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CLINICAL STUDY

Screening for ophthalmic involvement in asymptomatic patients with metastatic breast carcinoma

S Fenton[1], EG Kemp[1] and AN Harnett[2]

Abstract

Background **Breast carcinoma metastasises to the eye more frequently than is clinically recognised. The incidence is perhaps not appreciated, either because of the more common involvement and consequences of spread to major organs (such as lung, liver, or bone) or because a number of eye lesions are small and asymptomatic. Over a 6-month period, all patients with locally advanced or metastatic breast cancer were screened for ocular involvement and as a result management recommendations made.**
Materials and methods **Between January 2001 and June 2001, 68 patients with known locally advanced or metastatic breast carcinoma were referred for a screening ophthalmic examination. The aim of the study was to assess the frequency of asymptomatic ocular metastases by breast carcinoma in visually asymptomatic patients. The recognition and early treatment of both ocular metastases and ocular manifestations of metastatic breast carcinoma are important in maximising the quality of life in this group of palliative patients. These patients were all referred and recruited from the Beatson Oncology Centre and Breast Unit at the Western Infirmary, Glasgow by the oncologist (ANH). Examination included visual acuity assessment, slit-lamp examination, tonometry, and indirect ophthalmoscopy.**
Results **The median time from diagnosis of breast carcinoma to ophthalmic screening was 5 years (range 6 months–23 years). No patient had any evidence of choroidal metastases on ophthalmic examination. Four patients (5.8%) had ophthalmic manifestations of metastatic breast carcinoma and a further two had ocular complications of treatment. One patient had a restrictive motility problem from a metastatic deposit to her lateral rectus muscle and another had corneal punctate epitheliopathy secondary to a seventh nerve palsy. A further patient had coarse nystagmus from cerebellar metastases and the final patient of the four had a Horner's syndrome from metastases in the neck. In addition, two patients had symptomatic dry eyes whose onset coincided with commencement of chemotherapy.**
Conclusion **Ophthalmic manifestations of metastatic breast carcinoma occurred in 5.8% of asymptomatic patients. Orbital metastases were documented in one patient. No case of choroidal metastases was observed in this group with advanced or metastatic disease. Therefore, patients do not need to be routinely screened particularly for choroidal metastases.**
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Keywords: ocular metastases; metastatic breast carcinoma; ophthalmic screening for metastases

[1]The Ocular Oncology Unit
Tennent Institute of Ophthalmology
Gartnavel General Hospital
Glasgow, UK

[2]The Beatson Oncology Centre
Western Infirmary
Glasgow, UK

Correspondence:
S Fenton
Knockion Cunningham Road
Dalkey, Dublin
Ireland
Tel: +353 21 4922652
Fax: +353 21 4922656
E-mail: fentons@shb.ie

Introduction

Metastatic breast carcinoma is the most common primary tumour to metastasise to ocular structures.[1]

The incidence of ocular metastases among patients with breast carcinoma in clinical series has been reported to vary between 8 and 10%.[2,3] The occurrence of ocular metastases may not be appreciated because of the dominant clinical picture of metastases in other organs. Treatment options have increased and are prolonging survival, and thereby may increase the possibility of ocular metastases. Although the

highly vascular posterior choroid is the most frequent site of involvement, patients can be completely asymptomatic unless vision is threatened.

The recognition of ocular manifestations of metastatic disease and early treatment of metastases are important in maximising the quality of life in these patients. We undertook a pilot study to examine the frequency of ophthalmic manifestations of metastatic breast carcinoma in visually asymptomatic patients and to determine the frequency of asymptomatic ocular metastases.

Methods

Between January 2001 and June 2001, 68 patients with known advanced or metastatic breast carcinoma were referred for a screening ophthalmic examination. These patients were visually asymptomatic. They were recruited from the Beatson Oncology Centre by the oncologist (ANH). Ethical approval was sought but felt not to be required by the Ethics Committee and so the study was explained to patients and verbal consent obtained. One patient refused to take part. Examination included visual acuity assessment, slit-lamp examination, tonometry, and indirect ophthalmoscopy.

Results

The mean age of the patients was 60 years (range 36–77, median 62 years). One of the 68 patients was a male with metastatic breast cancer. The mean time from diagnosis of breast carcinoma to ophthalmic screening was 6.3 years (median 5 years). The mean duration of metastases was 19 months. In all, 45% of patients (31) had metastases to one site, 30% of patients (21) had metastases to two sites, 9% (six) had metastases to three sites, and 11% (eight) had metastases to four sites. The remainder 5% (four) had documented widespread metastases.

The most frequent site of involvement was bone followed by lung, soft-tissue involvement, liver, CNS, and others. In total, 54% of patients had bony metastases, 30% had pulmonary metastases, 26% had soft-tissue metastases, 20% had liver metastases, and 4% had brain or CNS metastases.

