ORIGINAL ARTICLE

Final Diagnosis in Patients Referred with a Diagnosis of Neuroretinitis

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ABSTRACT

The purpose of this study was to determine final diagnosis of patients referred with a diagnosis of neuroretinitis. A retrospective study of 40 patients with optic disc oedema with macular star (ODOMS) referred with a diagnosis of neuroretinitis was conducted. The final diagnosis was neuroretinitis in 26 patients (65%), with most of these patients (96.1%) having unilateral involvement. Main underlying aetiologies included cat scratch disease (30.8%), rickettsiosis (19.2%), and idiopathic neuroretinitis (23.1%). The remaining 14 patients (35%) had ODOMS that had been mistaken for neuroretinitis. Of these patients, 42.8% were found to have a previously unknown malignant systemic hypertension in association with bilateral ODOMS. Neuroretinitis, usually unilateral, should be differentiated from other causes of unilateral or most often bilateral ODOMS that may masquerade as neuroretinitis, mainly malignant systemic hypertension. This is essential to avoid inappropriate work-up and management and subsequent potential visual or systemic morbidity.

Keywords: Cat scratch disease, macular star, neuroretinitis, optic disc oedema, rickettsiosis, systemic hypertension

INTRODUCTION

Neuroretinitis is a particular form of optic neuropathy typically characterised by acute unilateral visual loss with optic disc oedema and macular exudates arranged in a partial or complete star figure around the fovea.¹ It occurs more often in the third and fourth decades of life, with no gender predilection, and it is mostly unilateral.^{1,2} Neuroretinitis has been associated with a wide variety of infectious or inflammatory conditions, with cat scratch disease being the most common identifiable cause.^{1,2} On the other hand, a number of non-infectious and non-inflammatory disorders may present with optic disc oedema with macular star (ODOMS) that might be mistaken for neuroretinitis.^{1,2} Data on the rate of various conditions causing or mimicking neuroretinitis are lacking. The purpose of the current study was to assess diagnostic accuracy and aetiological

spectrum in patients with ODOMS referred with a diagnosis of neuroretinitis.

METHODS

We retrospectively reviewed the charts of 40 consecutive patients (47 eyes) with ODOMS referred to the Department of Ophthalmology of Fattouma Bourguiba University Hospital (Monastir, Tunisia) with a diagnosis of neuroretinitis. Cases were classified as having neuroretinitis or a condition mistaken for neuroretinitis, and any specific underlying aetiology was noted. All patients underwent a comprehensive history taking and detailed ophthalmic examination including measurement of Snellen best-corrected visual acuity (BCVA), slit-lamp examination, tonometry, and dilated fundus examination with contact or non-contact lenses. Fundus photography and optical coherence

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tomography (OCT) were performed in all patients. Fluorescein angiography was performed when necessary.

All patients with a final diagnosis of neuroretinitis underwent a comprehensive ocular and systemic history, including an extensive review of medical systems. Exposure history was explored, including recent travel, unpasteurised and uncooked foods, and animal contacts. Physical examination and laboratory work-up, including a complete blood count, erythrocyte sedimentation rate, C-reactive protein tests, and serum biochemical analysis, were performed when indicated. Serology tests for *Bartonella henselae* were performed in patients who had contacts with cats. Anterior chamber paracentesis for polymerase chain reaction for *Toxoplasma gondii* DNA was performed in selected cases. Further, according to the clinical suspicion, other serologic and immunologic tests were performed when indicated.

In patients with ODOMS mistaken for neuroretinitis, investigations were performed according to suspected underlying aetiology, including blood pressure measurement, cardiovascular examination, measurement of cerebrospinal fluid pressure, and visual field testing.

Mean follow-up was 12 months (range: 6–36 months). The study was approved by the local ethics committee of our institution.

RESULTS

Mean age of our patients was 37 years (range: 12–32 years). Thirty patients (75%) were male and 10 patients (25%) were female. Mean initial BCVA was 20/200 (range: 20/400–20/20).

Final diagnosis was concordant with initial diagnosis of neuroretinitis in 26 patients (65%), and discordant in the remaining 14 patients (35%).

Of 26 patients (27 eyes) with neuroretinitis, cat scratch disease was recorded in 8 patients (30.8%) (Figure 1), rickettsiosis in 5 patients (19.2%) (Figure 2), toxoplasmosis in 2 patients (7.7%), toxocariasis in 1 patient (3.8%), idiopathic vasculitis, aneurysms, and neuroretinitis (IRVAN) in 1 patient (3.8%), tubulointerstitial nephritis and uveitis (TINU) syndrome in 1 patient (3.8%), Behçet disease in 1 patient (3.8%), Vogt-Koyanagi-Harada disease in 1 patient (3.8%), and idiopathic neuroretinitis in 6 patients (23.1%) (Table 1).

