BILATERAL METASTATIC CARCINOMA OF THE CHOROID

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Metastatic carcinoma of the choroid and other ocular structures is of sufficiently rare occurrence to make the following report of interest. Carcinoma involving the intra-ocular and extra-ocular tissues is regarded as a secondary growth arising from a primary neoplasm situated elsewhere in the body. In about 70 per cent. of such cases the primary growth is a carcinoma of the mammary gland, other primary foci being the lungs, stomach, prostate, etc. At times the primary growth cannot be located during life, and its presence is revealed only by a general autopsy.

The ocular lesion may be the only visible evidence of metastasis, hence in all cases of carcinoma a systematic ocular examination should be performed. In this condition the media are clear, permitting a distinct view of the fundi. The characteristic finding is the choroidal tumor, which is flat and of grayish color. It is situated temporally around the posterior pole, where it is thickest, and sometimes extends from the ora serrata to and around the optic disc. It is covered and surrounded by a flat retinal detachment which obscures a view of its contour. The carcinomatous tissue may invade one or several ocular structures, or these foci may occur independently of one another. A differentiation between them is usually impossible, even in serial eye sections.

Transillumination is frequently of no avail, owing to the posterior location of the growth. Tonometric examination is also of little value, since the tension does not increase until late complications set in. When the retrobulbar tissue be-

comes markedly involved, there will be disturbed motility and exophthalmos.

The rapid development of the choroidal tumor causes detachment of the retina, resulting in a sudden marked deterioration of vision, which in one-fourth of the cases is bilateral. Simultaneous affection of both eyes is rare, as a rule first one eye and then the other becoming involved. When the disturbance in vision is bilateral, a tumor can generally be recognized in each eye.

It is usually impossible to differentiate between a unilateral flat carcinoma without a known primary growth and a flat sarcoma of the choroid. However, if clinically the growth suggests a flat sarcoma, enucleation should be considered in order to establish a diagnosis and give a prognosis.

The cancer cells are transported from the original focus to the ocular structures by means of the blood stream. These cells form emboli in the ocular vessels, and these emboli finally break through the vessel walls into the surrounding tissues.

Metastatic choroidal carcinomas occur most often in women, and the growth in both men and women usually appears between the ages of thirty and sixty. The lapse of time between the occurrence of carcinoma of the breast and the appearance of ocular manifestations is variable—it may be weeks or even years. The outlook for life, even when the lesion is unilateral, is unfavorable; when the condition is bilateral, the prognosis is still graver. In unilateral cases death may be delayed for a few years, whereas in bilateral cases it is seldom delayed more than a few months.

Treatment is generally palliative, since the condition is a generalized one (carcinomatosis). In a very few cases radium and *x*-ray therapy have been tried with some success.

The typical pathologic change in the ocular structure consists principally in the presence of cancerous cellular elements. These are similar in structure to those found in the primary growth, but their arrangement varies according to

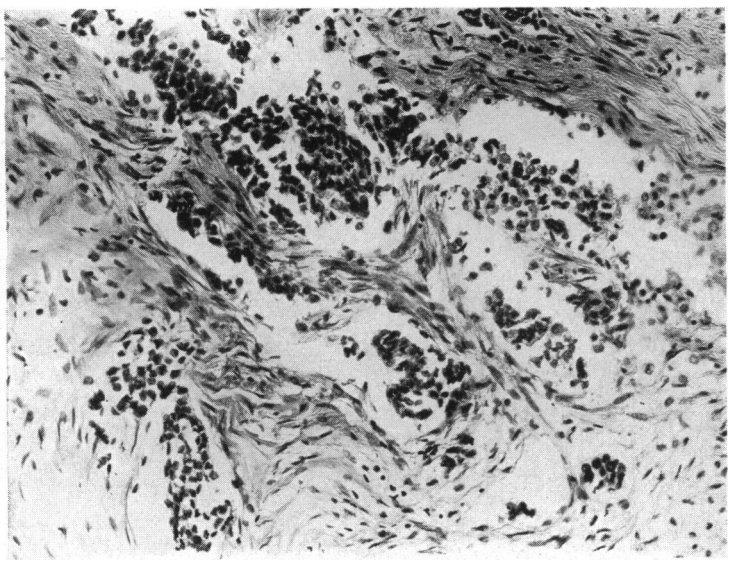

Fig. 1.—Photomicrograph (medium high power) of the breast tumor, showing nests of tumor cells separated by edematous fibrous tissue.

