1809 ICG-A Reveals Subclinical Choroidal Changes In Patients with Metastatic Malignant Disease

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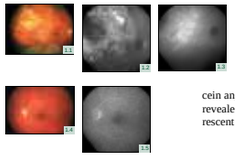
Objective

The purpose of this poster is to characterize unique ICG-Afindings in 5 cancer patients with established systemic malignancies.

Methods

Five patients with systemic malignancies underwent complete ophthalmic examination including fluorescein and pulse ICG angiography evaluation as part of a metastatic work-up. Four of five patients had previously identified metastatic ocular disease in at least one eye (lung, breast); while the fifth was grossly uninvolved OU (skin melanoma).



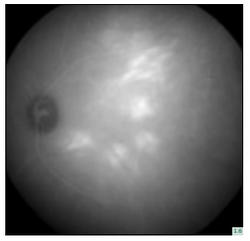
Patient 1

Patient 1 (metastatic lung cancer) demonstrated exudative retinal detachment with massive choroidal tumor infiltration OD (1.1-1.3); normal fundoscopy and fluorescein angiography OS (1.4 & 1.5). Pulse ICG-A revealed multi-focal 1/2-1 disc diameter hyperfluorescent choroidal lesions within the macula OS (1.6).

Results

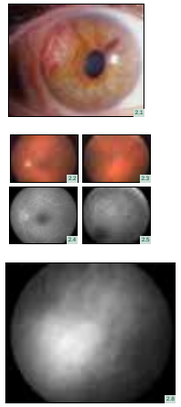
Eyes with normal findings on clinical fundoscopy or fluorescein angiography revealed patchy multifocal hyperfluorescent streaks in the posterior pole or mid-periphery in the late inversion phase of ICG-A.

Patient	Primary Malignancy	Sex	Age	Sites of Metastasis	Interval:Dx of 1° Malignancy to Metastasis	Interval: Metastasis to ICG-A	Pulse ICG-A Findings
1	Lung Cancer *[Non-smallcell/adenocarcinoma]*	Female	47	Thyroid, Choroid Brain	8 mths	1 week	Posterior Pole:patchy multifocal hyperfluorescent streaks in clinically uninvolved eye.
2	Breast Cancer *[Infiltratingductal]*	Male	57	Iris, Bone Skin, Choroid	0 mths	1 week	Posterior Pole/Periphery:patchy multifocal hyperfluorescent streaks OU.
3	Breast Cancer *[Infiltratingductal]*	Female	38	Bone Choroid	34 mths	2 weeks	Posterior Pole:patchy multifocal hyperfluorescent streaks in clinically uninvolved eye.
4	Breast Cancer *[Infiltratingductal]*	Female	52	Brain, Choroid Bone	24 mths	1 week	Periphery:patchy multifocal hyperfluorescent streaks OU.
5	Skin Cancer *[Malignant Melanoma - Clark Level V]*	Male	60	Dermal Metastasis	0 mths	4 weeks	Periphery:patchy multifocal hyperfluorescent streaks OU.



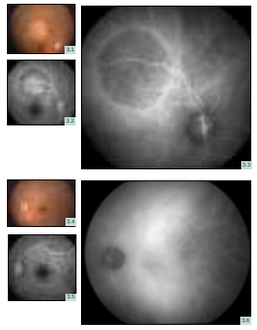
Patient 2

Patient 2 (male breast cancer) demonstrated a 4mm metastatic iris tumor involving the angle of the right eye (2.1). Fundoscopy and fluorescein angiography were normal OU (2.2-2.5). Pulse ICG-A(2.6) revealed diffuse peripapillary hyperfluorescence OD (2.7-2.8) and subtle, diffuse multi-focal streaks of hyperfluorescence in the midperphery.



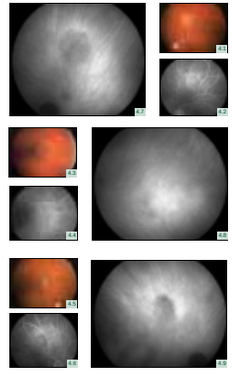
Patient 3

Patient 3 (breast cancer) demonstrated choroidal metastatis in the right eye (3.1-3.3) with normal fundoscopy and FA OS (3.4-3.5). Pulse ICG-Arevealed patchy multifocal hyperfluorescent streaks in the posterior pole of the uninvolved eye. (3.6).



