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Differential Diagnosis of Acute Bilateral Uveitis in the Rheumatologist's Office☆

Diagnóstico diferencial de uveítis bilateral aguda en la consulta del reumatólogo

To the Editor,

Given the multiorgan involvement in systemic diseases, there is a growing trend toward the establishment of multidisciplinary services for outpatient care. In recent years, we are witnessing the creation of units shared with dermatologists, pulmonologists or nephrologists and, recently, ophthalmologists. Uveitis is an isolated condition in 50% of the cases; however, a detailed interview, thorough physical examination and general laboratory tests with an immunological study reveal an underlying rheumatic disease in the remaining 50%.[1] There are conditions, like the spondyloarthropathies and sarcoidosis, with which uveitis is frequently associated; however, there are less common diseases that we should not overlook.

We report the case of a 46-year-old woman with a history of hepatitis C virus, endometriosis and migraine who presented with red eye and a sharp pain in her left eye. She was diagnosed with anterior uveitis and, once infection had been ruled out as the cause, was treated with topical glucocorticoids. Over the following weeks, she developed anterior uveitis in her right eye and it appeared anew in the contralateral eye, neither of which resolved completely with the treatment. She had no accompanying clinical manifestations or signs or symptoms suggestive of autoimmune or infectious disease. Laboratory tests revealed acute renal failure, with a creatinine level of 2.15 mg/dL and proteinuria of 1 g in 24 h, with no microhematuria, glycosuria or sterile pyuria. Given the suspicion of an underlying systemic disease, the patient was referred for further evaluation. She underwent an immunological study that included rheumatoid factor, antineutrophil cytoplasmic antibodies (ANCA) and antinuclear antibodies (ANA), all of which were negative; her complement and immunoglobulin levels were normal, tests for HLA-B27 and HLA-B51 were both negative, and her angiotensin-converting enzyme level was normal. In view of the progressive deterioration of her glomerular filtration rate, renal biopsy was performed. The results of the histological study were consistent with acute tubulointerstitial nephritis. On the basis of the clinical, analytical and histological findings, she was diagnosed with tubulointerstitial nephritis with uveitis (TINU), and a regimen of oral glucocorticoids was begun at doses of 0.5 mg/kg/day, and tapered until they were discontinued after 8 months of treatment. The patient's renal function returned to normal, the proteinuria disappeared and, after 12 months of follow-up, she has had no new episodes of uveitis.

Acute tubulointerstitial nephritis with uveitis (TINU syndrome) is an uncommon disorder that is somewhat unknown to rheumatologists. It should be considered in the differential diagnosis of those patients with recurrent uveitis who are frequently to be found in our offices.[1] Depending on the pattern of presentation, the differential diagnosis of uveitides includes the diseases summarized in Table 1. The differential diagnosis of acute anterior uveitis should include spondyloarthropathies, cytomegalovirus infections, herpes simplex or herpes zoster, relapsing polychondritis, systemic lupus erythematosus, Behçet's disease and TINU syndrome. Bilateral involvement further limits the alternatives to spondyloarthropathies, Behçet's disease and TINU syndrome. Thus, it is very important that the study of these patients include the determination of renal function and urinalysis. This syndrome was first described in 1975 by Dobrin et al.[2] and, to date, some 250 cases have been reported,[3–5] the majority in the pediatric, ophthalmology and nephrology literature. The mean age at presentation is 15 years (range: 9–74 years), and there is female predominance. The risk factors reported for the development of acute tubulointerstitial nephritis include infections, drugs (anti-inflammatory agents, antibiotics) and autoimmune diseases.[1,4–6] The presenting clinical signs and symptoms of interstitial nephritis are generally nonspecific: fever, weight loss, fatigue and malaise. The usual

Table 1
Differential Diagnosis of Uveitides According to Their Most Common Pattern of Presentation.

Type of uveitis	Associated diseases
Acute anterior	
Unilateral	Spondyloarthropathies, cytomegalovirus, herpes simplex, herpes zoster, relapsing polychondritis, systemic lupus erythematosus, Kawasaki disease
Bilateral	TINU syndrome, spondyloarthropathies, Behçet's disease
Chronic anterior	Juvenile chronic arthritis, Sjögren's syndrome, sarcoidosis, tuberculosis
Intermediate	Multiple sclerosis, Lyme disease, Whipple's disease, sarcoidosis, TINU syndrome
Posterior	Toxoplasmosis, cytomegalovirus, tuberculosis, syphilis, Sjögren's syndrome, Vogt-Koyanagi-Harada syndrome, sarcoidosis, Behçet's disease
Panuveitis	Vogt-Koyanagi-Harada syndrome, sarcoidosis, Behçet's disease, juvenile chronic arthritis, tuberculosis
Retinal vasculitis	Behçet's disease, systemic lupus erythematosus, granulomatosis with polyangitis, syphilis

☆ Please cite this article as: Prior-Español Á, Martínez-Morillo M, Holgado-Pérez S, Juega FJ. Diagnóstico diferencial de uveítis bilateral aguda en la consulta del reumatólogo. Reumatol Clin. 2016;12:174–175.

