- HS, Roberfroid M. Characteristic variations of serum alkaline DNase activity in relation to response to therapy and tumor prognosis in human lung cancer. *Eur J Cancer Clin Oncol* 1988, 24, 1337–1343.
- 3. Economidou-Karaoglou A, Lans M, Taper HS, Michaux JL, Roberfroid M. Variations in serum alkaline DNase activity. A new means for therapeutic monitoring of malignant lymphomas. *Anticancer Res* 1988, 61, 1838–1843.
- 4. Economidou-Karaoglou A, Brasseur F, Lans M, Taper HS, Roberfroid M. Variations in serum alkaline DNase activity in rats during growth and treatment of tumors sensitive or resistant to therapy. *Int J Cancer* 1989, 43, 956-959.
- Shepherd JH. Revised FIGO staging for gynaecological cancer. Br J Obstet Gynaecol 1989, 96, 889–892.
- Loiselle J-M, Carrier R. Désoxyribonucléase sérique chez le cancéreux. Rev Can Biol 1963, 22, 341-346.
- Beaven GH, Holiday ER, Johnson EA. Optical properties of nucleic acids and their components. In: Chargoff E, Davidson JN, eds. The Nucleic Acids. New York, Academic Press, 1955, 493–553.
- Kurnick NB. Desoxyribonuclease activity of sera of man and some other species. Arch Biochem Biophys 1953, 43, 97–107.
- Economidou-Karaoglou A, Opsomer M, Lans M, Taper HS, Deckers C, Roberfroid MB. Predictive value of serum alkaline

- DNase activity variations in treatment of head and neck cancer. *Acta Oncol* 1990, 29, 163-166.
- Spandidos DA, Ramandanis G, Garas J, Kottaridis SD. Serum deoxyribonucleases in patients with breast cancer. Eur J Cancer Clin Oncol 1980, 16, 1615-1619.
- Lykourinas M, Constantinidis C, Spantidos A, Manthopoulos A, Dimopoulos C. The role of acid and alkaline DNases as tumour markers in cancer of the genitourinary tract. *Urol Res* 1982, 10, 67-70.
- Gupta S, Herriott RM. Nucleases and their inhibitors in the cellular components of human blood. Arch Biochem Biophys 1963, 101, 88-95.
- 13. Lindberg MU, Skoog L. Purification from calf thymus of an inhibitor of deoxyribonuclease I. Eur J Biochem 1970, 13, 326-335.
- Lazarides E, Lindberg U. Actin is the naturally occurring inhibitor of deoxyribonuclease I. Proc Natl Acad Sci 1974, 71, 4742-4746.
- Åvall Lundqvist E, Economidou-Karaoglou A, Sjövall K, et al. Serum alkaline DNase activity in normal or nonhospitalised individuals. Clin Chim Acta 1989, 185, 35-44.

Acknowledgements—We are grateful to Prof. M. Roberfroid, Université de Louvain, Brussels, Belgium for providing the standard enzyme preparations, and to Eva Blad for technical assistance.

Eur J Cancer, Vol. 27, No. 10, pp. 1315–1316, 1991. Printed in Great Britain

0277-5379/91 \$3.00 + 0.00 © 1991 Pergamon Press plc

# An Unusual Cause of Diplopia in a Cancer Patient

Antoinette van der Heijden, Albert Twijnstra, Willy P.M.A. Lamers, Pierre S.G.J. Hupperets and Gerard Freling

A 47-year-old woman with metastatic infiltrating lobular carcinoma of the breast developed diplopia. Computed tomography of the orbits showed enlargement and irregularity of the right inferior rectus and inferior obliques muscles. Biopsies of these muscles contained breast carcinoma cells. This case report discusses the causes of diplopia in cancer patients, with special attention to the diagnostic problems of metastasis in extraocular muscles. The possible combined occurrence of metastasis in the leptomeninges and extraocular muscles is also to be borne in mind if the latter diagnosis is not to be missed.