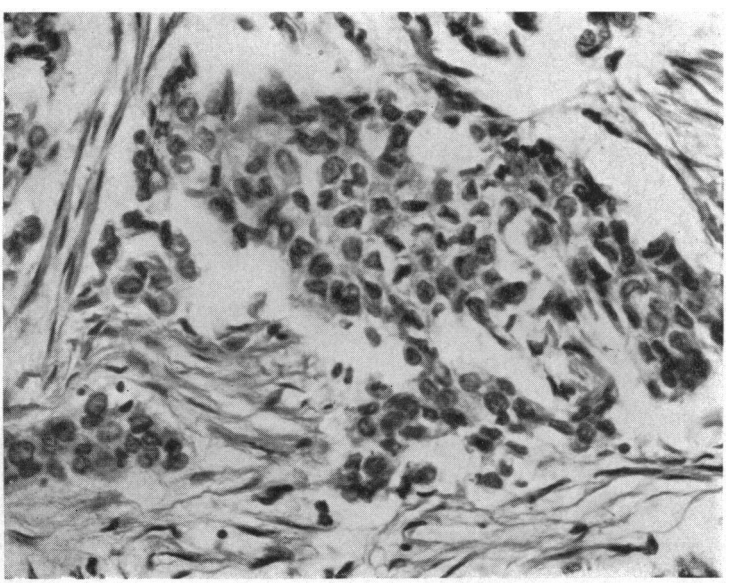

Fig. 2.—Photomicrograph (high power) of an area from the breast tumor showing large carcinomatous cells.

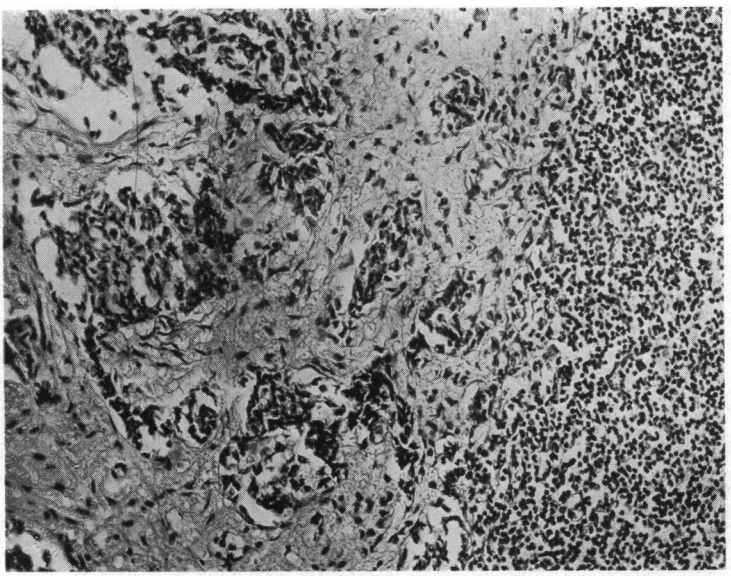

Fig. 3.—Photomicrograph (medium high power) showing metastatic focus of carcinoma in regional lymph node surrounded by lymphocytic infiltration.

