Original Research Article

Ocular masquerade syndrome

Tasneem A F[1], Vittal Nayak I[2], Mohammad Mehdi Raji[3*], Aniket Ginodia[4], Pooja B Wagganavar[5], Kavya Krishnarao Deshapande[6]

[1]Professor, [2]Professor and HOD, [3,4,5]Resident, Department of Ophthalmology, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, INDIA.

Email: alhajftasneem@Gmail.com, vittalvn1@Gmail.com, dr.raji@yahoo.com, aniketginodia@gmail.com, poojavgnr@gmail.com, deshpandekavya6@gmail.com

Abstract

Ocular Masquerade syndrome is a group of disorders that occurs with chronic ocular inflammation which is usually misdiagnosed as a chronic idiopathic uveitis. due to neoplastic or nonneoplastic underlying diseases. The term "Masquerade syndrome" was first used by Theodore in 1967. Some of these underlying diseases are critically life threatening therefore early and accurate diagnosis is very important because early treatment can even delay the mortality and improved surveillance of patient. We present a series of three patients with chronic uveitis who were diagnosed as ocular masquerade syndrome due to Spermatocytic Seminoma of testis, Pleomorphic adenoma of soft palate and Hodgkin's lymphoma in our hospital from 2014 till 2016.

Key Words: Masquerade syndrome, chronic uveitis, spermatocytic seminoma of testis, pleomorphic adenoma of soft palate, Hodgkin's lymphoma, Intraocular, tumor.

***Address for Correspondence:**
Dr. Mohammad Mehdi Raji VIMS and RC, #82, EPIP Area, Whitefield, Bangalore-560066, Karnataka State, INDIA.
Email: dr.raji@yahoo.com

Received Date: 04/01/2017 Revised Date: 31/01/2017 Accepted Date: 13/02/2017
DOI: https://doi.org/10.26611/1009124

Access this article online	
Quick Response Code:	Website: www.medpulse.in
	Accessed Date: 23 February 2017

INTRODUCTION

Masquerade syndromes are those conditions that include the presence of intraocular cells but are not due to immune-mediated uveitic entities. These may be divided into neoplastic and nonneoplastic conditions. Masquerade syndromes account for nearly 5% of all patients with uveitis at tertiary referral.[1] The term 'Masquerade syndrome' was first used in ophthalmology by Theodore in 1967 to describe a conjunctival carcinoma that presented as chronic conjunctivitis[2]. Neoplastic masquerade syndromes can occur due to lymphoid or nonlymphoid malignancies which totally account for 2%-3% of all patients seen in tertiary uveitis referral clinics. The vast majority of these are patients with intraocular involvement from primary CNS lymphoma[3,] other lymphoid neoplastic masquerade syndromes may occur secondary to leukemia[4], systemic lymphoma and uveal lymphoid proliferations[5]. Table 1 shows list of nonlymphoid malignancies which could cause masquerade syndrome.

Table 1: Causes of Masquerade Syndrome Secondary to Nonlymphoid Malignancies

Sr. No	Particular
1	Uveal Melanoma[6]
2	Retinoblastoma[7]
3	Juvenile Xanthogranuloma[8]
4	Metastatic Tumors (E.g.; From Lung **and** Breast Cancers)
5	Bilateral Diffuse Uveal Melanocytic Proliferartion[9]

Masquerade syndrome also can occurred due to some nonneoplastic conditions. (Table 2)

Table 2: Nonneoplastic Causes of Masquerade Syndrome

Sr. No.	Particular
1	Retinitis Pigmentosa
2	Ocular Ischemic Syndrome[10]
3	Chronic Peripheral Rhegmatogenous Retinal Detachment[11]
4	Intraocular Foreign Bodies
5	Pigment Dispersion Syndrome
6	Bacterial Uveitis (E.g.; due to Nocardia, Tropheryma Whipplei)
7	Fungal Endophthalmitis (E.g.; due to Candida, Aspergillus, Coccidioides immitis)

