EXTENDED REPORT

Decreased prevalence of asymptomatic choroidal metastasis in disseminated breast and lung cancer: argument against screening

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Aim: To determine the frequency of visually asymptomatic choroidal metastases in patients with disseminated breast and lung carcinomas in order to establish optimal patient management policies.

Methods: All patients with confirmed metastatic disease treated in our institution between January 2002 and December 2003 were invited to undergo a funduscopy examination and a B-scan ultrasound evaluation.

Results: Of the 169 study participants, 77 had breast cancer (64 with metastases in one organ and 13 with multiple-organ involvement) and 92 had lung cancer (85 with metastases in one organ and 7 with multiple-organ involvement). No patient with metastatic breast cancer and two patients with metastatic lung disease (each with multiple-organ involvement) were found to have choroidal metastases. The choroidal metastases were detected by both the funduscopy and ultrasound examinations.

Conclusions: The 2.17% incidence of choroidal metastasis in disseminated lung cancer and the 0% incidence in disseminated breast cancer speaks against the practicality of screening for early detection of choroidal metastasis among these patients, even though it would lead to early implementation of appropriate, often vision saving, therapeutic management. Its low incidence probably testifies to progress achieved by enhanced systemic oncological treatment policies that have been introduced into routine patient management over the past few years.

Breast and lung carcinomas are the most common primary sites for choroidal metastases.¹ The incidence of choroidal metastasis from metastatic breast cancer was 0–9.7% in clinical trials^{2–5} and up to 30% in histopathological trials.⁶ The incidence of choroidal metastases from metastatic lung cancer was reported to be 2–6.7% in clinical trials.^{2–7} The need for screening for asymptomatic choroidal metastasis among patients with disseminated disease continues to be a matter of controversy.⁸ Although a metastasis causes considerable visual disability and presents a very difficult therapeutic challenge, the cost of conducting numerous examinations on unaffected individuals is obviously high. As such, there must be compelling evidence of clinical benefits for operating an early detection programme in asymptomatic patients. We designed this study to determine the frequency of choroidal metastases in patients seen in our medical centre, who had disseminated breast and lung cancer, in order to determine whether such a clinical screening programme was justified. Our goal was to identify a subgroup of patients with early choroidal involvement who would profit from early implementation of appropriate changes in treatment.

METHODS

The local institutional review board approved the study. The participants were consenting patients with proved disseminated lung or breast cancer to at least one site. Between January 2002 and December 2003, 169 unselected patients were screened for choroidal metastases in the Department of Ophthalmology, Tel Aviv Sourasky Medical Center, a large urban university-affiliated tertiary care institution in Tel Aviv, Israel. Patients were referred for screening by their treating doctors in the institution's departments of oncology and internal medicine, as well as by doctors in various internal medicine departments in which the inpatients were hospitalised. None of these patients had any ocular symptomatology:

study recruits with symptomatic visual disturbance which could be related to choroidal metastases were excluded. All enrolled patients underwent systemic evaluation for brain, liver, lung and bones metastases. Ophthalmological screening consisted of visual acuity testing, slit-lamp examination, binocular indirect ophthalmoscopy and B-scan ultrasonographic examination. During indirect ophthalmoscopy, special attention was given to the typical ophthalmoscopic aspect of metastasis, including a greyish-white appearance of lesions with mottling of the pigment epithelium and visible elevation. Detailed B-scan ultrasonographic examination was carried out to detect any prominent lesions or choroidal thickening. In the case of a suspected lesion, the diagnosis of metastasis was confirmed by an A-scan ultrasonographic examination. All indirect ophthalmoscopic examinations were conducted by a single retina specialist (AB), and all B-scan examinations by a B-scan ultrasonographic specialist (MN), and the data were collected by a non-blinded investigator.

The incidence of metastases for each type of cancer was correlated with the number of organs involved by metastatic spread.

