

Case Report

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An Unusual and Missed case of Streptococcal Pharyngitis Presenting as Membranoproliferative Glomerulonephritis; case Report

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Streptococcal pharyngitis is common in the pediatric age group. Although its treatment is simply achieved by administration of a single dose of benzathine penicillin, oral penicillin for 10 days, or azithromycin for 5 days, it has serious complications such as rheumatic fever (RF) and chorea if left untreated. Treatment of pharyngitis does not prevent glomerulonephritis but prevents the spread of streptococci that can cause an epidemic in glomerulonephritis if they are of the nephritogenic strain. Post Streptococcal Glomerulonephritis (PSGN) is common in school age children and usually has a benign course as more than 95 percent of the cases recover the acute phase and less than 5 percent progress in their course to Rapidly Progressive Glomerulonephritis (RPGN) and ultimately about one percent develop End Stage Renal Failure (ESRF). Herein, we present a 12-year-old male with a history of untreated streptococcal pharyngitis who first came to our clinic with a history of arthralgia and arthritis, fatigue, hematuria, petechia, purpura, elevated levels of Blood Urea Nitrogen (BUN) and Creatinine (Cr), and low grade fever. Echocardiography revealed endocarditis which was treated. However, renal failure required renal replacement therapy (RRT), and massive proteinuria needed renal biopsy which revealed membranoproliferative glomerulonephritis (MPGN).

Keywords: Streptococcal Infections; Membranoproliferative; Glomerulonephritis; Pharyngitis; Renal failure.

Running Title: An Unusual Case of Streptococcal Pharyngitis Presenting as MPGN

Introduction

Streptococcal pharyngitis is one of the most common infectious diseases in children; it is caused by a variety of M type streptococci such as 12, 49, [1- 4]. Type 12 is usually responsible for pharyngitis and type 49 for pyoderma; they can cause glomerulonephritis (GN) by immune complex deposition in the kidney. When GN is due to streptococcal pharyngitis; the patient develops

acute nephritic syndrome 1-2 weeks after pharyngitis and when GN is due to streptococcal pyoderma, the signs and symptoms develop 3-6 week later. Although its treatment is simply achieved by administration of a single dose of benzathine penicillin, oral penicillin for 10 days, or azithromycin for 5 days, it has serious complications such as rheumatic fever (RF),

chorea, lymphadenitis, and abscess, if left untreated. The treatment of pharyngitis does not prevent glomerulonephritis but prevents the spread of streptococci that can cause an epidemic in glomerulonephritis if they are of the nephritogenic strain.

Post Streptococcal Glomerulonephritis (PSGN) is common in school age children [5] and usually has a benign course as more than 95 percent of the cases recover the acute phase and less than 5 percent progress in their course to Rapidly Progressive Glomerulonephritis (RPGN); ultimately about one percent develops End Stage Renal Failure (ESRF). Herein, we present a 12-year-old male with a history of untreated streptococcal pharyngitis who first came to our clinic with arthralgia, hematuria, petechia, purpura, and elevated levels of Blood Urea Nitrogen (BUN) and Creatinine (Cr).

Case Report

The patient was a 12-year-old boy from Aligudarz in the east central part of Iran. He presented and was admitted with arthralgia in the lower limbs, generalized edema, ascites, melena, petechia and hematuria. In the local hospital, a diagnosis of hench schoenlein purpura (HSP) with renal complications was made and treatment with prednisolone was started. About 4 days later, edema, ascites and petechia alleviated but renal function deteriorated and BUN and Cr had a rising trend; for this reason, he was referred to our hospital. At presentation, he had periorbital edema, low grade fever, a pansystolic murmur in the heart and splinter hemorrhage in the subungual area. Bacterial Endocarditis was considered and echocardiography was requested. The first echocardiography was normal which was not acceptable and another echocardiography by a different cardiologist was requested, revealing a medium size (7mm) vegetation on the atrial surface of the anterior Mitral Valve (MV) leaflet, moderate Aortic Insufficiency (AI), and moderate Mitral Regurgitation (MR).

Treatment with penicillin, vancomycin, and rifampicin was prescribed and Peritoneal Dialysis (PD) started as the serum level of urea was around 180 and the serum level of creatinine was around 5- 6 mg/dl. The patient had severe hypertension due to RF and volume overload. Auxiliary therapies, calcitriol, Calcium carbonate, vitamins, minerals and methylprednisolone were started. Hydralazine, nifedipine, and furosemide were administered for hypertension, and digoxin

was started for heart failure. During the early days of hospital stay, he had a high fever. Blood and PD fluid were negative in sepsis work-up. The fever gradually subsided, and renal function returned to normal. The last Echocardiography 2 months after the start of treatment revealed very small endothelialized vegetation in the MV with moderate mitral insufficiency and aortic insufficiency. At routine follow-up, renal function was stable but proteinuria remained in the nephrotic range; renal biopsy was performed and examined under light, immunofluorescence and electron microscopy. The results were compatible with membranoproliferative glomerulonephritis (MPGN). Based on renal biopsy results, high dose pulsed methylprednisolone was initially prescribed for 3 days and continued with high dose oral prednisolone.

