# Neoplastic Masquerade Syndromes in Patients With Uveitis

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• PURPOSE: To identify the demographic and clinical characteristics, along with the frequency, of neoplastic masquerade syndromes in a tertiary uveitis clinic.
• DESIGN: A retrospective observational cohort.
• METHODS: Demographic and clinical data on all patients presenting to the National Eye Institute (NEI) with uveitis between 2004 and 2012 were used to compare neoplastic masquerade syndromes and uveitis.
• RESULTS: A total of 853 patients presenting with uveitis were identified. Of these, 21 (2.5%) were diagnosed with neoplastic masquerade syndromes. The average age at presentation of masquerade syndrome patients was 57 years (median, 55; range, 38–78); for uveitis, 42 years (median, 43; range, 3-98) ($P = 0.0003$). There were 48% females in the masquerade syndromes group, compared with 59% females in the uveitis group. African American patients represented 9% of the masquerade syndrome patients and 36% of uveitis patients ($P = 0.01$). Mean worse eye visual acuity was 0.89 (20/160) in neoplastic masquerade syndromes, and 0.66 (20/100) in the uveitis group ($P = 0.21$). Of masquerade syndrome patients, 90% had posterior inflammation, compared with 63% of uveitis patients ($P = 0.006$). Of those with masquerade syndromes, 48% of patients had unilateral disease, compared with 27% of the uveitis patients ($P = 0.04$).
• CONCLUSIONS: Patients with neoplastic masquerade syndromes were more likely to be older, male, or non-African American and to have posterior segment inflammation and unilateral disease. Patients with masquerade syndromes also had worse visual acuity than did uveitis patients. These differences in clinical characteristics may help to raise the suspicion for neoplastic masquerade syndromes. (Am J Ophthalmol 2014;157:526–531. Published by Elsevier Inc.)

THE TERM *MASQUERADE SYNDROME* IS CLASSICALLY used to describe conditions that include as part of their manifestation the presence of intraocular infiltrating cells that are not due to immune-mediated uveitis entities.[1,2] The term *masquerade syndrome* was first used in ophthalmology by Theodore in 1967 to describe a conjunctival carcinoma that presented as chronic conjunctivitis.[3] Hematologic malignancies, retinoblastoma, retinal detachment or degeneration, and intraocular trauma are just a few of the disorders that may masquerade as uveitis, with intraocular lymphoma representing the most common neoplastic masquerade syndrome.[1,4] Neoplastic masquerade syndromes are known to represent a minority of cases seen in uveitis clinics, yet specific information regarding their prevalence or clinical characteristics is scarce, at best.[4] The importance of accurate and timely diagnosis cannot be overstated because making the correct diagnosis can be life saving.

The goal of this study was to identify the proportion of patients with masquerade syndromes in a tertiary uveitis clinic and to determine the baseline clinical characteristics of patients with masquerade syndromes.

## MATERIALS AND METHODS

ALL PATIENTS PRESENTING TO THE NATIONAL EYE INSTITUTE (NEI) between 2004 and 2012 with the preliminary diagnosis of uveitis were identified using a database search of the NEI's electronic medical records. A standard screening protocol for uveitis was followed for each patient, including erythrocyte sedimentation rate, complete blood counts, chemistries, HLA-B27 typing, determination of serum angiotensin-converting enzyme levels, urine analysis, tuberculosis testing, and serologic tests for syphilis. Because of the tertiary nature of our clinic, non-malignant masquerade syndromes, such as retinal detachment or trauma, are very rare and were not included in our search. The clinical, ophthalmologic, and laboratory data at baseline for the identified patients were collected in retrospective chart reviews. All patients were seen under an Institutional Review Board (National Institutes of Health)–approved clinical research protocol.

The baseline clinical characteristics of the neoplastic masquerade syndrome patients and the uveitis patients were gathered, with particular attention to sex and age at the onset of symptoms and presentation, anatomic site of uveitis, posterior segment findings, presumed initial diagnosis, definitive diagnosis, interval between the onset of symptoms and the time of final diagnosis, diagnostic

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procedures performed, presence and anatomic location of intraocular inflammation, and initial and final best-corrected visual acuity. The anatomic location and the activity of the inflammation were determined by using Standardization of Uveitis Nomenclature (SUN) criteria.[5] The initial best-corrected visual acuity was calculated by taking the mean of the logMAR visual acuity in better and worse eyes for bilateral cases and in the affected eye for unilateral cases.

Demographic and clinical data are presented with descriptive statistics. Univariate comparisons of characteristics between neoplastic masquerade syndrome patients and uveitis patients were made by using 2-sample *t* tests for continuous variables and $\chi^2$ tests for categorical variables. A 2-sided *P* value less than 0.05 was considered statistically significant. Because of the small sample size in the neoplastic masquerade group, a multivariate analysis was deemed inappropriate.