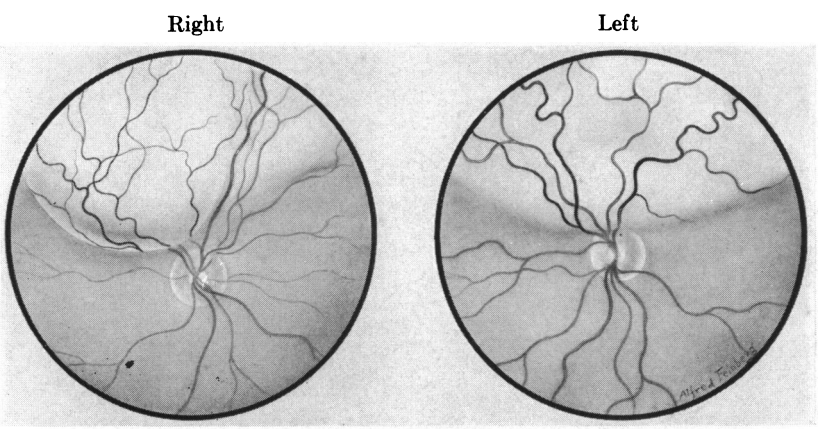

Fig. 4.—A drawing of the fundus of each eye on admission, showing a bilateral flat retinal detachment due to bilateral metastatic carcinoma of the choroid.

the nature of the tissues which they invade or infiltrate. In the choroid the cellular type of carcinoma predominates: the cells replace the vessels of the choroid, arranging themselves in strands or cords; small nests of epithelial cells form alveoli sparsely surrounded by fibrous tissue. The retrobulbar invasion is usually of the alveolar or scirrhous type of carcinoma. The sclera, optic nerve, and optic sheath may be involved similarly, whereas the retina, iris, and ciliary body are rarely affected.

CASE REPORT

F. J., female, single, aged twenty-seven years, was admitted to the New York Skin and Cancer Unit of the Post-Graduate Medical School and Hospital on July 17, 1934, complaining of local pain caused by a mass in the left breast. The pain first occurred in September, 1933. Her family and previous personal history had no bearing on her present condition. She was pale and obese. A complete physical examination revealed nothing abnormal except the breast condition. The right breast was normal. In the outer half of the left breast a large mass could be felt; it was hard, diffuse, and somewhat infiltrated. Both axillae, but especially the right, showed enlarged nodes. A diagnosis of carcinoma of the left breast was made, and an operation was advised. A radical mastectomy was performed on August 10, 1934.

Pathologic diagnosis of the removed tumor was scirrhous carcinoma of the breast (grade 2). Microscopic examination of sections of the breast showed a growth of epithelial cells arranged in nests and surrounded by a fibrous stroma (figs. 1 and 2). The nodes showed a similar structure (fig. 3).

Ten days after the operation the wound became infected. The infection lasted for four days, after which the wound healed. The patient remained in the hospital for one month. During this time she complained of pain in the right sacro-iliac region, but *x*-ray examination of this area yielded negative results. After being discharged, she frequently returned to the hospital for *x*-ray therapy. At her last visit to the clinic she complained of marked visual disturbances in both eyes, and was thereupon referred to the eye department of the Post-Graduate Hospital.

Ophthalmologic Report.—The patient was admitted to the eye ward on October 15, 1935. Four months before this date the vision in both eyes had suddenly become defective, first one eye

and then a little later the other eye, being affected. The visual disturbance was accompanied by general malaise, cough, and pain in the right hip joint. Physical examination and laboratory reports were negative. After an *x*-ray examination and a study of the lungs, Dr. H. W. Meyer diagnosed the condition as a metastatic pulmonary malignancy.

The external appearance of the eyes was normal, with the exception of a moderate dilatation of the pupils; the latter reacted sluggishly to light and in accommodation. The vision was excentric, and was equal in the left eye to 5/200 and in the right to 3/200. The field of vision in both eyes was defective, but no accurate determination could be made owing to lack of cooperation. No exophthalmos or loss of motility could be observed in either eye. In both eyes the intra-ocular tension was normal and the ocular media were clear.

