

**Case Report****The Hidden Salmon Patch: Ocular Lymphoma Mistaken as Vogt Koyanagi Disease**

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**Abstract**

Ocular inflammation from various causes may have similar clinical presentation thus careful clinical evaluations are mandatory particularly when the disease appear to be resistant to treatment. This paper reports a case of ocular lymphoma which was initially treated as Vogt Koyanagi Harada disease at a different centre. A 65-year-old Sudanese man complained of gradual worsening left eye vision. Careful ocular and slit lamp examination revealed a conjunctival lesion with choroidal infiltration as well as exudative retinal detachment. Computed tomography scan (CT scan) showed left eye axial proptosis, and a homogenous enhancing mass at the posterior coat of the globe. Tissue biopsy of the conjunctival lesion revealed marginal Zone B cell (MALT type), low grade, non-Hodgkin's lymphoma. AS the ocular signs and symptoms progressed, chemotherapy was initiated. The proptosis, exudative retinal detachment, disc hyperemia and swelling improved after chemotherapy. The post treatment CT scan showed reduction of the posterior ocular coat mass. The possibility of malignant lymphoma should be considered in patients with resistant uveitis despite administration of corticosteroid. Ocular lymphoma is an indolent tumour with good prognosis. Careful ocular examination, adequate imaging studies followed by early surgical biopsy will contribute to early diagnosis.

**Keywords:** intraocular lymphoma, MALT lymphoma, orbital neoplasms, uveitis, Vogt Koyanagi Harada disease

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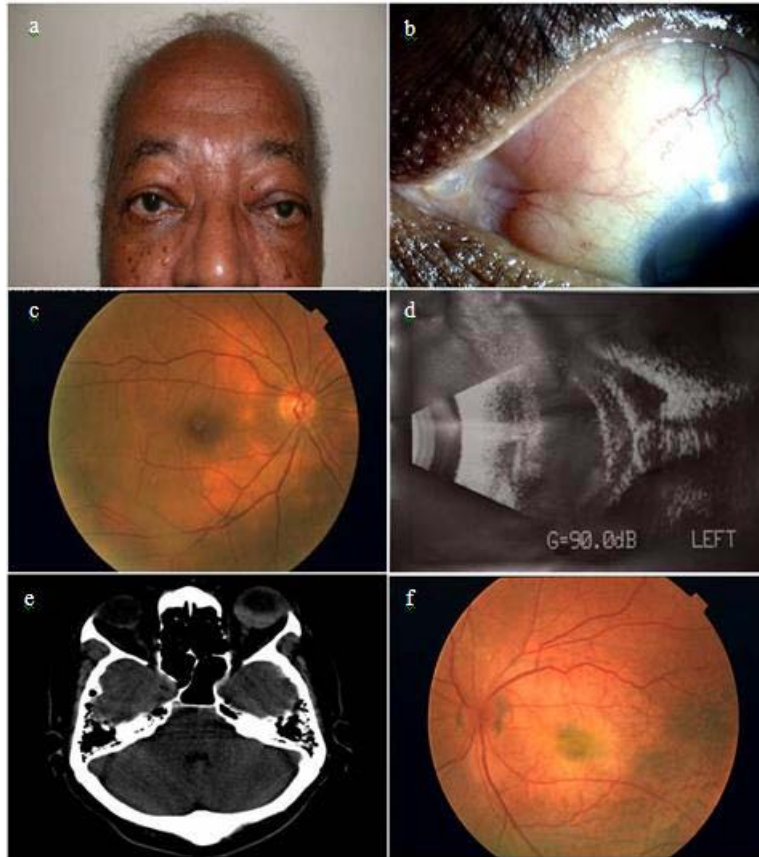
**Introduction**

About 5 to 10% of extranodal lymphomas are orbital lymphomas. They are uncommon, making up only 1% of all non-Hodgkin's lymphoma (1,2). However, in adults aged 60 years and older, the most common primary orbital tumour is lymphoma (3).