It is usually bilateral but may have asymmetrical involvement[12]. Sites of ocular involvement can include the vitreous, retina, subretinal pigment epithelium (sub-RPE), and any combination thereof. The most common complaints of patients are decreased vision and floaters[1]. Examination reveals a variable degree of vitritis with the variable presence of anterior chamber cells. Retinal examination classically reveals creamy yellow subretinal infiltrates with overlying RPE detachments[1]. Sometimes, there is a lack of inflammatory features such as keratic precipitates and synechiae[12]. Many of these patients are mistakenly diagnosed with an autoimmune uveitis and treated with anti-inflammatory medication. This can improve the vitreous cellular infiltration, but the effect is not long lasting and the uveitis often becomes resistant to therapy[1]. We present a series of three patients with ocular masquerade syndrome due to different causes who were admitted in our hospital from 2014 till 2016.

CASE REPORT

CASE 1

A 35-year-old male presented with painless, unilateral blurring of vision in left eye since 15 days with history of infertility and a mass in left testis from 3 months. On examination of left eye, visual acuity was counting finger at 2m. Conjunctiva showed congestion with dilated, tortuous episcleral vessels present in all 4 quadrants. Cornea appeared steamy with loss of normal sheen. Posterior surface of cornea also showed multiple mutton fat KP's, which were brownish white in colour of variable sizes, present in a triangular fashion in the inferior part. Anterior chamber contained 4+ cells and 1+ to 2+ flare. There was loss of normal iris pattern (muddy iris). Pupil was 5mm, round, regular and sluggishly reactive. Iris pigments were present on anterior capsule of the lens with early cortical cataract. Intraocular pressure of 18mm of Hg was recorded on applanation tonometery. Fundus of left eye revealed hazy media with 4+ vitritis. Disc appeared slightly hyperaemic with normal vessels. Rest of the details could not be seen as media was hazy. In right eye, visual acuity was 20/20. No abnormality was found in right eye except early cortical sclerosis. Transscrotal open biopsy was taken from left testicular mass and sent for histopathology, in which the reports suggested spermatocytic seminoma of testis. (Fig.1)

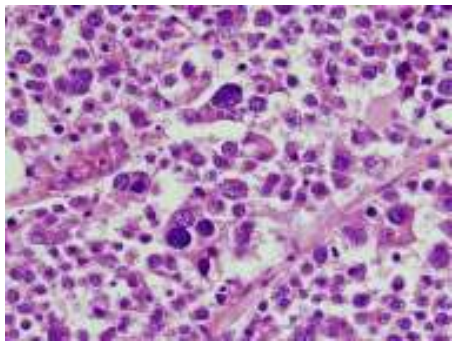

Figure 1: Spermatocytic Seminoma histopathology

Abdominopelvic CT scan revealed retroperitoneal and left external iliac lymphadenopathy with bilateral enlarged adrenal glands. CT thorax showed no evidence of metastasis, but pneumatocele were present bilaterally in the lung fields. Palliative therapy was planned, followed which chemotherapy with Bleomycin, Etoposide and Cisplatin (BEP) 4 cycles was to be started. Blood and urine investigations were normal. Tumor markers were also within normal limit. Our patient was simultaneously started with treatment for uveitis. Prednisolone acetate 1% eye drop 2 hourly, Nepafenac 0.1% eye drop 8 hourly, Homatropine 2% eye drop 12 hourly, Timolol maleate 0.5% eye drop 12 hourly, lubricant eye gel 8 hourly, cap Indomethacine SR 75 mg once daily with cap vit A, vit C and vit B complex was given. With these treatment patient showed no improvement in both signs and symptom. Was referred for immunologist opinion Unfortunately, the patient passed away, in midst of the treatment due to cardio-respiratory arrest[13].