The fundus lesion present in both eyes was significant, and consisted of a tumor mass in the choroid. The growths in both eyes were practically identical in configuration, size, color, and location (fig. 4). The mass was flat, sharply circumscribed, of grayish hue, and moderately pigmented. The tumor was covered by a flat retinal detachment, located posteriorly in the upper temporal and nasal area of the fundus. The choroidal growth in both eyes was elevated 3 mm. The optic disc and retinal vessels appeared to be normal, and no hemorrhages or exudates were visible. *Fundus diagnosis:* Bilateral carcinoma of the choroid (metastatic).

During the patient's stay of one month at the hospital the foregoing picture of the fundi remained practically stationary. She was then discharged, and on November 27, 1935, was transferred to Bellevue Hospital on the service of Dr. Webb W. Weeks. I was given the opportunity of examining her frequently. After a short time she became cachectic, and the ocular condition became aggravated. In the right eye vision was reduced to an amaurosis, the pupil was widely dilated and fixed, the ocular conjunctiva was chemotic, the fundus ischemic, and the retinal detachment seemed to be complete. The tumor mass was now elevated 4 mm. The optic disc showed a moderate papilledema surrounded by numerous small hemorrhages. The retinal veins became engorged and tortuous, the arteries were narrowed, and the intra-ocular tension rose to 56 mm. Hg (Schiötz). The exophthalmometer reading was 20, and motility of the eye was restricted in all directions, causing pain on motion. The cornea, anterior chamber, and media were clear. In the left eye vision was reduced to light perception and faulty

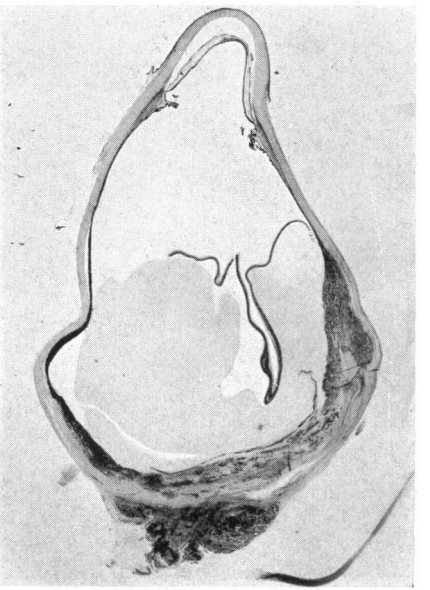

Fig. 5.—Photomicrograph (low power) of the right eyeball, showing carcinomatous involvement of the choroid, sclera, and retrobulbar tissue.

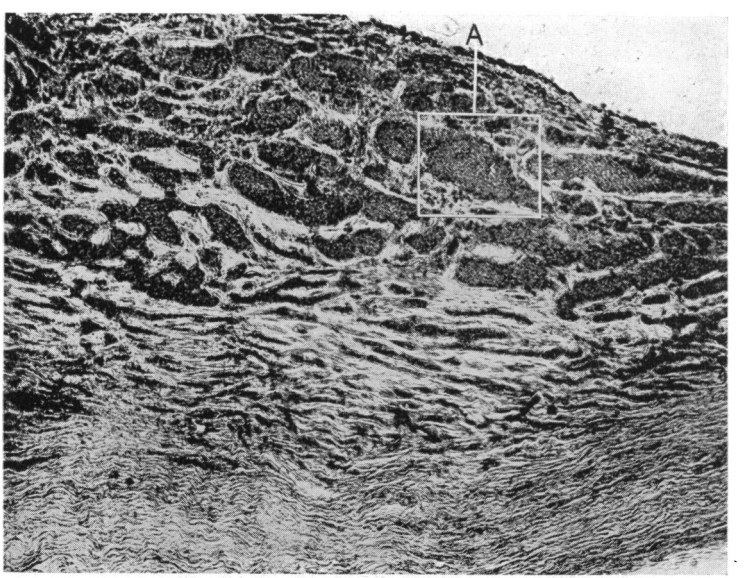

Fig. 6.—Photomicrograph (low power) of the tumor of the choroid (right eye) resembling the tumor of the breast.