Extranodal marginal-zone B-cell lymphomas of mucosa-associated lymphoid tissue (MALT) lymphomas are the majority of orbital or conjunctival non-Hodgkin's lymphomas (4). Primary uveal lymphoma which is usually unilateral is quite an uncommon disease. On the other hand, primary vitreoretinal lymphoma can invade the central nervous

system (CNS) due to its aggressive nature and may be bilateral (5).

Palpebral swelling, blepharoptosis, proptosis, tumour formation and diplopia are among the features of primary malignant lymphoma (6). Orbital lymphoma can either be a primary disease or secondary from systemic lymphoma. Knowles et al. (7) reported that systemic lymphoma was associated with orbital lymphoma in 35% of cases, involving the conjunctiva in 20% of cases and eyelid in 67% of cases. Systemic lymphoma can develop in patients with solely orbital disease even after several years.



**Figure 1:** (a) Proptosis with bilateral upper lid fullness (b) Conjunctival salmon patch underneath the upper lid (c) Multiple choroidal infiltrates in the right fundus (d) B-scan showing a thickened choroid and retinal detachment (e) CT Scan of the orbit revealing a left axial proptosis with a homogenous enhancing mass at the posterior aspect of the globe (f) Left fundus shows a swollen optic disc and a choroidal mass

This is a case report of a successfully managed case of primary uveal lymphoma with conjunctival and orbital extension, initially masquerading an ocular inflammatory disorder, i.e. Vogt Koyanagi Harada disease. This case highlights the importance of early detection and diagnosis of masquerade syndrome in elderly patients.

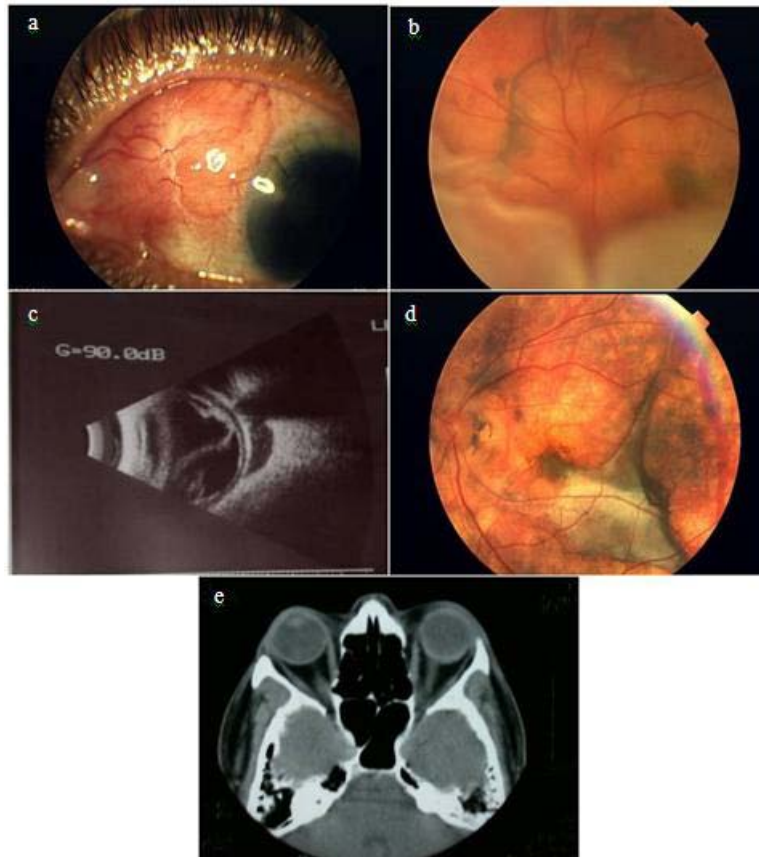
### Case Report

A 65-year-old Sudanese male was referred to Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Eye Centre with a provisional diagnosis of Vogt Koyanagi Harada disease of the left eye. Prior to presentation, he had been on 6 months of oral prednisolone for painless red left eye and progressive blurring of vision. Unfortunately, despite treatment, his condition did not improve. He denied any other ocular or systemic symptoms. He had no significant past medical, ocular, family or drug history. On presentation, his right visual acuity was 6/9 N5 and left visual acuity was CF N48. There was no relative

