EXUDATIVE AMD REFRACTORY TO ANTI VEGF THERAPY
IN PATIENTS WITH MALIGNANCY

Irene Tan MBBS(Hons)
Randev Mendis BSc(Hon), MBChB(UK), MRCS(Edin), FRCOphth(UK) , FRANZCO(Australia)

Purpose

Choroidal neovascularization (CNV) and malignancy are dependent on vascular endothelial growth factor (VEGF) for progression.

Systemic VEGF production is required and augmented in malignancy. It is possible that this increased systemic production could induce, augment and sustain secondary CNV from any cause. Furthermore this could also lead to poor response to anti VEGF agents.

There is paucity in the literature documenting this association

Methods

This was a descriptive study of consecutive patients presenting with CNV and malignancy or patients while on treatment for CNV who developed malignancy between 2012 and 2015, at the Canberra Retina Clinic, Canberra, Australia.

Nine patients with CNV secondary age related macular degeneration (AMD), myopia and chronic central serous retinopathy (CCSR) were identified.

CNV was confirmed with standard imaging studies that included fluorescein angiography and spectral domain ocular coherence tomography. The cancer type, stage, treatment and temporal relation to wet CNV presentation were obtained from case record.

Refractory response to anti VEGF agents in patients with CNV was defined as persistence of sub-retinal and intra-retinal fluid on a monthly treatment schedule with the standard dose of these agents. Similar response was recorded with all three commercially available anti VEGF agents.

Results

There were six patients with CNV secondary to AMD and co existent cancer. Two patients had bilateral wet AMD. One patient had CNV secondary to myopia and the other patient CNV secondary to chronic central serous retinopathy. The male female distribution was 50% in patients with AMD. The patient demographic data, imaging data, cancer type and treatment and neovascualr AMD subtype and anti VEGF agent used are detailed in table 1 and figure 1.

Conclusion

Active malignancy of any type was associated with a poor response to anti VEGF agents in this group of patients with CNV secondary to AMD, CCSR and myopia. Treatment and remission from cancer was associated with response to anti VEGF treatment. These results require further investigation as these may benefit from dose escalation for control.

