Comment

Although ICG angiographic studies of CRAO have been published,[1,2] CRAO with cilioretinal artery sparing has not been reported to date. Cilioretinal arteries are usually derived from short posterior ciliary arteries but have also been shown to arise directly from the choroidal vessels in the subhuman primate model.[3] Approximately 25% of eyes with CRAO have cilioretinal sparing of part of the macula.[4]

In our case, ICG angiography allowed us to follow all the stages of CRAO with cilioretinal sparing. The early-phase ICG angiogram showed normal background fluorescence only in the region of the cilioretinal artery, which contrasted sharply with the adjacent hypofluorescent areas supplied by the CRA. Although vascular filling defects and blocking substances such as pigment, haemorrhage and exudation have been included in the causes of hypofluorescence seen in ICG angiograms,[5] special attention to CRAO with cilioretinal sparing has not been reported. Diffuse pallor of the retina due to intracellular oedema, cellular necrosis and accumulation of cellular debris may cause hypofluorescence surrounding the area of cilioretinal sparing in which normal background fluorescence is present. The retinal arteries did not fill completely, even in the middle phase, but our most striking finding was the persistent staining of the retinal vessels at 45 min after injection. In contrast, FFA showed no fluorescence at the late stage. This persistent staining may be caused by a combination of the protein-binding properties of ICG and the retinal vessel damage, which can not be documented with FFA. ICG angiography does not reveal the details provided by FFA when imaging the normal retinal vasculature, but our case shows that, with some pathological conditions, ICG angiography may highlight abnormalities of the retinal and choroidal circulation.

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Sir,

Bilateral choroidal metastases as the first sign of metastatic gestational choriocarcinoma

The uvea is the most common site of ocular metastases, with the choroid accounting for approximately 80% of all metastatic ocular disease.[1] Uveal metastases represent the most common uveal malignancy, being more common than primary uveal melanoma.[2,3] Uveal metastases are spread haematogenously, with the posterior pole (particularly the submacular choroid) most often involved.[4] A metastatic tumour of the uvea is the initial clinical manifestation of systemic cancer in approximately 17% of patients.[5]

Gestational trophoblastic neoplasia is the term applied to choriocarcinoma and related tumours. Choriocarcinoma develops in 1 in 40 000 term pregnancies; in contrast, it develops in approximately 3–5% of patients with a molar pregnancy. In approximately 50% of patients with choriocarcinoma the disease develops following a hydatidiform mole; in approximately 25%, following a term pregnancy; and in 25%, following an abortion (spontaneous, therapeutic or ectopic). Aside from direct tissue examination, one of the hallmarks of diagnosis is an elevated urine or serum titre of human chorionic gonadotrophin (hCG), the 'pregnancy hormone', which is produced by this tumour in large quantities. Non-gestational choriocarcinomas derive from germ cells of the testis or ovary. Because of a propensity for haematogenous spread, all the blood-rich organs are at significant risk for metastatic disease. Metastatic disease can be found in the lung, genitourinary system, brain, liver, spleen and gastrointestinal tract.[6]

Gestational choriocarcinoma rarely metastasises to the eye, and only few cases of mestastasis to the choroid have been reported.[7–14] We report here an unusual case of gestational choriocarcinoma that presented as bilateral choroidal metastases and serous retinal detachment.

Case report

A 41-year-old woman presented to the retina service, King Abdulaziz University Hospital, with a 2-month history of decreased vision in both eyes. On examination, the patient was found to have a visual acuity of counting fingers in both eyes. Slit-lamp examination yielded normal results and the intraocular pressure was 12 mmHg bilaterally. Dilated fundoscopy showed bilateral, multiple, yellow, elevated choroidal lesions involving the macular and juxtapapillary areas with total bullous sensory retinal detachments (Fig. 1). The choroidal lesions showed moderate- to high-amplitude internal reflectivity on ultrasonography. A fluorescein angiogram