## RESULTS

A TOTAL OF 853 PATIENTS WITH COMPLETE DATA AND UVEITIS or ocular inflammation as the presenting diagnosis were identified. The average follow-up time for these patients was 5 years ± 4 years (median, 4; range, 0–27 years). The National Eye Institute (NEI) is a tertiary care center that accepts referrals from all over the world, including people of all ethnicities and ages. Nevertheless, most of the patients in this study were either Caucasian (46%) or African American (36%) and were referred from the mid-Atlantic region of the United States. Also, patients 21 years of age or younger represented 17% of our cohort. This is reflective of the average uveitis population, in which only 10% to 15% are children.[6] Less than 5% of patients were excluded due to incomplete data or follow-up.

Of the 853 patients, 21 (2.5%) were identified as having neoplastic masquerade syndromes, and 832 were diagnosed as having non-masquerade uveitis, of which 62 (7%) had infectious uveitis and 770 (93%) had non-infectious autoimmune uveitis.

For patients with neoplastic masquerade syndromes, the average length of time between the onset of symptoms and definitive diagnosis was 8 months (median, 7; range, 1–28 months). The average time to diagnosis from presentation to NEI was 2 months. The most commonly identified neoplasm among the patients with masquerade syndrome was primary intraocular/vitreoretinal lymphoma (PIOL/PVRL) (17 of 21; 81.1% of the neoplastic masquerade syndromes; 17 of 853; 2.0% of all cases of uveitis). Other masquerade syndromes were identified as follows: mucosal associated lymphoid tissue lymphoma of the optic nerve sheath (n = 1); chronic lymphocytic leukemia (n = 1), human T-lymphotropic virus T-cell leukemia (n = 1); and non-Hodgkin lymphoma (n = 1). Of the 21 (66.7%) patients, 14 were diagnosed using diagnostic vitrectomy and/or ocular tissue biopsy (optic nerve sheath biopsy [n = 1] or chorioretinal biopsy [n = 1]). Of the 14 vitrectomies, 12 were performed immediately upon referral, while the other 2 were followed first on immunosuppressants due to initial favorable response and were biopsied after 12 months of follow-up. Of the 21, 4 (19.0%) patients were diagnosed by brain biopsy (2) or lumbar puncture and cytology (2), and the other 3 (non-Hodgkin lymphoma, chronic lymphocytic leukemia, and human T-lymphotropic virus leukemia) were diagnosed systemically (Table 1).

When compared with patients with non-masquerade uveitis, patients with masquerade syndromes were more likely to be older, with an average age of 57 years (range, 38–78 years), as opposed to 42 years (range, 3–98 years) in the uveitis group (mean difference = 15.0; 95% confidence interval [CI] for the difference, 6.9-23.1; $P = 0.0003$). The proportion of patients 50 years of age or older was 95% in the masquerade group, compared with 38% in the uveitis group (odds ratio [OR], 32.7; 95% CI, 4.4-244.5; $P = 0.0001$). No patient 21 years of age or younger was diagnosed with a neoplastic masquerade syndrome. A total of 48% (10/21) of the masquerade syndrome patients were female, compared with 59% (489/832) in the uveitis group (OR, 1.6; 95% CI, 0.7-3.7; $P = 0.19$). Among the patients with masquerade syndrome, 13/21 (62%) were Caucasian, compared with 389/832 (47%) in the uveitis group (OR, 1.9; 95% CI, 0.8-4.5; $P = 0.13$). There were significantly fewer African American patients among the masquerade syndrome patients (2/21; 10%) compared with the uveitis group (301/832; 36%) (OR, 0.2; 95% CI, 0.04-0.80; $P = 0.01$) (Table 2).

The baseline visual acuity in the worse- and better-seeing eyes was not significantly different for the masquerade syndrome patients (logMAR 0.89 and 0.29 in the worse- and better-seeing eyes, respectively), compared with the uveitis group (logMAR 0.66 and 0.36 in the worse and better eyes, respectively) (mean difference, 0.23; 95% CI, −0.58-0.13; $P = 0.21$ and mean difference, 0.1; 95% CI, −0.19-0.33; $P = 0.59$, respectively).

Of the 21 patients with masquerade syndromes, 19 (90%) as opposed to 522 of the 832 uveitis patients (63%), presented with intermediate, posterior, or panuveitis (OR, 0.2; 95% CI, 0.0-0.77; $P = 0.006$). The proportion of patients with active intraocular disease, as determined by the presence of cells in the anterior chamber or vitreous haze on examination at the initial visit, was almost identical in the 2 groups, with 14/21 (67%) among the masquerade syndrome patients and 560/832 (67%) in the uveitis group. The proportion of individuals with unilateral disease, as opposed to bilateral disease, was higher in the masquerade group (10/21; 48%) than in the uveitis group (222/832; 27%) (OR, 2.5; 95% CI, 1.05-6.0; $P = 0.05$).