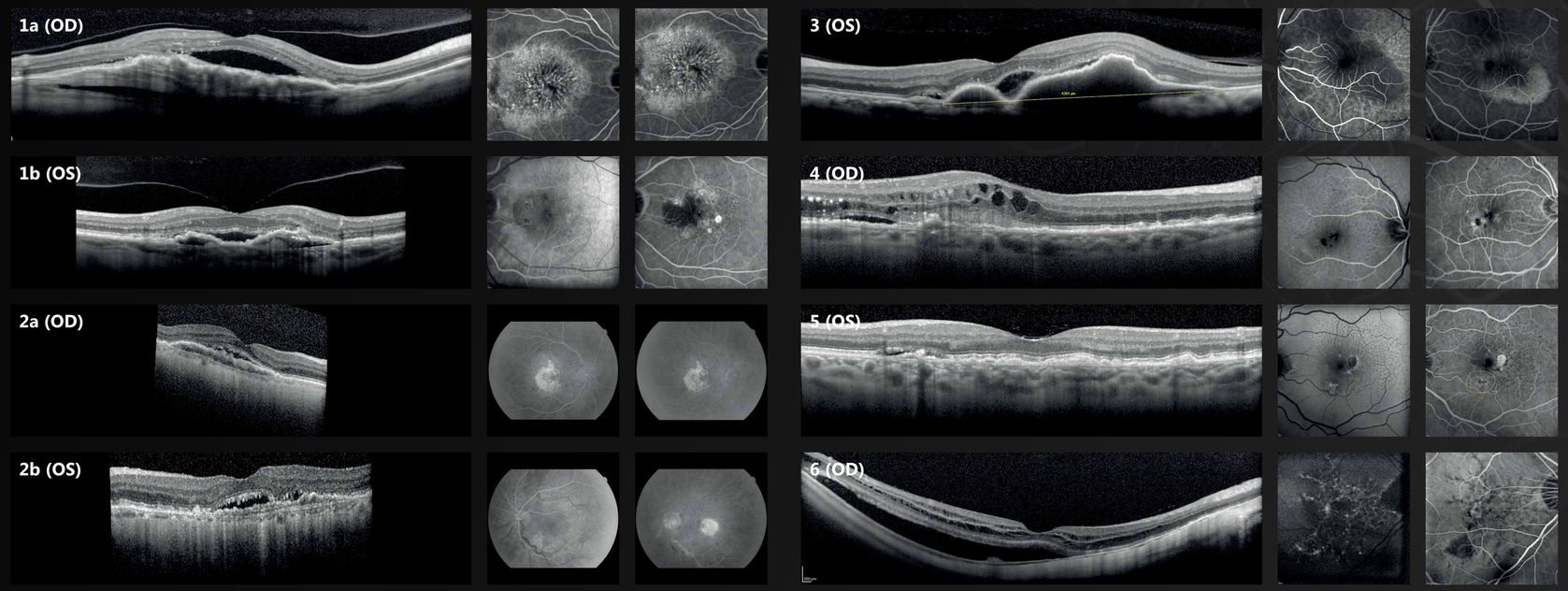

Table 1: Summary of cases

Pt	Age	Sex	BCVA on presentation		Latest BCVA		Eye affected	Diagnosis	Type of cancer	Time interval between cancer diagnosis and AMD diagnosis or deterioration	Anti-VEGF treatment†	No. of injections	Cancer treatment	Cancer outcome	AMD outcome
			OD	OS	OD	OS									
1	80	M	CF	6/9-1	6/12-2	6/9	OD	Exudative AMD with large subfoveal CNV	Grade 2 distal pancreatic non-functioning neuroendocrine tumour	6 months	R A	15 2	Distal pancreatectomy and splenectomy	In remission	Left eye developed exudative AMD 4 months later but with anti-VEGF treatment both eyes now have good control of exudative features
2	71	M	6/15	6/6	6/15-2	6/12	OD	Large central PED with CNVM progression*	Right lung T3N2M0 adenosquamous carcinoma	2 months	R A	20 9	Planned for pneumonectomy but inoperable. Chemotherapy (gemcitabine, carboplatin, vinorelbine), radiotherapy and immunotherapy with nivolumab but ceased after a month	Metastasis of cancer	Left eye developed PED with serous component 13 months later Latest review – OD persistent SRF and PED but left eye nil SRF/IRF
3	60	F	6/5	6/12	6/6-2	6/9-1	OS	PED + SRF + occult CNV	Left breast high grade ductal carcinoma in situ	6 weeks	R A	4 9	Wide local excision, sentinel lymph node biopsy and adjuvant radiotherapy.	In remission	Left eye trace subretinal fluid
4	88	F	6/12	6/6-2	6/9	6/9	OD	Subfoveal occult CNV	Right breast T2 N0 M0 grade 3 invasive ductal carcinoma	6 months	R	15	Wide local excision, sentinel lymph node biopsy & adjuvant radiotherapy. Recurrence – mastectomy, adjuvant radiotherapy and endocrine therapy with letrozole	Possible liver metastasis	PED, nil SRF/RF
5	74	M	6/9-1	6/6-2	6/6-3	6/9	OS	Exudative AMD*	Stage yp T3 N3a M0 gastric adenocardinoma	3 months	R A	10 2	Total radical gastrectomy, neoadjuvant chemotherapy (MAGIC chemoprotocol using erpirubicin, cisplatin and fluorouracil)	In remission	PED and SRF
6	83	F	6/12-2	6/9	6/12+2	6/6-1	OD	Subfoveal CNV AMD*	Stage 3c melanoma	2 months (between discontinuation of chemotherapy and vision deterioration)	R A	3 3	Resection, axillary lymph node clearance. Local recurrence and metastatic disease à BRAF inhibitor vemurafenib but ceased after a month	Recurrence and metastatic disease	Reduction in SRF

R, Ranibizumab; A, Aflibercept; TNM, tumour-node-metastasis system classifies cancer by the size and extent of the primary tumour (T), involvement of the regional lymph nodes (N), and the presence or absence of distant metastases (M); yp, pathological data following systemic therapy prior to surgery (American Joint Committee on Cancer, 2016).
*Patient had known stable AMD before sudden deterioration; †All patients received Ranibizumab and was then switched to Aflibercept except for patient 2 who received Ranibizumab, Aflibercept and then switched back to Ranibizumab and patient 4 who have received only Ranibizumab.