CASE 2

A 29 year old female patient attended to our outpatient department with complaint of floaters and blurred vision in left eye since 1 month. Patient had a history of whitish swelling inside the oral cavity since 5 years. It was insidious in onset and non-progressive without any other systemic symptoms. Intraoral examination revealed a single ovoid whitish mass measuring 3×4 cm in diameter at the junction of soft and hard palate on the right side, which was firm, compressible with smooth surface and non-tender extending to the anterior pillar area with bilateral jugulodigastric lymphadenopathy without tenderness. Ophthalmic examination revealed visual acuity of 20/20 in right eye and 20/200 in left eye with normal colour vision in both eyes. Extra ocular movements were full range and painless. Right eye examination was within normal limits. Left eye examination showed mild bulbar conjunctiva hyperemia, multiple fine KP's in inferior quadrant of corneal endothelium, 3+ cells and 2+ flare in anterior chamber. Pupil was 4 mm in size, round, regular and reactive to

light. IOP was 16 mmHg in both eyes. Fundus examination in left eye showed slightly hazy media with 3+ vitritis. Optic disc was normal in size, shape and color with cup/disc ratio of 0.6 and normal vessels. Foveal reflex normally presented. Indirect ophthalmoscopy also revealed pars planitis, which suggested non-granulomatous intermediate uveitis of the left eye. OCT of macula was normal in left eye. CT-scan of palate revealed a well-defined hypodense soft palate lesion involving palatine tonsil and uvula with narrowing of nasopharyngeal area. FNAC biopsies from soft palate lesion was done and sent for histopathology, in which the report showed clusters of epithelial and myoepithelial cells embedded in mucopolysaccharide background, suggested pleomorphic adenoma of palate. After routine preoperative investigations, the patient was planned for surgical excision. Histopathologic report of excised lesion confirmed the same diagnosis.(Fig.2) Abdominopelvic CT scan, ultrasonography, chest X-Ray and lumbo-cervical X-ray were normal. Mantoux test, blood and urine investigations were normal. Tumor markers were also within normal limit. Surgical excision for palatine mass was planned for the patient. Patient received uveitis treatment for left eye. Prednisolone acetate 1% eye drop 2 hourly, homatropine 2% eye drop 8 hourly and timolol maleate 0.5% were started topically in left eye and tablet prednisolone 50 mg per day was started systemically and had been tapered over 6 weeks. Patient improved and since no any other cause for uveitis was detected it was inferred that patient's final ocular diagnosis as masquerade syndrome secondary to pleomorphic adenoma of palate.

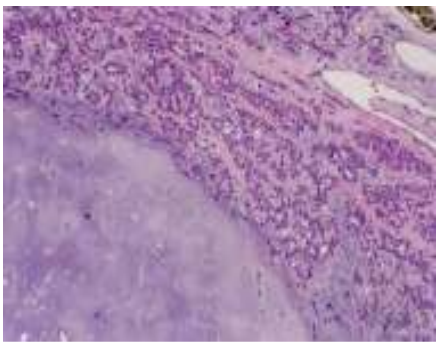

Figure 2: Pleomorphic Adenoma of Palate histopathology

CASE 3

A 32 year old female patient attended our outpatient department with complaint of blurring vision in left eye associated with swelling of left side of neck over a period of 2 months. She had history of low grade fever, night sweating and significant weight loss in recent few months. She was a known case of classical Hodgkin's lymphoma and received two courses of chemotherapy with ABVD regimen (Adriamycin, Bleomycin, Vinblastine and Dacarbazine) with two weeks interval ten years back. She did not have any remarkable past ocular history. Physical examination revealed level III middle jugular round lymph node on left side of neck measuring 6×6 cm without any other lymphadenopathy in the body. Patient did not have any neurological symptom or sign. On ocular examination she had best corrected visual acuity of 6/12 in right eye and counting fingers at 2 meter in left eye. Anterior segment examination with Slit lamp biomicroscopy revealed mild ciliary injection with fine keratic precipitates on the back of cornea with 1+ anterior chamber cells without flare in the right eye and mild ciliary injection with inferior mutton-fat keratic precipitates on the back of cornea with 3+ anterior chamber cells without flare in the left eye. Ocular movement was normal in both eyes. The intraocular pressure was 16 mmHg in both eyes. Dilated fundus examination showed 2+ vitreous cells with retinitis, focal perivascular sheathing and cystoid macular edema in the right eye and 3+ vitreous cells with optic disc edema, occlusive vasculitis of small retinal veins and cystoid macular edema in the left eye. There was no any evidence of intraocular mass lesion in both eyes. Systemic investigations included: Complete Blood Count with differential classification, Sedimentation Rate, Anti-Nuclear Antibody, Rheumatoid Factor, Human Immunodeficiency Virus test, Anticardiolipin antibody, Chest and Sacroiliac X-Ray, Toxoplasma gondii and cytomegalovirus serologies, Immuno-Histo-Chemistry study and whole body Positron Emission Tomography Scan which all supported the patient's first diagnosis of relapsed classical Hodgkin's lymphoma stage IB with both eyes panuveitis more severe in left eye presenting as Masquerade syndrome. Patient has been treated with systemic and topical corticosteroid. After 2 weeks of maximal ocular treatment her vision minimally improved to 6/9 partial in the right eye and 6/60 in the left eye. Patient has been referred to medical oncology service. Patient received two courses of ABVD regimen with 2 weeks interval.