The causes of the remaining 14 cases (20 eyes) of ODOMS masquerading as neuroretinitis included a previously unknown malignant hypertension ($n=6$; 42.8%) (Figure 3), branch retinal vein occlusion ($n=3$; 21.4%), idiopathic intracranial hypertension ($n=2$; 14.3%), diabetic papillopathy ($n=2$; 14.3%) (Figure 4), and anterior ischaemic optic neuropathy ($n=1$; 7.1%) (Table 2).

FIGURE 1 Red-free fundus photograph of the left eye of a 34-year-old patient with cat scratch disease shows optic disc oedema with telangiectatic vessels and a macular star.

FIGURE 2 Fundus photograph of the left eye of a 35-year-old patient with rickettsial disease shows optic disc oedema and a complete macular star.

TABLE 1 Causes of neuroretinitis in the present series.

Cause	Number of patients (N = 26)	%
Cat scratch disease	8	30.8
Rickettsiosis	5	19.2
Toxoplasmosis	2	7.8
Toxocariasis	1	3.8
IRVAN	1	3.8
TINU syndrome	1	3.8
Behçet disease	1	3.8
Vogt-Koyanagi-Harada disease	1	3.8
Idiopathic neuroretinitis	6	23.1

Note. IRVAN = idiopathic retinal vasculitis, aneurysms and neuroretinitis; TINU = tubulointerstitial nephritis and uveitis.

Systemic investigations in patients with previously unknown systemic hypertension revealed renal failure in 2 patients, and pheochromocytoma in 1 patient.

Patients with cat scratch disease and those with rickettsiosis were treated with doxycycline

FIGURE 3 A 29-year-old otherwise healthy man was referred for suspicion of infectious neuroretinitis in both eyes. Fundus photographs (A, B) show arterial narrowing, multiple cotton-wool spots, and a partial macular star in both eyes, and superficial peripapillary retinal haemorrhages in the left eye. Physical examination revealed a previously unknown severe systemic hypertension.

FIGURE 4 Fundus photograph of the left eye of a 33-year-old patient with diabetic papillopathy mistaken for neuroretinitis. Note the presence of optic disc oedema, optic disc telangiectatic vessels, and a macular star associated with retinal hard exudates due to clinically significant macular oedema.

TABLE 2 Systemic or ocular conditions masquerading as neuroretinitis.

Condition	Number of patients (N = 14)	%
Previously unknown systemic hypertension	6	42.8
Branch retinal vein occlusion	3	21.4
Idiopathic intracranial hypertension	2	14.3
Diabetic papillopathy	2	14.3
Anterior ischaemic optic neuropathy	1	7.1

200 mg/day for 4–6 weeks. Patients with ocular toxoplasmosis were treated with a combination of pyrimethamine (100 mg on day 1, followed by 50 mg/day), azithromycin (500 mg on day 1, followed by 250 mg/day), and folinic acid (15 mg/day) for 4 weeks. Three patients received additional corticosteroid therapy with gradual tapering. Patient with toxocariasis

was treated with prednisone (1 mg/kg/day, followed by a gradual tapering over 6 weeks).

Patient who presented IRVAN was treated by panretinal laser photocoagulation in both eyes together with intravitreal injection of acetamide of triamcinolone in one eye.

Patients with systemic hypertension were referred to cardiovascular specialist.

Patients with idiopathic intracranial pressure elevation were treated with oral acetazolamide.

Mean final BCVA was 20/32 (range: 20/200–20/20) in patients with neuroretinitis and 20/50 (range: 20/400–20/20) in patients with ODOMS masquerading as neuroretinitis. Visual prognosis appears to be good, with a final BCVA $\geq 20/40$ in 22 eyes (81.5%) in patients with neuroretinitis and in 12 eyes (60%) in patients with ODOMS masquerading as neuroretinitis.