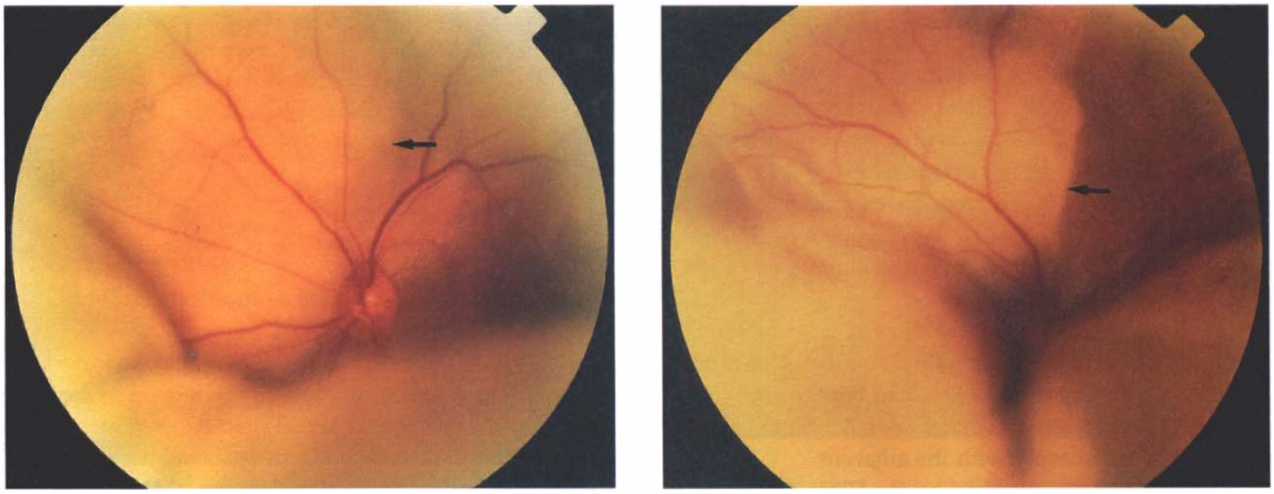

Fig. 1. *Fundus photographs at presentation show tumours in the posterior poles (arrows) and bullous retinal detachments.*

showed early blockage and late staining. The initial impression was bilateral choroidal metastases with unknown primary site.

Because a routine pregnancy test was positive, consultation was obtained with the gynaecology service. The patient had had 7 full-term pregnancies and 3 abortions. The last pregnancy was complicated by a hydatidiform mole 18 months prior to presentation, which was confirmed histologically. The patient was followed up at her local hospital by serial assays of serum beta-human chorionic gonadotrophin (βhCG) for 5 months and the levels were reported to be within normal limits. Over the year prior to presentation she was lost to follow-up, and her menstrual periods were irregular. Transvaginal ultrasonography showed a large empty uterus and uterine fundal mass measuring 5 cm in diameter. Colour Doppler imaging revealed the rich vascularity of the mass and increased blood flow in the mass and surrounding myometrium. The serum βhCG level was 10784 IU/l (normally less than 5 IU/l), and diffuse metastatic involvement of the lungs was shown on the chest roentgenogram. Upper abdominal ultrasonography and a CT scan revealed no evidence of liver or nodal metastases. No evidence of brain metastases was shown on the CT scan. A diagnosis of uterine choriocarcinoma with choroidal and lung metastases was made.

One day prior to the initiation of chemotherapy the patient developed severe uterine bleeding for which hysterectomy was performed. Histological examination revealed invasive uterine choriocarcinoma involving two-thirds of the myometrium. A combination chemotherapy regimen of etoposide, methotrexate and actinomycin D alternating with cisplatin, vincristine and bleomycin was initiated on the fifth post-operative day. Two weeks later the choroidal metastases showed progression and the retinal detachment became more bullous bilaterally. Lung metastases became worse (more than 40% lung opacification), and the serum βhCG level was markedly elevated (18110 IU/l). Because of the poor response to initial chemotherapy the patient was treated with a 7-day course of radiotherapy to both orbits. Intravenous methylprednisolone was added to ameliorate inflammation secondary to tumour necrosis. One week after completion of radiotherapy there was no clinical evidence of improvement, serum βhCG level increased to 38273 IU/l and lung metastases worsened (more than 50% lung opacification). Death occurred 48 days after her ophthalmic admission because of respiratory failure.

