Choroidal Tuberculoma with Membranous Glomerulonephritis

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We report treatment of a 24-year-old man with membranous glomerulonephritis (MGN) who developed a solitary choroidal tuberculoma in association with miliary tuberculosis during steroid therapy. In June 1995, the patient had developed nephrotic syndrome. He had refused renal biopsy at that time. So we treated him with corticosteroids having assumed a diagnosis of minimal change nephrotic syndrome. After initial corticosteroids and diuretics therapy for 5 months, his generalized edema resolved but proteinuria (3 positive) continued, suggesting the presence of other forms of glomerulonephritis. Renal biopsy performed in January 1996. The patient was diagnosed as having MGN. The patient was closely observed over a period of 34 months and remained stable without steroid therapy. However at 34 months, generalized edema was again noted and steroid therapy at high dosage was initiated. After 5 months of steroid therapy, he developed miliary tuberculosis and a solitary choroidal mass. An antituberculosis chemotherapeutic regimen was started and after a further 5 months, all clinical symptoms and signs of the pulmonary lesion were resolved and a measurable shrinking of the choroidal mass was recorded.

Key Words: Membranous glomerulonephritis, miliary tuberculosis, choroidal tuberculoma

INTRODUCTION

Tuberculosis is a still common disease particularly in developing countries with associated risk factors, whether introduced in an individual or a population, including HIV infection, diabetes mellitus, lymphoma, any chronic debilitating disease, gastrectomy, cancer, and immunosuppressive therapy.¹ Although its major impact is pulmonary, tuberculosis is actually a disseminated disease. Uveal involvement in tuberculosis has been described in the primary, recurrent, and miliary forms of this disease.² The common findings are uveitis and choroidal tuberculosas (solitary or multiple) as a part of hematogenous spread.³,⁴

Here is presented a case of a man with miliary tuberculosis who developed a rapidly growing choroidal tuberculoma. The choroidal lesion was documented clinically with fundus photography, ultrasound, and fluorescein angiography, and dramatic improvement was observed with antituberculous medication.

CASE REPORT

A 24-year-old male with a history of MGN was hospitalized at the end of April 1999 because of high fever, headache, night sweats and decreased vision of the right eye. MGN had initially been confirmed by renal biopsy for proteinuria in January 1996. On first admission, the serum creatinine level was 0.9mg/dl and laboratory findings were indicative of nephrotic syndrome. For 34 months the patient had remained stable without medication. At approximately 34 months after diagnosis the patient had developed generalized edema and abdominal distension. The proteinuria was reduced and the edema relieved.
with daily doses of 60 mg of prednisolone. After 5 months of steroid therapy, he developed the symptoms of April 1999. The basic dose of prednisolone which had been maintained at 10 mg was interrupted due to fever and sweating before admission. He had no significant ocular history.

His height was 166 Cm, weight 55 Kg. Physical examination at initial presentation revealed a febrile state, temperature 39.7°C, with a blood pressure of 110/90 mmHg, a respiratory rate of 20 per minute, and a heart rate of 130 beats per minute. No lymphadenopathy was present. Coarse breath sounds could be heard over both lung fields without rales. There was no skin rash.

Initial laboratory values showed a hemoglobin level of 11.2 g/dl and a hematocrit count of 34.2%. The white blood cell count was 8.39 × 10^9/L, with a differential of 88% neutrophils, 7% lymphocytes, 3% monocytes and 1% eosinophils. The Westergren erythrocyte sedimentation rate was 111 mm/hr. The platelet count was 478 × 10^9/L. Blood chemistry revealed a total serum protein level of 4.8 g/dl, albumin 2.2 g/dl, AST 49 U/L, ALT 30 U/L, triglyceride 149 mg/dl, cholesterol 172 mg/dl, BUN 24.2 mg/dl, creatinine 2.1 mg/dl, calcium 8.2 mg/dl and phosphate 3.7 mg/dl with normal serum electrolyte. The serum C3 and C4 levels were 125.8 and 30.6 mg/dl, respectively (reference range: C3 88-201 mg/dl, C4 16-47 mg/dl). The urinalysis was reported as showing 500 mg/dl of proteinuria, 5-9 red blood cells, 5-9 white cells per high-power field and oval fat bodies. In a 24-hour sampling of urine, the protein level was 6095 mg, creatinine 754 mg and the creatinine clearance rate was 28.7 ml/min. The tests for antistreptolysin O titer, ANA, LE cell, VDRL, hepatitis B surface antigen, hepatitis C virus antibody, hantavirus antibody, leptospirosis antibody, Rickettsia tsutsugamushi antibody, toxoplasma antibody, mycoplasma antibody, widal test, rubella virus Ig M and rheumatoid factor were all negative. Blood cultures remained sterile. Three separate smears of sputum for AFB were negative.

Chest roentgenogram taken on admission showed left CP angle blunting and accentuation of the interstitium. High resonance computed tomography (HRCT) disclosed diffuse scattered, small fine nodules in the entirety of both lung fields. Antituberculous chemotherapy was begun with once daily administrations of isoniazid (400 mg), ethambutol (1,200 mg), rifampin (600 mg), pyrazinamide (1.5 g) and pyridoxine (50 mg).

