Breast	36	3 (8.3)
Prostate	24	1 (4.2)
Urinary tract	16	0
Uterus	20	1 (5.0)
Oral cavity, pharynx	20	1 (5.0)
Skin	14	2 (14.3)
Pancreas	28	1 (3.6)
Ovary	16	1 (6.3)
Neuroblastoma	2	1 (50)
Granulosa cell tumour	1	1 (100)
Liver, biliary passages	13	1 (7.7)
Unknown primary	3	1 (33.3)
Gastrointestinal	5	1 (20.0)
Adenocarcinoma	11	1 (9.1)
Other sites*	111	0
Total carcinomas	510	25 (5.1)

*Includes oesophageal, brain, hepatocellular, gastric, not specified, thyroid, adrenal, testicular.

cancer cases; and in the Wisconsin study, no macroscopic metastases were seen in 81 lung cancer cases. There was no statistical difference between these two values (p=0.31). In short, the frequency of ocular metastases in patients dying of carcinomas overall and lung cancer in particular have not changed in the past 12 years.

The overall frequency of gross intraocular metastasis in the present series has decreased from 4.7% to 1% over the past 12 years (p=0.005). However, the frequency of metastases in eyes from patients with carcinomas has not changed with time (p=0.38). This decrease may be attributable to improvements in the treatment of lymphoproliferative malignancies.

The American Cancer Society provides estimates of the frequency of new cancer cases and cancer deaths in the United States annually.¹³ Extrapolating from these figures and from our data, a conservative estimate of the number of ocular metastases among fatal cases of cancer in the United States can be made (Table 6). In 1993, there were 526 000 cancer deaths, 149 000 from lung cancer and 43 600 from breast carcinoma. Based on our data, 66 000 cancer patients will have ocular metastases and among these, approximately 9100 with fatal lung carcinoma and nearly 4000 with fatal breast carcinoma.

Our results support previous data on frequency of ocular metastases.^{3 7} As cancer therapy improves, patients with metastatic cancer are surviving longer.⁴ Thus, one might expect to see more patients with ocular metastases. Additionally, 12–46% of patients with metastatic tumours present initially with ocular metastases and no other findings.^{11 14} Timely detection of ocular metastases in patients with

Table 5 Comparison of the frequency of ocular metastases

Study	Number of cases	Frequency of ocular metastases (%)
Bloch and Gartner ⁷	230	10.0
Nelson <i>et al</i> ³	562	9.3
Present study	741	12.6

Table 6 An estimate of ocular metastases in the United States in 1993

Site of primary malignancy	Estimated cancer deaths in 1993 ¹⁴	Percentage with ocular metastases	Estimated number of patients with ocular metastases
Lung	149 000	6.1	9089
Breast	46 300	8.3	3843
Prostate	35 000	4.2	1470
Oral	7700	4.8	370
Skin	6800	14.3	972
Pancreas	25 000	3.6	900
Ovary	13 300	6.3	838
Cervical	4400	8.3	365
Multiple myeloma	9400	29.0	2632
Leukaemia	18 600	34.2	6361
Lymphoma	22 000	22.2	4884
Total	526 000	12.6	66 272

cancer is important because radiation therapy may improve vision and the quality of life in the remaining time the patients are alive.

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