afferent papillary defect detected. Intraocular pressure was 16 mmHg in both eyes. His left eye was noted to be proptosed (Fig. 1a) and there were fullness of the upper lids bilaterally. Further careful evaluation revealed conjunctiva salmon patch lesions underneath both upper lids (Fig. 1b).

On funduscopy, the right fundus revealed multiple choroidal infiltrations with mild optic disc swelling (Fig. 1c). Unfortunately, patient also had left eye dense cataract which obstructed his fundus view. However, the B-scan ultrasound investigation of the left eye showed a thickened choroid with retinal detachment (Fig. 1d). Systemic examination was normal. Based on these findings, a diagnosis of bilateral ocular lymphoma was made.

Further blood investigations performed were unremarkable. CT scan of the orbit confirmed a left axial proptosis, and showed a homogenous enhancing mass at the posterior aspect of the globe (Fig. 1e). Additional CT brain, abdomen, thorax and bone



**Figure 2:** (a) Left conjunctival salmon patch appear to have increased in size (b) Worsening of left optic disc swelling with a development of an inferior exudative retinal detachment (c) Development of an inferior exudative retinal detachment on B-Scan (d) Improvement of optic disc hyperaemia with development of subretinal fibrosis after chemotherapy (e) Improvement of the left axial proptosis with reduction of the mass posterior to the globe after chemotherapy

marrow biopsy were normal. Tissue biopsy of the conjunctival lesion revealed marginal zone B-cell (MALT type), low-grade, non-Hodgkin's lymphoma, which confirmed the diagnosis. He was then referred to the Haematology team who initially decided on conservative management at that time. He underwent an uncomplicated left extracapsular cataract extraction with intraocular lens (IOL) implantation. However, his left eye vision did not improve.

The fundus photograph after surgery better demonstrates his left swollen optic disc and choroidal lesion affecting the macula (Fig. 1f).

He was initially observed over a 6 months period. However, the conjunctival lesion became more injected and swollen (Fig. 2a) and the left optic disc became more hyperaemic and swollen although his vision remained the same. He also developed an inferior exudative retinal detachment (Fig. 2b & Fig. 2c).

At this stage he was then commenced on chemotherapy (Rituximab, Cyclophosphamide,

Vincristine, Prednisolone) by the Haematology team which improved the proptosis, exudative retinal detachment and disc hyperaemia and swelling (Fig. 2d). The post treatment CT also showed reduction of the posterior ocular coat mass (Fig. 2e).

To date, this patient remains well. His vision is stable and repeat CT scans thereafter reveals no evidence of recurrences.

## Discussion

Non-Hodgkin's lymphoma of the orbit is uncommon, involving only 1% of cases. Approximately, 90% and 50-78% of all primary eye lymphomas are ocular adnexal marginal zone B-cell (MALT type) lymphoma in Japan and Korea, and Western countries respectively (8).

Lymphoid tumours in the conjunctiva can be an isolated lesion or part of systemic lymphoma manifestation (9). Knowles et al. (7) reported that systemic lymphoma was associated with orbital

lymphoma in 35% of cases, with conjunctival lymphoma in 20% of cases, and with eyelid lymphoma in 67% of cases.

At presentation, the orbit (40%) is the most commonly involved tissue, the conjunctiva is involved in 35-40% of cases, 10-15% in the lacrimal gland and 10% involving the eyelid. Only 10-15% of cases are bilateral. The term 'salmon patch' is widely used as clinically, the lesion is comparable to that of smoked salmon; as it is a pink, diffuse and slightly raised infiltrate in the stroma or underneath the Tenon's fascia at the fornices (10).