Ocular examination on June 5, 1999, revealed that the best corrected visual acuity in the right eye was finger counts and 20/20 in the left eye. Ophthalmoscopy revealed a yellowish subretinal mass, measuring 3 × 3 disc diameters in area, adjacent to the optic nerve head, behind and elevating the macula (Fig. 1). Fluorescein angiography (Canon, CF-60UV, Utsunomiya, Japan) and B-scan ultrasonography (Sonomed, B-3000, New York, USA) confirmed a large subretinal mass in the posterior pole with a surrounding retinal detachment (Fig. 2, and 3). MRI displayed

![Fig. 1. Fundus photograph of right eye showing yellow subretinal lesion, which is elevating the macula.](image1)

![Fig. 2. Fluorescein angiography at the time of presentation showing diffuse hyperfluorescine of the subretinal mass with a surrounding ring containing less hyperfluorescine due to serous retinal detachment.](image2)
a well-demarcated hyperechoic mass in the right eye (Fig. 4). Based on the clinical history, laboratory findings, and the appearance of the fundus, a diagnosis of choroidal tuberculoma was made. Choroidal biopsy and histopathological studies were considered for further diagnosis but could not be undertaken as the patient refused consent.

During the next month, the patient’s right eye became painful and the choroidal lesion continued to grow. Ophthalmoscopy revealed the subretinal mass grown to 9 × 7 disc diameters in area (Fig. 5). On July 8, 1999, the vision in his right eye decreased to hand motions and the patient complained of more severe eyeache with an associated headache.

Following an additional one month of chemotherapy, the choroidal lesion started to decrease in size and the vision in his right eye improved to finger counts. And after a further five months of antituberculous chemotherapy, his pulmonary and ocular conditions were improved. Although the patient’s visual acuity was not improved, the size of the choroidal lesion was dramatically decreased (Fig. 6). However the presence of proteinuria (4 positive) was still noted and serum creatinine level was 1.6 mg/dl.

DISCUSSION

Intraocular tuberculosis, while a rarity, can present as a variety of clinical forms. The choroid is the commonly affected site and is usually associated with hematogenous spread from other...
active infected foci. Whereas choroidal tubercles are usually small, multiple, and bilateral, tuberculomas are usually solitary, more well defined, may measure up to 7 mm in diameter, and have less surrounding edema. Histologically they are similar to other tuberculous lesions and may be either caseating or noncaseating granulomas.

It has been suggested that ocular tuberculosis may occur more often in immunocompromised states such as occurring in cases of AIDS, drug abuse, diabetic nephropathy and prolonged intake of steroid. Shiono et al. reported a case of miliary tuberculosis with disseminated choroidal hemorrhage and tubercles in both fundi. The patient had been diagnosed with nephrotic syndrome and had been taking steroids for 7 months. However, renal biopsy had not been performed. Choroidal tubercles can occur with pulmonary tuberculosis in a variety clinical circumstances without any evidence of miliary tuberculosis, or they can occur with acute miliary tuberculosis. Bouza et al., reporting on the underlying predisposing conditions and risk factors in the clinical course of ocular tuberculosis, found that the most frequent underlying disease was HIV infection (45%), followed by chronic liver disease (38%), and that the most important independent factor was miliary tuberculosis.

In patients without evidence of systemic involvement, the diagnostic possibility of a large tuberculoma should be considered in conjunction with choroidal hemangioma, sarcoidosis, foreign body presence, metastatic disease, and melanoma. The presumed diagnosis of choroidal tuberculoma may lead to the subsequent diagnosis and treatment of a systemic focus.

Routine ophthalmic investigation, opthalmoscopy, fluorescein angiogram, and ultrasonogram etc., are nonspecific tests for a choroidal mass. A definitive diagnosis of ocular tuberculosis from available clinical symptoms, signs, and routine examination is elusive because it requires the detection of the Mycobacterium tuberculosis bacilli in ocular tissues or secretions, by microscopy or culture. The results of the PPD skin test are not helpful in the endemic area. Currently, new diagnostic techniques are needed to confirm the mycobacterial infection of the eye as soon as possible. Molecular biology techniques like the amplification of DNA by polymerase chain reaction (PCR) may in the future become rapid, sensitive, and specific tools for the identification of pathogens in ocular liquid or tissue samples.

Management of intraocular tuberculosis often is difficult if it is not diagnosed at an early stage. Any patient evidencing disease symptoms highly suggestive of intraocular tuberculosis should be treated with a multi-drug regimen, especially in the presence of an active focus. The initiation of early therapy will be of benefit to the patients in avoiding delayed complications like an enucleation. Generally, the therapeutic course of treatment for miliary tuberculosis is an initial intensive phase of chemotherapy combined with the four drugs, isoniazid, ethambutol, rifampin, and pyrazinamide, for 2 months followed by the continuation phase. The optimal length of therapy has never been tested in large controlled trials. The American Thoracic Society recommends 6 to 9 months in adults. We used the three drugs isoniazid (400 mg), ethambutol (800 mg) and rifampin (600 mg) during the continuation phase.

In our case, the choroidal tuberculoma occurred in the presence of preexisting MGN, which was being treated with high dose steroid therapy. We would like to conclude by emphasizing several points based on this case and our review of available literature. First, it is important in immunocompromised cases to begin the antituberculous chemotherapy in endemic areas in order to treat the ocular lesion regardless of the identification of the active focus. Second, early recognition of choroidal tuberculoma with proper techniques can prevent serious complications such as enucleation from arising. Third, physicians need to be comprehensively aware that patients with steroid therapy are highly susceptible to M tuberculosis.

REFERENCES

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