DISCUSSION

Masquerade syndromes are those conditions that include the presence of intraocular cells but are not due to immune-mediated uveitic entities. These may be divided into neoplastic and nonneoplastic conditions.[1] Ocular masquerade syndrome was found in 5% of all of the uveitis patients.[14] Neoplastic masquerade syndromes can be due to lymphoid or nonlymphoid malignancies. The vast majority of these are patients with intraocular involvement from primary CNS lymphoma[3], other lymphoid neoplastic masquerade syndromes may occur

secondary to leukemia4, systemic lymphoma and uveal lymphoid proliferations[5]. For the proper diagnosis of Masquerade syndrome careful consideration to patient's past medical, ocular and familial history are very important. General physical examination and ocular examination and even response of ocular inflammation to the treatment can distinguish the underlying cause including any malignancy. The systemic workup should include Complete Blood Count with differential classification, Sedimentation Rate, Anti-Nuclear Antibody, Rheumatoid Factor, Human Immunodeficiency Virus test, Anticardiolipin antibody, Mantoux test, Chest CT scan, Sacroiliac X-Ray, Toxoplasma gondii and cytomegalovirus serologies, Immuno-Histo-Chemistry study. Spermatocytic seminoma is a type of germ cell tumour (GCT), accounting for less than 1% all GCTs. Unlike other GCTs, spermatocytic seminoma does not arise from intratubular germ cell neoplasia and is not associated with a history of cryptorchidism or bilaterality. The most common presentation of testicular cancer is a painless testicular mass. Although approximately two thirds of men with GCT have diminished fertility, it is an uncommon initial presentation.[15] For the diagnosis, the tumor markers, Ultrasonography of scrotum, CT abdomen and pelvis, CT thorax and histopathology of the tumour, help identify the testicular mass as spermatocytic seminoma of testis. A solid intratesticular mass in a postpubertal male should be considered a GCT until proven otherwise.[15] Inguinal orchidectomy with high ligation of the spermatic cord is performed. Testis sparing surgery for GCT is done if there is a small tumour in either a solitary testis or synchronous bilateral testicular masses. If elevated before orchidectomy, serum tumour marker levels should be measured after orchidectomy to determine if levels are declining, stable or rising. In our patient left hemiscrotectomy with high inguinal orchidectomy was done. Further palliative radiotherapy was planned, followed which chemotherapy with BEP 4 cycles was to be started. Tumours arising in the minor salivary glands account for upto 22% of all salivary gland neoplasm.[16] Pleomorphic adenoma (PA) is the commonest benign tumour to arise in the minor salivary glands. Majority are malignant with only 18% being benign. The commonest site of occurrence of pleomorphic adenomas of minor salivary glands is the palate followed by lip, buccal mucosa, floor of the mouth, tongue, tonsil, pharynx, retromolar area and nasal cavity.[17] The diagnosis of PA is established on the basis of history, physical examination, cytology, and histopathology. CT scan and MRI can provide information on the location and size of the tumor and extension to surrounding superficial and deep structures.[18] The treatment is strictly wide local excision with the removal of periosteum or bone if they are involved.[19] Both Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL) can present as inflammation or infection in the eye. Ocular involvement in Hodgkin's lymphoma is relatively rare, often occurring late in the course of the disease,[20] and can present with posterior uveitis or anterior uveitis with hypopyon or hyphema formation. Most of the patients have many systemic symptoms like fever, weight loss and lymphadenopathy. Ocular involvement in NHL is more common rather than Hodgkin's lymphoma and it has two different clinical forms: systemic NHL with ocular metastasis and NHL of the central nervous system presenting as Masquerade syndrome. In all patients with systemic NHL with ocular metastasis the choroid is infiltrated by malignant cells.[21] Most of patients with intraocular lymphoma clinically are presented with a refractory uveitis and complaining of eye pain, diminished vision and floaters due to associated vitritis.[22] The pathogonomic fundus changes included small, well-defined, round, yellow-white, dome shaped masses in the sub-RPE space with retinal hemorrhage, exudates, disc edema, vascular sheathing, vasculitis and retinitis.[23] A definitive diagnosis requires cytological confirmation of malignant lymphocytes. The best diagnostic method is cerebrospinal fluid sampling by lumbar puncture for the cytological study. If negative, then the next diagnostic option is to obtain vitreous sample by standard three-port pars plana vitrectomy for the cytological study. The diagnosis can finally be established in 95% of patients.[24] It has been suggested that the diagnostic value of vitrectomy may be improved by adding analysis for interleukin-10 (IL-10) and interleukin- 6 (IL-6). Whitcup and colleagues[25] demonstrated that the IL-10/IL-6 ratio was greater than 1 in all of 5 patients with intraocular lymphoma and in none of 13 control patients with intraocular inflammation unrelated to a malignant process. The early and accurate diagnosis is very important because early treatment can even delay the mortality and improved surveillance of patient.