#### Eur J Cancer, Vol. 27, No. 10, pp. 1315–1316, 1991.

#### INTRODUCTION

A SUBSTANTIAL proportion of cancer patients develop neurological complications during the course of their disease [1]. Diplopia in a cancer patient requires neurological evaluation. The most common cause of diplopia in cancer is leptomeningeal metastasis or metastasis to the base of the skull. Metastasis to the brainstem can also cause diplopia, in which case it is usually accompanied by involvement of other cranial nerves or long tracts [2]. Orbital metastasis of solid tumours is rare, and metastasis into the extraocular muscles has seldom been described.

In this report we describe an unusual case of metastasis of breast cancer in two extraocular muscles of the right eye without infiltration of the orbit.

Correspondence to A. van der Heijden.

A. van der Heijden and A. Twijnstra are at the Department of Neurology; W.P.M.A. Lamers is at the Department of Ophthalmology; P.S.G.J. Hupperets is at the Department of Internal Medicine; and G. Freling is at the Department of Pathology, University Hospital Maastricht, Postbox 5800, 6202 AZ Maastricht, The Netherlands. Revised 1 July 1991; accepted 18 July 1991.

## CASE REPORT

A 47-year-old woman was admitted to the hospital with diplopia in April 1988. She had been well until 5 years earlier, when she had a mastectomy for an infiltrating lobular carcinoma of the left breast. She subsequently underwent adjuvant chemotherpy because of the presence of metastasis in the axillary nodes. She remained well until April 1988, when she developed enlarged left axillary and left cervical nodes. Biopsy confirmed breast cancer. Further examination revealed bone metastasis. She started treatment on tamoxifen and bisphosphonate capsules.

In April 1988 she complained of painless diplopia on left lateral gaze. There were no other neurological symptoms. There was no history of previous neurological problems. On neurological examination the patient was alert and full oriented. Visual acuity and visual fields were normal; optic fundi were normal; pupils were equal in size and reactive. Both orbital regions appeared normal. There was an impaired adduction and downwards gaze of the right eye without ptosis. The external movement of the left eye was normal in all directions. Ocular media were clear. Results of the remainder of her neurological and

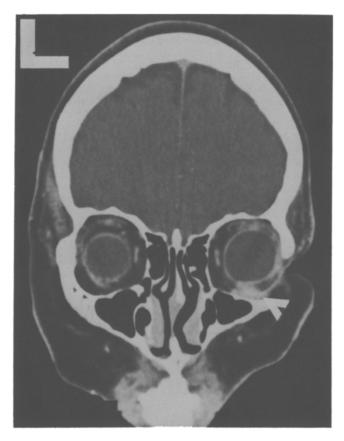


Fig. 1. Orbital CT showing enlargement of the rectus inferior muscle and the obliquus inferior muscle (arrow) of the right eye.

neuro-ophthalmological examination were normal. Computed tomography (CT) of the brain and a lumbar puncture revealed no abnormal findings.

Follow-up 3 months later showed an improvement of the movement of the right eye. 6 months later, diplopia had progressed, with progressive medial limitation approximately 50% of normal and elevation approximately 25% of normal. At that time there was also a palpable mass in the right orbit just below the eye. CT of the orbita showed an enlargement of the right inferior rectus and inferior obliquus muscles (Fig. 1).

Lumbar puncture showed the cerebrospinal fluid to be clear and colourless and containing no tumour cells. Protein and glucosis contents were normal. An open biopsy of the right musculus rectus inferior and musculus obliquus inferior was performed, whereby as much tumour as possible was excised. Histological examination of the ocular muscle biopsy showed slight fibrosis and infiltration with small carcinoma cells in so-called "indian file" formation, corresponding the primary infiltrating lobular carcinoma of the breast. Furthermore, immunohistochemically the tumour cells in the biopsy showed expression for oestrogen receptors.

The patient was treated with radiotherapy to the right orbit. Follow-up after 1 year revealed almost normal vision and a diminished diplopia.