Finally, he was receiving prednisolone 50 mg every other day and mycophenolate mofetil 500 mg twice daily, which resulted in a dramatic decrease in proteinuria from the nephrotic range to trace on urinalysis and around 300 mg in 24 hour urine collection. At last, on the outpatient visit, the patient was well with mild proteinuria (218 mg in 24 hours). Results of his laboratory investigations during his treatment were as is shown in table 1.

In this situation; detailed history was taken and revealed that at the age of 6, he had a sore throat and high fever (symptoms and signs of pharyngitis) that was treated only with acetaminophen as a common cold. Two weeks later when he presented with migrating arthritis, the pain was attributed to weakness and growing pain, and rheumatic fever (RF) was missed and untreated.

Several months later when he was unwell and had fatigue and exercise intolerance again, the condition was related to hypovitaminosis and multivitamin was prescribed. Retrospectively looking, in this stage, he probably had rheumatic carditis which was missed and again left untreated. The low grade fever and fatigue continued and he developed sub acute bacterial endocarditis with one of the major complications, i.e. severe glomerulonephritis as a result of chronic infection, leading to renal failure requiring dialysis.

Discussion

Every human being experiences sore throat several times in his/her life. It has many causes such as viral, bacterial, and immunologic

conditions. The treatment of pharyngitis prevents RF and its complications such as carditis but does not prevent glomerulonephritis although it keeps from the spread of streptococci that can cause an epidemic in glomerulonephritis if they are of the nephritogenic strain.

Table 1. Results of laboratory investigations during admission

Date	Urea	Cr	K	Na	Other laboratory Results
16.4.2007	80	1/3	5/6	136	U/A: alb 3+ WBC:30 RBC: 40
26.4.2007	139	2/9	5/7	132	Blood WBC: 7300 Hgb: 10 g/dl Plt: 231000 K/mcL ESR: 35 mm/hr CRP: 3+ ASOT: 333
8.5.2007	182	5/8	3/2	124	U/24h: Volume: 2500 Protein: 2260 mg/24 hr Cr: 485 mg/24 hr
10.5.2007	132	5/2	4/5	135	U/C: Neg PT,PTT: N Alb: 1.9 g/dl Total Pr: 5.6 g/dl
18.5.2007	140	5/1	4/4	136	ESR: 141 mm/hr Ca. 7.5, P. 3.5 mg/dl Alk.p. 288
20.5.2007	130	5/3	3/8	139	B/C negative for 2 time
30.5.2007	46	2/2	3	143	Triglyceride: 231 mg/dl Cholesterol: 182 mg/dl
20.6.2007	43	1/4	5/2	140	Uric acid: 3.4 mg/dl
21.6.2007	58	1/7	5/9	140	S/E: OK
23.6.2007	50	1/8	5/6	136	C3: 114 (N), C4: 15 (N) CH50: 130 = N
26.6.2007	78	1/5	4/3	133	ANA, Anti dsDNA: = N CIC: Non detective IgG, IgM, IgA: N

U/A: Urinalysis, N: Normal, Hgb: Hemoglobin, ESR: Erythrocyte Sedimentation Rate, CRP: C - reactive protein, ASTO: Anti Streptolysin O, ANA: Anti Nuclear Antibody, CIC: Circulating Immune Complex

Post streptococcal GN is most common in children aged 5-12 years and uncommon before the age of 3 years. In the typical form of the disease, acute nephritic syndrome develops 1-2 weeks after an antecedent streptococcal pharyngitis or 3-6 weeks after a streptococcal pyoderma. The history of a specific infection may be absent in the patients because symptoms may be mild or may resolve without a specific treatment while complications overtake afterwards. On the other hand, MPGN, which is classified in 3 types, is caused by several etiologies. Although most of them are idiopathic [6,7], there are reports of dense deposit disease associated with monoclonal gammopathy [8, 9],

polymorphisms in complement factor H (CFH) and C3 genes [10], PR3-ANCA-Positive Periodic Fever Syndrome [11], etc.

The presented case is an extreme example of missing a simple disease that progressed to dramatic and life threatening conditions, i.e. RF, bacterial endocarditis, and MPGN. This patient have no history of GN days or weeks after throat infection, but his GN was the endpoint after bacterial endocarditis and was MPGN as confirmed by renal biopsy. Unfortunately, blood cultures in our hospital at that time were mostly negative even in highly suspicious cases of infection such as this patient that had vegetation in the mitral and tricuspid valves.

Conclusion

The life threatening consequences of an easily treatable pharyngitis result from the lack of the routine physical examination of the patients with fever, as was the case in our patient for several times. We reemphasize the value of physical examination before any laboratory test and imaging study and before any prescription.

Conflict of Interest

Authors have no conflict of interest to declare.

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