CONCLUSION

Spermatocytic Seminoma of testis, Pleomorphic adenoma of soft palate and Hodgkin's lymphoma are by no mean the only malignancies that masquerade as ocular inflammation. There are many diseases both malignancies and nonmalignant etiologies that can manifest as chronic uveitis. Masquerade syndromes represent the uncommon presentation of rare disease. The primary diagnosis for the related underlying cause if not proper can lead to inappropriate therapy, which may not be effective to control the intraocular inflammation and cause irreversible effect on the patient's final visual outcome. In

case of any unresponsive chronic intraocular inflammation to maximal medical therapy always Masquerade syndrome due to neoplastic or nonneoplastic entities should be ruled out. A proper diagnostic approach and careful general examination in such cases include making a list of possible differential diagnosis will help in early diagnosis of a Masquerade syndrome. Treatment of the malignancy or underlying condition is required to control the uveitis and also plays a life-saving role to the patient.

REFERRENCES

1. Moorthy RS, Rao PK, Read RW, Van Gelder RN, Vitale AT, Bodaghi B *et al*. Intraocular Inflammation and Uveitis. In: Gregory LS, Cantor LB, Weiss JS. Basic and Clinical Science Courses. 2014 ed. San Francisco: American Academy of Ophthalmology; 2014-2015:281-289.
2. Theodore FH: Conjunctival carcinoma masquerading as chronic conjunctivitis. Eye Ear Nose Throat Mo 1967; 46:1419-1420.
3. Chan CC, Fisson S, Bodaghi B. The future of primary intraocular lymphoma (retinal lymphoma). *Ocul Immunol Inflamm.* 2009; 1 7(6):375- 379.
4. Kincaid MC, Green WR. Ocular and orbital involvement in leukemia. *Surv Ophthalmol.* 198 3; 27(4):211 -232.
5. Jakobiec FA, Sacks E, Kronish JW, Weiss T, Smith M. Multifocal static creamy choroidal infiltrates. An early sign of lymphoid neoplasia. *Ophthalmology.* 198 7; 94(4):397- 406.
6. Fraser DJ Jr, Font RL. Ocular inflammation and hemorrhage as initial manifestations of uveal malignant melanoma. Incidence and prognosis. *Arch Ophthalmol.* 1979; 97(7):1311-1314.
7. Bhatnagar R, Vine AK. Diffuse infiltrating retinoblastoma. *Ophthalmology.*1991; 98(11):1657-1661.
8. Zamir E, Wang RC, Krishnakumar S, Aiello Leverant A, Dugel PU, Rao NA. Juvenile xanthogranuloma masquerading as pediatric chronic uveitis: a clinicopathologic study. *Surv Ophthalmol.* 2001; 46(2):164- 171.