Systemic lymphoma can develop in patients with solely orbital disease even after several years. Several studies have shown the risk of developing systemic lymphoma after 5 and 10 years is around 30% and 79% respectively (11,12). Bilateral orbital involvement, eyelid and lacrimal gland lymphoma were significant factors for the development of systemic lymphoma (11). Besides that, high number of tumours as well as location of the tumour at an extralimbal site (fornix or midbulbar conjunctiva) are also predictive of systemic lymphoma (12).

Patients with uveitis at extreme age and non responsive to corticosteroids should be suspected to have masquerade syndrome. In tertiary uveitis centres, 2-3% of all patients seen have neoplastic masquerade syndromes. The commonest cause of neoplastic masquerade syndromes is primary CNS lymphoma (PCNSL), of which 98% are non-Hodgkin's B-cell lymphoma (13).

At presentation, the disease may be unilateral however after several months bilateral involvement may be seen. Anterior examination of the eye with slit-lamp biomicroscopy often shows keratic precipitates on corneal endothelium, mild anterior segment inflammation, with aqueous cells and flare, and rarely pseudohypopyon. Chorioretinal infiltration without cystoid macular edema, vasculitis with perivascular sheathing of retinal vessels, disc edema, and exudative retinal detachments with variable degree of vitritis may be seen.

In all cases of suspected orbital lymphoma, tissue biopsy of the lesion is mandatory to confirm the diagnosis. It is usually difficult to differentiate benign and malignant lymphoid tumour clinically. Presence of systemic lymphoma must be excluded via a thorough systemic evaluation. On histopathological examination, layers of lymphocytes are seen and

categorised as malignant lymphoma or 'reactive lymphoid hyperplasia'. Commonly, it is B-cell lymphoma and T-cell lymphoma is rarely noted (14). There are 2 types of ocular lymphomas; Primary vitreoretinal lymphoma and primary uveal lymphoma. Primary vitreoretinal lymphoma is common and maybe bilateral. It can invade the CNS due to its aggressive nature (5). It typically presents with significant vitritis unresponsive to immunosuppressant with variable amount of retinal or uveal involvement. It is of large B-cell tumour in origin and ocular disease usually precedes CNS disease. Early accurate diagnosis and treatment allows improved prognosis.

In contrast, primary uveal lymphoma is generally unilateral and rare. In the literature, there had been only 60 to 80 cases reported (5). This disease is said to occur as a result of proliferation of low grade malignant histiocytes and lymphocytes in the choroidal tissue with subsequent involvement of conjunctiva or orbital tissues. However, MALT lymphoma arising from the conjunctiva with secondary uveal infiltration was recently published in a report (5). The diagnosis of primary uveal lymphoma can only be made after excluding systemic involvement at presentation as well as histopathological confirmation of the lesion. As illustrated in our patient's case, the biopsy of the salmon patch underneath our patient's left upper eyelid was done immediately upon diagnosis which confirmed the diagnosis of low grade, marginal zone B-cell (MALT type), non-Hodgkin's lymphoma.

Orbital lymphomas are indolent tumours which are normally localised (stage I E, Ann Arbor Staging System) and have good response to local radiotherapy or chemotherapy with favourable outcome. Various treatment options are available for these patients. Currently, there are only specific management plan for primary gastric MALT lymphoma. Meanwhile, for ocular lymphoma, the effectiveness surgical intervention, radiotherapy and chemotherapy are reported with no significant survival difference (15).

## Conclusion

It is important to have a high index of suspicion in uveitis patients who are non responsive to corticosteroids, especially in the extreme age group as the diagnosis of malignancy might be delayed. Systemic lymphoma can develop in patients with solely orbital disease even after several years. Therefore, patients with orbital lymphoma should have a long term systemic multidisciplinary follow-up.

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