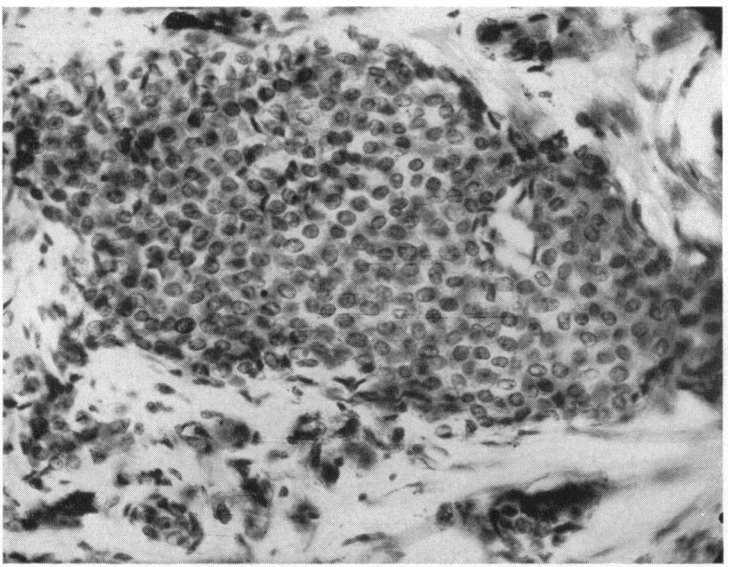

Fig. 7.—Photomicrograph (high power) of area A shown in figure 6, showing slight degeneration in cellular nest.

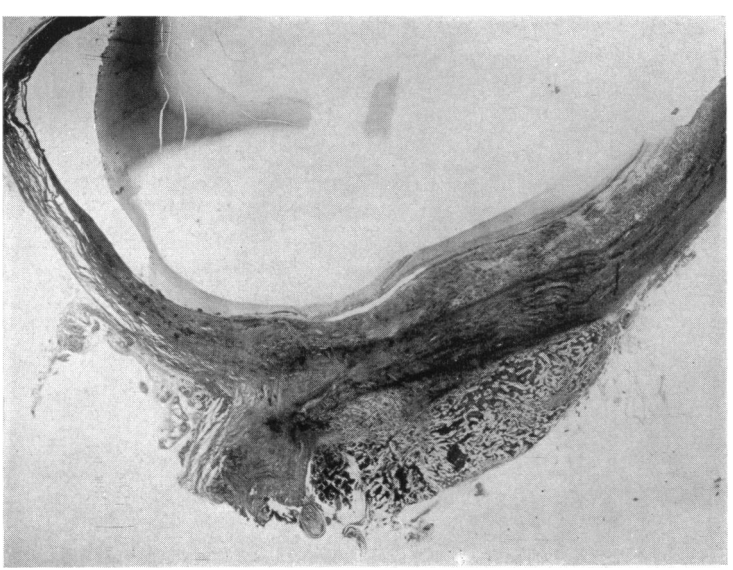

Fig. 8.—Photomicrograph (medium high power) showing metastatic focus in retrobulbar tissue and optic nerve (right eye).

projection. The lids, cornea, anterior chamber, and iris were normal. The pupil was widely dilated and fixed. Fundus examination disclosed two large retinal detachments in the lower quadrant and a recent one in the upper temporal area. The circumscribed mass visible above the disc was elevated 5 mm. and retained its grayish color, but its outline was less distinct. No hemorrhages or exudates were present. The disc was hyperemic and elevated, indicative of an incipient papilledema. The media remained clear and the retinal vessels normal. Intra-ocular tension was 29 mm. Hg (Schiötz), and exophthalmometer reading was 18. *Fundus diagnosis:* Bilateral carcinoma of the choroid (metastatic) with bilateral retinal detachment and moderate bilateral papilledema.