DISCUSSION

To the best of our knowledge, our study is the first to evaluate diagnostic accuracy and to characterise aetiological spectrum in patients referred with a diagnosis of neuroretinitis. Our data show that the diagnosis of neuroretinitis could be confirmed in 65% of patients. Conversely, a substantial proportion of patients (35%) were found to have a masquerade syndrome. The patient's history, pattern of visual loss, and results of ophthalmic and general examination can help to differentiate neuroretinitis from other causes of ODOMS. In fact, a history of fever, skin rash, contact with a cat, scratch or inoculation site, and travelling in endemic area is rather to be associated with neuroretinitis. On the other hand, advanced patient's age, history of diabetes, systemic hypertension, or other cardiovascular morbidity should incite clinician to rule out other causes of ODOMS. In addition, laterality of optic nerve involvement is an important feature to differentiate neuroretinitis from other causes of ODOMS. In fact, the majority of

neuroretinitis cases are unilateral, and bilateral involvement is uncommon. In case of bilateral involvement, other causes of ODOMS should be ruled out before a diagnosis of neuroretinitis can be made.

A previously unknown systemic hypertension was by far the most common cause of ODOMS mistaken for neuroretinitis (42.8%) in our series. The association in both eyes of ODOMS with arterial narrowing, cotton wool spots, and superficial peripapillary retinal haemorrhages are indicative of hypertensive retinopathy.²⁻⁶ Optic disc oedema and retinopathy resolves after the hypertension is controlled. Blood pressure should be a part of initial work-up in patients with bilateral ODOMS even in young patients and in the absence of history of systemic hypertension. It is important to measure blood pressure repeatedly in the presence of normal initial readings, since high blood pressure can be paroxysmal for certain aetiologies of hypertension such as pheochromocytoma.³ Treatment of malignant hypertension should not be over-aggressive; in fact, several cases of a rapid reduction in vision and infarction of the optic nerve have been reported in patients after aggressive reduction of the blood pressure.^{3,4,7}

Our findings, together with those from previous reports, show that an array of conditions other than systemic hypertension can present with ODOMS that may mimic neuroretinitis. These include branch retinal vein occlusion, diabetic papillopathy, idiopathic intracranial hypertension, anterior ischaemic optic neuropathy, posterior vitreous traction, disc and juxtapapillary tumours including angioma, melanocytoma, and melanoma, and infiltrative and toxic optic neuropathy.^{2,8} The patient's history and a careful analysis of clinical findings associated with ODOMS can help to establish the definitive diagnosis.

Results of our study show that cat scratch disease is the most common aetiology of neuroretinitis, recorded in 30.8% of cases. In a previous study, 64.3% of 14 patients with neuroretinitis had evidence of past or present cat scratch disease infection.⁹ Neuroretinitis has been reported to occur in 1–2% of patients with cat scratch disease.¹⁰ Rickettsial disease was found to be the second most common cause of neuroretinitis in our series (19.2% of neuroretinitis cases). In a previous series, neuroretinitis was recorded in 25% of eyes of patients with rickettsial ocular disease.¹¹ Rickettsial disease should always be considered in the differential diagnosis of neuroretinitis in a patient living in or travelling back from a region endemic for rickettsiosis, even in the absence of systemic signs. Neuroretinitis has been associated with an array of other bacterial, viral, parasitic, and fungal infections.^{1,2} Proper clinical diagnosis of any of these infections is based on epidemiological data, history, systemic symptoms and signs, and the pattern of eventual associated

ocular findings. The association of foci of retinitis or retinochoroiditis on fundus examination may orient to infectious aetiology of neuroretinitis. Diagnosis is confirmed by serologic testing and/or polymerase chain reaction. Neuroretinitis also has been reported in the setting of a variety of inflammatory and non-inflammatory disorders, including sarcoidosis, inflammatory bowel disease, periarteritis nodosa, IRVAN syndrome, and post-vaccination.^{1,2} In nearly one quarter of our cases, neuroretinitis was idiopathic. Diagnosis of idiopathic neuroretinitis should be a diagnosis of exclusion, made after ruling out other known causes of neuroretinitis.^{1,2} A non-specific viral illness has been reported before or during visual loss.^{1,2}

Neuroretinitis is usually a self-limited disorder with a good visual prognosis^{1-2,12-13}; however, few reports describe recurrent cases of neuroretinitis with progressive visual loss.^{2,14-15} The overall visual prognosis in our series appears to be good, with a final BCVA $\geq 20/40$ in 81.5% of eyes in patients with neuroretinitis and in 60% eyes in patients masquerading as neuroretinitis.

In conclusion, besides cat scratch disease, an array of other infectious and inflammatory conditions may present with neuroretinitis. Clinician also should be aware that ODOMS associated with unknown malignant hypertension or other non-inflammatory conditions may masquerade as neuroretinitis. An accurate differential diagnosis is mandatory to avoid inappropriate work-up and management and subsequent potential visual or systemic morbidity.

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