At the time of ophthalmic examination, all patients were receiving systemic treatment. This included palliative radiotherapy, chemotherapy, and hormonal therapy alone or in combination. Hormonal therapy included tamoxifen, aromatase inhibitors, and medroxyprogesterone acetate.

Four patients (5.8%) had ophthalmic manifestations of metastatic breast carcinoma. One patient had a restrictive motility problem from a metastatic deposit in the lateral rectus muscle, confirmed on CT scan and biopsied for which she received orbital radiotherapy. The onset of diplopia corresponded with her scheduled clinic visit and she was asymptomatic until this time. This same patient had a metastatic deposit to her lateral rectus muscle 2 years previously, which previously showed an excellent response to orbital radiotherapy. One patient had corneal punctate epitheliopathy secondary to lagophthalmos from a seventh nerve palsy requiring intensive lubricants and a further patient had coarse nystagmus from cerebellar metastases. Finally, one patient demonstrated a Horner's syndrome from metastases in the neck. No patient had macroscopic choroidal metastases. In addition, two patients had symptomatic dry eyes, the onset of which coincided with commencement of their chemotherapy, and were treated with topical lubricants.

Incidental eye findings causing impaired visual acuity but not subjective symptoms included posterior subcapsular lens opacities in one patient, age-related macular degeneration in one patient, uncorrected refractive error in one patient, and anisometropic amblyopia in two patients.

Discussion

The aim of our study was to determine the frequency of ocular involvement in visually asymptomatic patients with advanced or metastatic breast carcinoma and particularly to detect the presence of asymptomatic choroidal metastases where early recognition and treatment may avoid visual loss. Ophthalmic manifestations of metastatic breast carcinoma occurred in four asymptomatic patients.

Previously, much of our knowledge has come from autopsy studies. The rate of ocular metastases is expectedly higher in these studies since occult microscopic disease can be detected. Of 741 autopsy cases examined where cancer was the cause of death at John Hopkins Hospital over a 4-year period, 36 cases died of breast carcinoma. No case had macroscopic ocular metastases, but 3/36 (8.3%) had microscopic metastases.[4] Bloch and Gartner[5] also observed ocular metastases in 36% of patients who died of breast cancer, and Font and Ferry[6] found a similar incidence of ocular metastases in 41% of patients who died from breast cancer.

A clinical study by Mewis and Young[3] found an incidence of 9% for choroidal metastases in asymptomatic patients who had metastatic breast carcinoma. In their study group, the median age was 51 years and the median interval between the diagnosis of the primary tumour and that of uveal metastases was 3 years. The median age of our patients was 11 years older and the median time to ophthalmic screening was 6 years. This is within the range when choroidal

metastases can be expected[7]. The fact that no case demonstrated uveal metastases in our study might have been accounted for by treatment with chemotherapy or hormonal therapy for metastatic disease, which may possibly have caused regression of uveal metastases.

In a study by Wiegel *et al*,[8] patients with metastases from breast carcinoma in more than one organ and specifically with lung and brain metastases had a significantly higher risk of choroidal metastases compared with patients with only one site of metastases. The incidence of choroidal metastases in their group was 7% (6/120) and increased to 11% when there was more than one site of metastases. This is not supported by our study where patients with both brain and lung metastases still did not have choroidal metastases.

One patient had an orbital metastasis. Orbital metastases from breast carcinoma are much less common than choroidal metastases. However, metastatic disease accounts for 2.5–13% of all orbital tumours and breast carcinoma is the most common source of orbital metastases, accounting for 29–50%.[1,9–11] Discrete muscle metastases are considered unusual and constituted 9% of orbital metastases in one series[12].

The high incidence of breast carcinoma (one in every eight women will be affected[13]) and prolonged survival because of effective treatment may in part explain its metastatic frequency. The median presentation for orbital involvement is in the sixth decade of life and occurs on average 4.5–6.5 years after primary tumour diagnosis, and the majority have concomitant nonorbital metastases at the time of presentation. Our patient was 53 years old with concomitant soft-tissue and bony metastases. She had orbital radiotherapy for metastases to her lateral rectus muscle 2 years earlier with full recovery and had been asymptomatic until her screening ophthalmic examination.

In conclusion, a spectrum of ophthalmic manifestations of metastatic breast carcinoma was seen including cranial nerve involvement, Horner's syndrome, nystagmus, and orbital metastases. These findings occurred in 5.8% of patients. No case of choroidal metastases was observed in this group with advanced metastatic disease. As a result of this study, we recommend that routine ophthalmic assessment is not performed in asymptomatic patients with advanced or metastatic breast cancer.

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