During the patient's four months' stay in the hospital several *x*-ray examinations were made. These showed the presence of metastatic foci in the lungs, skull, ribs, and long bones. She gradually became extremely cachectic, and died on March 30, 1936. *Final diagnosis:* Carcinomatosis with metastases to the eyes.

A general autopsy was refused, but removal of the eyeballs was permitted. These organs were fixed and stained in the usual manner, and were then sent to me through the courtesy of Dr. Edward Gresser.

REPORT ON THE ENUCLEATED EYES

Right Eye.—The eyeball was misshapen, owing to manipulation following enucleation.

Macroscopic examination (fig. 5) showed the anterior segment of the eye to be normal. The retina was detached. The posterior segment showed a thickening of the choroid, principally on its temporal side, and most prominent around the posterior pole. The choroid appeared to be flattened and stretched from the disc to the region of the ora serrata. On the nasal side of the disc, extending anteriorly for a short distance, there was a flat thickening of the choroid. The sclera presented a few dark spaces—probably carcinomatous foci. Surrounding the head of the optic nerve, at the apex of the retro-orbital region, were dark, malignant areas, more apparent on the temporal side, in the neighborhood of the posterior (short) ciliary vessels. The head of the optic nerve, behind the lamina cribrosa, was the seat of carcinomatous foci.

Microscopic study of eye sections revealed no lesions in the cornea, anterior chamber, iris, or vitreous. The retina was completely detached, but its structural layers, including the lamina vitrea, were normal. The important pathologic changes appeared

in the choroid (figs. 6 and 7). The vascular layers were replaced by carcinomatous tissues, arranged in acini which were filled with cancer cells. A few of their central areas showed degeneration, but no hemorrhages were found. The arrangement of the cancerous tissue was mainly of the glandular type, due to the structure of the choroid. There was some invasion of the lamina suprachoroidea. A few cancerous nests were seen between the lamellae of the sclera. The stem of the optic nerve fibers just behind the lamina cribrosa showed a few nests of carcinoma cells, possibly transported by the central retinal artery. Surrounding the head of the optic nerve in the retro-orbital tissue (fig. 8) the cancerous invasion was marked, appearing in the vicinity of the posterior ciliary vessels. The arrangement of the cancerous tissue in this area was mainly of the alveolar type, owing to the nature and structure of the retrobulbar tissue invaded by the metastases. Degeneration of the cells was noted in the center of a few acini, but no hemorrhages were visible.

Left Eye.—This eyeball (fig. 9) also was somewhat misshapen from manipulation. The media seemed to be clear. There was an artificial detachment of the retina. A thin mass could be seen encircling the posterior segment of the eye, and a thicker mass appeared posteriorly in the retrobulbar region.

Microscopic examination revealed nothing abnormal in the cornea, anterior chamber, iris, or lens. The layers of the detached retina, as well as the pigment epithelium and the lamina vitrea, appeared to be normal. The choroid was replaced by carcinomatous tissue, thinned out and extending from the ora serrata on the nasal side to the ora serrata on the temporal side. The flat growth was extremely cellular and apparently glandular in type. Some of the vessels in Sattler's layer were still recognizable. The choriocapillaris was partially replaced by carcinomatous tissue; vessels contained carcinomatous cells (fig. 10). A few chromatophores were visible. There was some invasion of the lamina suprachoroidea, and the scleral spaces contained many nests of carcinomatous tissue. The retro-orbital tissue surrounding the optic nerve head was markedly infiltrated with carcinomatous tissue of the alveolar type, and some of the capillaries of this region were filled with carcinoma cells.

Pathologic Diagnosis: Bilateral carcinoma of the choroid with involvement of other ocular structures (metastatic).