Comment

This case is unusual because the patient presented with bilateral multiple choroidal metastases with secondary retinal detachments leading to bilateral visual loss. The elevated serum βhCG level suggested the diagnosis of metastatic choriocarcinoma. Histological confirmation of the diagnosis was made after hysterectomy.

Gestational choriocarcinoma is a rare cause of choroidal metastasis. In 1970, Keates and Billig[7] described 12 previously reported cases in 7 male and 5 female subjects and presented one of their own in a female subject. Six additional cases have been described in 3 male subjects[8–10] and 3 female subjects[11–13] since that time, bringing the total reported cases of metastatic choroidal choriocarcinoma to 19. To our knowledge, ours is the fourth case of metastatic choroidal choriocarcinoma in which the ocular tumour caused the presenting symptom[11,12,14] and the second in which histological confirmation of the primary uterine lesion was obtained.[14]

The cornerstone of treatment of metastatic choriocarcinoma is chemotherapy.[6] To our knowledge there are 4 reported cases of choroidal metastases of choriocarcinoma in female subjects that responded to systemic chemotherapy.[7,11–13] Patients with choriocarcinoma who are found to have metastatic disease are classified as having a poor prognosis for treatment by chemotherapy when the following are present: (1) brain or liver metastasis; (2) urinary βhCG titre greater than 100 000 IU/24 h or serum βhCG titre greater than 40 000 IU/l; (3) failed previous chemotherapy; (4) long duration (last pregnancy > 4

months); and (5) antecedent term pregnancy.[6] In addition, Lurain and associates[15] noted that there are three factors primarily responsible for treatment failure: extensive disease, inadequate initial treatment, and failure of the chemotherapy protocol used.

Our case demonstrated several poor prognostic factors. The patient's clinical disease, dated from her molar pregnancy, was more than 15 months in duration. The patient had extensive disease at presentation with a large primary uterine lesion, bilateral diffuse lung metastases and bilateral multiple choroidal metastases. Despite prompt diagnosis and institution of combined chemotherapy and radiotherapy, her serum βhCG levels were massively increasing and the disease progressed rapidly. Following evacuation of the molar tissue it is recommended that patients require weekly βhCG determinations until the βhCG titre is within normal limits for 3 weeks. The titres are observed at monthly intervals for 6 months and then every 2–3 months for a further 6 months. Those patients who continue to show a plateau or rise in titres require chemotherapy.[6] In our case the disease was not recognised early because the patient had not been followed-up as recommended.

In conclusion, we report a case of metastatic uterine choriocarcinoma in which bilateral choroidal metastases were the initial manifestation of choriocarcinoma. Although choriocarcinoma is a rare cause of choroidal metastasis, it should be considered in the differential diagnosis in a young woman with choroidal metastases.

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Sir,

Central retinal artery occlusion associated with primary antiphospholipid syndrome

Antiphospholipid syndrome is a newly recognised entity. The clinical manifestations of this syndrome include hypertension, chronic renal failure, recurrent spontaneous abortions and deep vein thrombosis.[1] These manifestations are caused by arterial and venous thrombosis due to anticardiolipin antibodies, which may be the primary abnormality (primary antiphospholipid syndrome) or part of other systemic disease such as lupus erythematosus (secondary antiphospholipid syndrome).

As many as half of the patients with primary antiphospholipid syndrome may experience a decrease in visual acuity.[2] The funduscopic findings in primary antiphospholipid syndrome have recently been reviewed[2] and include retinal venous hypertortuosity, choriocapillary and retinal capillary dropout, vitreous haemorrhage or bands, serous macular detachment and optic disc oedema. Ischaemic optic neuropathy has also been described.[3] These findings were attributed to capillary vaso-occlusive disease and not to arterial occlusion and differ somewhat from the findings in secondary antiphospholipid syndrome, in which retinal arterial and vein occlusions may be quite frequent. We describe central retinal artery occlusion (CRAO) as a previously unreported complication of primary antiphospholipid syndrome.