### **DISCUSSION**

Diplopia in cancer patients may be due to leptomeningeal metastasis or metastasis to the base of the skull. Diplopia caused by brainstem metastasis is usually accompanied by involvement of other cranial nerves or long tracts [2]. However, metastasis into the brainstem may be too small to be detected by CT, and

magnetic resonance imaging (MRI) of the brain may be necessary [3]. Leptomeningeal metastasis can be difficult to detect and repeated lumbar punctures are often necessary to detect malignant cells.

A less common cause of diplopia, which appears to be increasing in frequency [4] is metastasis of solid malignancies into the orbits. Breast [5], lung and prostate cancer are the most common source of metastasis into the orbits [4–8]. An even less frequent cause of diplopia is metastasis into the extraocular muscles without infiltration of the orbits. In recent years a few case-reports have been published discussing, metastasis in extraocular muscles [5, 8–12].

The symptoms and signs are diplopia, unilateral proptosis (which may be very mild), limitation of ocular movement in the direction of action of the affected muscle, which can be tested by forced duction and sometimes pain in the affected eye. None of the reported cases showed a palpable orbitable mass.

Metastasis in the extraocular muscles can be detected by ultrasonography, by CT with special attention to the orbit and by MRI of the orbit. Li et al.[13] compared these three methods and concluded that MRI using a 0.15 T resistive magnet offered no distinct advantage over the combination of CT and ultrasound in the diagnosis of orbital tumours. It is likely that diagnosis of metastasis in extraocular muscles is not infrequently missed, especially when a cause for the diplopia has been identified. The finding of leptomeningeal and/or brain metastasis does not exclude metastasis in extraocular muscles [8]. The neurological examinations of patients with diplopia without other evidence of nerve dysfunction should include examination of the cerebrospinal fluid including culture and cytology, and CT with special attention for the orbit.

- Henson RA, Urich H, eds. Cancer and the Nervous System. Oxford, Blackwell, 1982.
- Adams RD, Victor M. Principals of Neurology. New York, McGraw-Hill. 1989.
- Pusateri ThJ, Sedwick LA, Margo CE. Isolated inferior rectus muscle palsy from a solitary metastasis to the oculomotor nucleus. Arch Opthalmol 1987, 105, 675-677.
- 4. Goldberg RA, Rootman J, Cline RA. Tumors metastatic to the orbit: a changing picture. Surv Opthalmol 1990, 35, 1-24.
- Mortada A. Binocular diplopia due to metastasis in orbital muscle from female breast cancer years after radical mastectomy. Orbit 1984, 3, 71-74.
- Boldt HC, Nerad JA. Orbital metastases from prostate carcinoma. Arch Opthalmol 1988, 106, 1403–1408.
- Freedman MI, Folk JC. Metastatic tumors to the eye and orbit. Patient survival and clinical characteristics. Arch Opthalmol 1987, 105, 1215-1219.
- 8. Weiss R, Grisold W, Jellinger K, Mühlbauer J, Scheiner W, Vesely M. Metastasis of solid tumors in extraocular muscles. *Acta Neuropathol* 1984, **65**, 168–171.
- Oosterhuis JA, Keizer de RJW, Wolff de-Rouendaal D, Kakebeeke-Kemme HM, Graaff de ML. Ocular and orbital metastasis of cutaneous melanomas. *Int Opthalmol* 1987, 10, 175–184.
- Shields CL, Shields JA, Eagle RC, Peyster RG, Conner BE, Green HA. Orbital metastasis from a carcinoid tumor. Computed tomography, magnetic resonance imaging, and electron microscopic findings. Arch Othalmol 1987, 105, 968-971.
- Arnold RW, Adams BA, Camoriano JK, Dyer JA, Acquired divergent strabismus: presumed metastatic gastric carcinoma to the medial rectus muscle. J Pediatr Opthalmol Strabismus 1989, 269, 50-51.
- Slavin ML, Goodstein S. Acquired Brown's synrome caused by focal metastasis to the superior oblique muscle. Am J Ophthalmol 1987, 103, 598-599.
- Li KC, Poon PY, Hinton P, et al. MR imaging of orbital tumors with CT and ultrasound correlations. J Comput Assist Tomogr 1984, 8, 1039-1047.