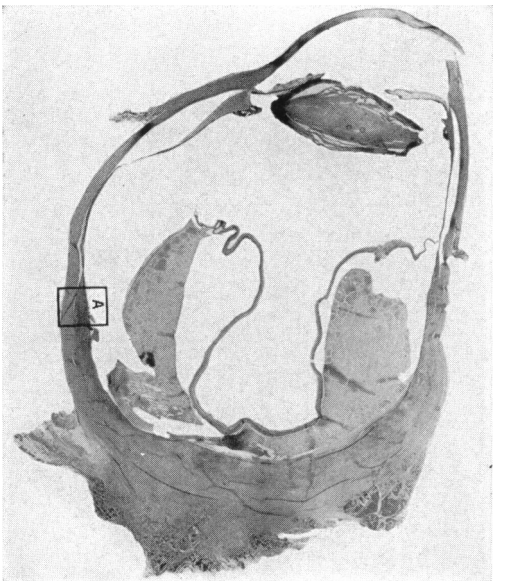

Fig. 9.—Photomicrograph (low power) of the left eyeball, showing carcinomatous involvement of the choroid, sclera, and retrobulbar tissue.

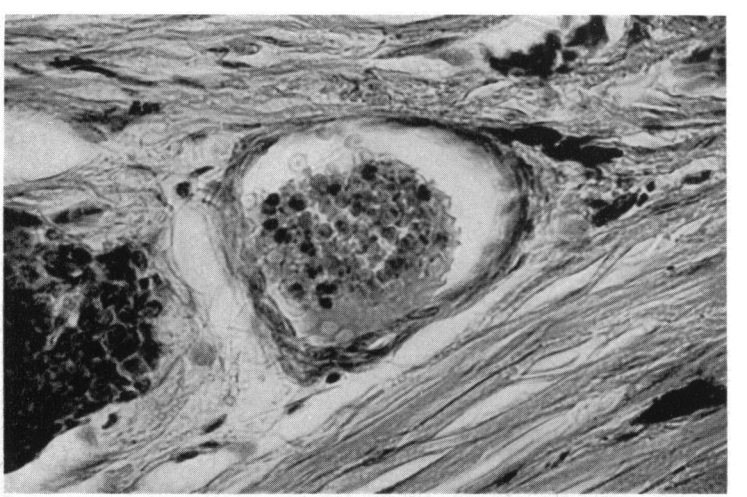

Fig. 10.—Photomicrograph (high power) of area A, figure 9, showing an enlarged blood vessel containing carcinomatous cells.

COMMENTS

1. Bilateral metastatic carcinoma of the choroid is rare; unilateral involvement occurs more often. One-fourth of the latter type of cases developed bilateral ocular metastases.

2. Carcinomatous metastases may occur in one or several ocular structures, due to an extension of the primary metastasis or to independent foci.

3. A view of the choroidal growth is often obscured by a flat retinal detachment. The finding of a primary carcinoma elsewhere in the body would suggest that the retinal detachment was caused by a metastatic choroidal carcinoma.

4. An ophthalmologic examination is advisable in cases of primary carcinoma occurring in any part of the body, as the eye lesion may be the only evidence of metastasis.

5. Further reports of ocular metastases are necessary in order to establish, by means of statistics, the relationship between these metastases and any primary carcinoma.

PRECANCEROUS MELANOSIS AND DIFFUSE MALIGNANT MELANOMA OF THE CONJUNCTIVA

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The fact that tissue may undergo certain changes prior to the development of malignant growth is well known. In the experimental production of epithelioma in animals a precancerous stage of varying duration has been observed. In the human, such examples are afforded by the senile dystrophy of the skin which manifests itself in a thinning of the derma, with pigment flecks, telangiectasis, and circumscribed keratosis. Similar changes are seen in xeroderma pigmentosum. Other examples are leukoplakia, Paget's disease of the nipple and adnexa, Bowen's disease, et cetera.