RESULTS

Patients with breast cancer

Altogether, 77 patients with breast cancer (all women) were screened during the study period. Their mean age was 62 (range 42–79) years. The mean time between the first diagnosis of the breast cancer to this ophthalmic screening was 5.7 years. In all, 64 (83.1%) of these patients had metastases in one organ and 13 (16.9%) had multiple-organ involvement. The most frequent site of involvement was the bone, followed by soft tissue, lung, liver and the central nervous system. None of the patients with breast carcinoma were found to have choroidal metastases either with ultrasonographic or with indirect ophthalmoscopic examination.

Patients with lung cancer

The 92 patients (54 men, 38 women) with lung cancer who were screened during the study period had a mean age of 65 (range 49–81) years. The mean time from diagnosis of the lung cancer to this ophthalmic screening was 1.3 years. In all, 85 (92.3%) of these patients had metastases in one organ and 7 (7.6%) had multiple-organ involvement. Two of the patients were found to have choroidal metastases both by ultrasonographic and by slit-lamp examination: one had two other involved organs and the other had three other involved organs.

DISCUSSION

The aim of our study was to determine the current incidence of asymptomatic choroidal metastases in patients with disseminated breast or lung cancer in order to decide whether a screening programme is justified. The figures cited in the literature are too outdated and are too inconsistent to determine sound policy: 0–9.7% in clinical trials^{2,4} for breast cancer and 2–6.7% in clinical trials^{2,7} for lung cancer.

Our data showed that there was no case of choroidal metastasis among the 77 patients with disseminated breast cancer and 2 cases (2.1%) in the group with lung cancer. The results for our breast cancer group are consistent with those recently published from a screening programme conducted by Fenton *et al.*³ They found no choroidal metastasis among 68 screened patients with advanced metastatic disease of the breast. By contrast, clinical studies published in 1967 by Albert *et al.*² and in 1982 by Mewis *et al.*⁴ found a frequency of 9% and 7%, respectively. A possible explanation for the low rate that was detected among our patients is that most studies with which it was compared were hospital-based series and included inpatients or patients with more advanced disease. It is impossible to compare our series to these two series, as the site and number of systemic metastases were not stated.

The difference between the older and the recent series may also be partially explained by the current more complex treatment of metastatic breast carcinoma by a more extensive arsenal of systemic treatment options. Importantly, choroidal metastasis is highly sensitive to both chemotherapy and radiotherapy,^{9–11} and the increased use of such treatment modalities among these patients may be responsible for the decreased detection rate of choroidal metastasis. Our patients with metastatic breast cancer receive different lines of palliative chemotherapy, at least one containing taxanes, which are known to penetrate choroidal tissue.¹²

Information on the frequency of choroidal metastasis in lung cancer is sparse. The finding of a 2.1% incidence of choroidal metastasis in our study group is considerably lower than the approximately 7% previously reported among 84 patients screened by Kreusel *et al.*⁷ between 1995 and 1998 in the University Hospital Benjamin Franklin (Free University of Berlin, Berlin, Germany), and the Eye Clinic, University of Essen (Essen, Germany). The low rate of choroidal metastasis among our patients may be explained by their healthier state: the number of metastases among Kreusel *et al.*'s⁷ patients was one in 44% and more than one in 66% of patients. Among our patients, 92.3% had metastases in one organ and 7.6% had multiple-organ involvement. Another probable contributing factor to the low rate is that our patients with metastatic lung cancer received the well-known combination of docetaxel and carboplatinum. As both these drugs show considerable penetration into choroidal tissue,^{12,13} it is reasonable to consider that

our results reflect a real change in the natural course of the disease brought about by chemotherapy.

Choroidal metastasis can cause major vision deterioration. A visual acuity of 6/60 or less was diagnosed at presentation in one third of patients with uveal metastases, and about one quarter of them will have bilateral disease.¹ Although aggressive treatment causes considerable reduction in metastasis size, most of these patients show no visual improvement after treatment.^{4,14} Moreover, patients presenting with already poor visual acuity are likely to remain with marked visual impairment even after aggressive treatment.¹⁵ If some of these individuals had been detected during early disease stages, appropriate treatment could have been started and the deterioration of vision could have been delayed, if not halted altogether. Unfortunately, the statistics testify against even reasonable cost effectiveness of implementing screening for asymptomatic choroidal metastasis among patients with disseminated breast and lung cancer.

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