9. Barr CC, Zimmerman LE, Curtin VT, Font RL. Bilateral diffuse melanocytic uveal tumors associated with systemic malignant neoplasms: a recently recognized syndrome. *Arch Ophthalmol.* 1982; 100(2):249-255.
10. Mendrinos E, Machinis TG, Pournaras CJ. Ocular ischemic syndrome. *Surv Ophthalmol.* 2010; 55(1):2-34.
11. Matsuo N, Takabatake M, Ueno H, Nakayama T, Matsuo T. Photoreceptor outer segments in the aqueous humor in rhegmatogenous retinal detachment. *Am JOphthalmol.* 1986; 101(6):673-679.
12. Sen HN, Chan Chi-Chao: Masquerade syndrome-Neoplasms. Yanoff: Ophthalmology, 4th edition, chapter 7.23, 788-792.
13. Tasneem AF, Shwetha BA, Kaur A, Benzy M. Ocular Masquerade Syndrome; A Case Report, Medplus-International Medical journal, September 2014; 1(9): 534-536.
14. Gass JD, Sever RJ, Grizzard WS, Clarkson JG, Blumenkranz M, Wind CA, *et al*. Multifocal pigment epithelial detachments by reticulum cell sarcoma. A characteristic funduscopic picture. Retina. 1984; 4(3):135-43.
15. Andrew J, Timothy D: Neoplasms of the testis.Wein: Campbell-Walsh urology 2011.10th edition. Chapter 31, 893-913.
16. Spiro SH (1986) Salivary Neoplasm: overview of a 35 years experience with 2807 patients. Head Neck Surg 8(3): 177–184.
17. Varghese BT, Sebastian P, Abraham EK, Mathews A (2003) Pleomorphic adenoma of minor salivary gland in the parapharyngeal space. World J Surg Oncol 1(1): 2.
18. Kaur S, Thami GP, Nagarkar NM. Pleomorphic adenoma of the hard palate. Indian J Dermatol Venerol Leprol 2003; 69:74-5.
19. Sreenivas SD. Pleomorphic adenoma of the palate: A case report. J Indian Dent Assoc 2011; 5:4.
20. Nussenblatt RB, Whitcup SM, Palestine AG. Masquerade syndromes. In: Nussenblatt RB, Whitcup SM, Palestine AG, eds. Uveitis: fundamentals and clinical practice. St. Louis: Mosby, 1996:385–395.
21. Saga T, Ohno S, Matsuda H, *et al*. Ocular involvement by a peripheral T-cell lymphoma. Arch Ophthalmol 1984; 102:399–402.
22. Whitcup SM, de Smet MD, Rubin BI, *et al*. Intraocular lymphoma. Clinical and histopathologic diagnosis. Ophthalmology 1993; 100:1399–1406.
23. Char DH, Ljung BM, Miller T, *et al*. Primary intraocular lymphoma (ocular reticulum cell sarcoma) diagnosis and management. Ophthalmology 1988; 95:625–630.
24. Buettner H, Bolling JP. Intravitreal large-cell lymphoma. Mayo Clin Proc 1993; 68:1011– 1015.
25. Whitcup SM, Stark-Vancs V, Wittes RE, *et al*. Association of interleukin 10 in the vitreous and cerebrospinal fluid and primary central nervous system lymphoma. Arch Ophthalmol 1997; 115:1157–1160.

Source of Support: None Declared
Conflict of Interest: None Declared