INTRA-OCULAR NEOPLASM TREATED WITH CYCLOPHOSPHAMIDE*†

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THE use of cyclophosphamide in treating intra-ocular neoplasms has been largely confined to cases of retinoblastoma; the following report illustrates its use in a case of disseminated anaplastic carcinoma affecting the eye.

Case Report

A 74-year-old woman was first seen in the Ophthalmic Out-Patients Department in July, 1965, having been referred by the Medical Clinic. She complained of "distorted vision" in the right eye which had started 2 weeks previously.

Examination.—There was a right infero-temporal retinal detachment (Fig. 1), cystic in appearance, with no visible retinal hole. The patient was therefore admitted to hospital for further investigation and treatment.

When questioned about her general health she reported a number of small haemoptyses during the preceding few months; otherwise she felt perfectly well. She was a housewife who looked after her very elderly husband and was a non-smoker. Physical examination at this time revealed no significant abnormalities, though a chest x ray revealed evidence of a partial right middle lobe collapse.

Treatment.—She was first treated for a few days with rest in bed and double padding of the eyes.

Progress.—Daily examination showed that the lesion was increasing rather than decreasing in size. At this time two small sub-conjunctival haemorrhages were seen in the right eye (Fig. 2).

FIG. 1.—Appearance of right infero-temporal retinal detachment before treatment with cyclophosphamide (August, 1965).

FIG. 2.—Subconjunctival haemorrhages in right eye at time of their first appearance.

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It was felt in view of these developments that the most likely diagnosis was that of a melanoma of the choroid, but the chest x-ray appearance suggested that a bronchial carcinoma should be excluded. The peripheral visual fields were charted (Chart 1). Enucleation of the eye was considered and was thought in the circumstances to be indicated.

CHART 1.—Upper temporal defect produced by retinal detachment, September 3, 1965.

CHART 2.—Decreased defect after treatment with cyclophosphamide, September 8, 1965.

CHART 3.—Increased defect with recurrence of tumour, December 6, 1965.

The patient now complained of a hard lump which had appeared in her neck. Physical examination (carried out about 2 weeks after the examination on admission) showed a hard mass in the thyroid gland and collapse of the lower lobe of the right lung. Two sub-cutaneous nodules had appeared on the abdominal wall, both about 3 cm. in diameter and surrounded by areas of haemorrhage. All these lesions had appeared during the 2 weeks and were obviously growing rapidly.

A biopsy excision of one of these was examined histologically and reported as:

"Highly anaplastic carcinoma in which numerous mitotic figures were present. A bronchial primary is the most likely diagnosis, but the possibility of a secondary malignant melanoma cannot be excluded".

Examination of the sputum revealed malignant cells of a similar histology.

Treatment.—In view of the obvious widespread dissemination of the tumour and its rapid rate of growth, it was decided that a cytotoxic agent would be the most effective form of therapy. The patient was therefore given a 4-week course of cyclophosphamide, 100 mg. being given intravenously each day, commencing early in August. Frequent white blood cell counts were performed during this time, a count of between 2,000–3,000 cells per c.mm. being regarded as an indication of the effectiveness of the drug. At the end of the fourth week, she was started on a dose of 50 mg. orally twice daily.

During the course of this treatment, the ocular lesion decreased until it had virtually disappeared (Fig. 3, opposite). There was, however, little alteration in the visual fields as recorded by perimetry (Chart 2). The other two deposits were also greatly reduced in size.

Further Progress.—The patient's general condition improved. In late September she had an episode of left foot drop, associated with an absent ankle jerk and absent vibration sense in the left leg below the knee. This was thought to be a carcinomatous peripheral neuropathy. It recovered slowly over the course of a few weeks.

Discharge.—The patient was discharged from hospital early in October, 1965, and continued to take cyclophosphamide 50 mg. twice daily. Her hair had become noticeably thinner but, apart from occasional nausea, this was the only obvious side-effect of the treatment.

Re-admission.—She remained fairly well until late November, when she had to be re-admitted to hospital complaining of dyspnoea and cough. The detachment had increased slightly in size and there was evidence again of right lower lobe collapse. The visual field on December 6 is shown in Chart 3.

Termination.—Her condition steadily deteriorated, in spite of the continued cytotoxic therapy, and she died on January 18, 1966.

FIG 3.—Flattened appearance of retina after completion of treatment (November, 1965).

Post mortem Examination.—There was a large necrotic tumour at the hilum of the right lung, with spread to the lymph nodes, thyroid, and adrenal glands. *Post mortem* examination of the right eye (performed at the Institute of Ophthalmology) showed a flat tumour of the temporal choroid with an associated retinal detachment (Fig. 4). Histologically this was a highly vascular tumour of the choroid situated between the equator and the disc on one side, and composed of ovoid cells, with deeply staining nuclei (Fig. 5). There were some areas of necrosis. The retina overlying the tumour was detached, but apart from cystic degenerative changes at the retinal periphery there was no other gross abnormality. The appearances were considered to be consistent with a diagnosis of secondary oat cell carcinoma. The left eye was normal.

FIG. 4.—*Post mortem* section of eye (January, 1966).

FIG. 5.—Microscopical appearance of tumour. Haematoxylin and eosin. $\times 425$.

Summary

A 74-year-old woman presented with a right retinal detachment in July, 1965, which proved to be secondary to an underlying neoplasm. She developed widespread metastases

over the course of the next few weeks. Treatment with intravenous cyclophosphamide was followed by virtual disappearance of the secondary deposits. In December, 1965, she developed total collapse of the right lung and died a few weeks later. *Post mortem* examination disclosed a carcinoma of the right bronchus with widespread metastases.

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