laboratory findings are leukocytosis, anemia, elevated acute phase reactant levels (erythrocyte sedimentation rate or C-reactive protein), microhematuria, proteinuria, glycosuria and/or pyuria. The ocular symptoms of uveitis include eye pain, red eye, loss of visual acuity and photophobia. The nephritis and uveitis do not normally present at the same time, a circumstance that further complicates the diagnosis. In 65% of the cases, nephritis is diagnosed first, in 21% it is uveitis that develops earlier, and in the remaining 15%, they appear simultaneously.[1] Mandeville et al.[6] published a number of diagnostic criteria that require histological confirmation or extensive clinical evidence of acute tubulointerstitial nephritis and of uveitis. The kidney disease can have a good prognosis if treatment is begun early with systemic glucocorticoids. However, tubulointerstitial fibrosis and deterioration of the chronic renal function may develop if the disease goes untreated. For this reason, early diagnosis is essential. Recurrence of the uveitis is common (41%), but does not predict or imply recurrences of the kidney disease.[7]

The TINU syndrome is a condition in which the renal involvement can have a good prognosis with systemic glucocorticoid therapy. It is important that we know about it and include it in the differential diagnosis of uveitides and in that of acute tubulointerstitial nephritides. We consider multidisciplinary units to be increasingly necessary for cases like the one described here, as they would enable more precise diagnostic and therapeutic approaches.

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Bilateral Sudden Sensorineural Hearing Loss in a Patient With Microangiopathic Antiphospholipid Syndrome☆

Anacusia súbita neurosensorial bilateral en un paciente con síndrome antifosfolípido primario microangiopático

To the Editor,

Sudden sensorineural hearing loss (SSHL) is defined as a sudden deterioration in auditory function of at least 30 dB; bilateral presentation (BSSHL) is extremely rare (<5% of all cases of SSHL).[1] The known etiological agents are viral infections, tympanic membrane perforation, vascular disorders and autoimmune diseases.[2] The autoimmune etiology was proposed by Ernst Lehnhardt in a patient with unilateral SSHL, who subsequently developed the same condition in the other ear.[3] He postulated that the damage to the first ear led to the development of antibodies that affected the contralateral ear. The first associations of BSSHL with rheumatic diseases were reported in the 1980s in patients with systemic lupus erythematosus (SLE) and anticardiolipin antibodies (aCL).[4] It was during the same period of time that Hughes pointed out the unusual presentations of thromboses, miscarriages and lupus anticoagulant in patients with SLE, an observation that would lay the foundations for the characterization of antiphospholipid syndrome (APS). Since then, the concept of APS has evolved considerably. In recent years, a variant with exclusively microangiopathic involvement (MAPS), in which virtually any organ can be affected, has been recognized.[5]

A 54-year-old man presented with BSSHL, headache and vertigo. He had had acute pancreatitis with secondary diabetes mellitus 4 years earlier and had a 7-year history of primary hypothyroidism. He underwent a neurotologic examination and, following audiometry, was diagnosed with bilateral neurosensory hearing loss, which was treated with transtympanic dexamethasone. A specialist in infectious diseases prescribed ganciclovir at a dose of 12 mg/kg/day for 10 days + prednisone at 50 mg/day for 4 weeks. Nerve conduction studies revealed short latency auditory evoked potentials with no response. Speech audiometry showed an absence of response to maximum intensities. The patient was referred to lip and face-reading therapy and to rheumatology because he had been found to have aCL. In the latter department, we reached a diagnosis of APS on the basis of high titers of IgM anti-β2 glycoprotein and aCL, a positive test for lupus anticoagulant and a prolonged activated partial thromboplastin time (aPTT). After immunological studies (Table 1), we ruled out the presence of lupus. In addition, in magnetic resonance imaging (MRI), we observed subcortical hyperintensity in bilateral frontal and parietal lobes, with normal vascular behavior and enhancement, findings that demonstrate microvascular involvement (Fig. 1). As the patient had never had large vessel thrombosis, we concluded that what he had was primary APS in its microangiopathic variant.

Table 1
Immunological Studies.

Test	Result
Antinuclear antibodies	80 homogeneous, 40 cytoplasmic
Anti-DNA antibodies	Negative
Anti-Sm antibodies	Negative
Lupus anticoagulant	1.69 (positive <1.2)
IgM anti-β2 glycoprotein	3350 (<8 U/mL)
IgG anti-β2 glycoprotein	6.8 (14.3 U/mL)
IgM anticardiolipin	>255 MPL (positive >15)
IgG anticardiolipin	46.3 GPL (positive >20.1)
Complement C3	296.7 mg/dL (90–180)
Complement C4	29.8 mg/dL (10–40)

GPL, IgG phospholipid units; MPL, IgM phospholipid units.

☆ Please cite this article as: Galicia-López A, Anda-Garay JC, García de la Peña M. Anacusia súbita neurosensorial bilateral en un paciente con síndrome antifosfolípido primario microangiopático. Reumatol Clin. 2016;12:175–177.