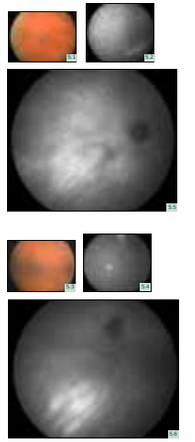
Patient 4

Patient 4 (breast cancer) demonstrated choroidal metastatis OU (4.1-4.6). Pulse ICG-Arevealed late phase patchy multifocal hyperfluorescent streaks in the periphery OU (4.7-4.9).



Patient 5

Patient 5 (skin melanoma) demonstrated symmetrical, irregular chorio-retinal RPE disturbances in a juxtapapillary and temporal macular distribution fundoscopically and on FA in both eyes (5.1-5.4). Pulse ICG-A revealed mid phase hypofluorescence and late phase hyperfluorescence in the midperiphery OU (5.5-5.6).



Discussion

Five patients with systemic carcinoma and ocular tumor metastases were examined with IV-FA and pulse ICG-A. All five demonstrated a specific ICG-A pattern of **Patchy Multifocal Hyperfluorescent Streaks (PMHS)** of the choroid, noted as an incidental finding. The PMHS pattern was not contiguous with clinically observable metastatic tumor lesions of the posterior segment, and always appeared as a discrete area of choroidal involvement.

Stephens & Shields (Ophthalmology 1979) found that the choroid was the most likely part of the eye to be first involved by metastatic tumors (93% of cases on histopathology). They found that metastatic eye disease presented first 31% of the time, while the primary tumor presented first 69% of the time. There was a striking difference by tumor type, with breast cancer presenting in the eye first only 12.8% of the time, while lung cancer presented in the eye first 70% of the time. Histopathologic reviews of metastatic breast cancer reveal tumor cells within the choroid with an acinar structure, filled with mucin centrally. Lung cancer metastatic to the choroid demonstrates cords and lobules of tumor, often containing vacules of mucin-like material.

As ICG dye is known to be lipophilic, we speculate that this pattern of increased relative fluorescence on pulse ICG-Amay represent:

- biochemical bonding of ICG to mucinous material within additional, but not yet clinically evident, foci of metatastasis,
- a change in vascular leakage due to a modification of the choroidal vascular phenotype which can be induced by metastatic tumors,
- alteration of a hypothetical carrier transport mechanism within the retinal vascular-RPE-choroidal complex capable of moving ICG dye more rapidly into the choriocapillaris intersitial space when compromised by early metastatic disease, or
- the influence of circulating serum tumor antibodies on the choroidal vasculature, a potential remote effect of cancer.

Conclusions

- Unique, sub-clinical ICG angiographic findings **(PMHS)** were revealed in patients with known malignancy. These areas were identified from survey photographs exposed during late phase pulse ICG-A.
- The etiology of these hyperfluorescent fundus lesions is inconclusive. They may represent early metastatic disease, tumor recurrence or regression, choroidal infiltration, or autoimmune related cancer associated retinopathy (CAR).
- We suggest that a pulse ICG angiogram with a photographic survey of the posterior pole and periphery of both eyes be performed in patients undergoing diagnostic evaluation of cancer.

References

Desmettre T, Devoisselle JM, Mordon S. Fluorescence properties and metabolic features of indocyanine green as related to angiography. Survey of Ophthalmology 2000;45:15.

Spencer WH. Ophthalmic Pathology:An Atlas and Textbook. Philadelphia, WBSaunders 1986.

Stephens RF, Shields, JA. Diagnosis and management of cancer metastatic to the uvea: A Study of 70 cases. Ophthalmology 86: 1336-1349, 1979

Stevens RA, Saine PJ, Cavender JC. Pulse Administration of ICG During Choroidal Angiography Increases Visualization of Vascular Details. IOVS Volume 40:4:S129, 1999.