SciMedCentral

Clinical Research in Infectious Diseases

Case Report

Vasculitis, a Rare Presentation of a Post-Streptococcal Syndrome

Andreia Luís Martins[1]*, António Eduardo Figueiredo[2] and Maria João Brito[3]

[1]*Pediatric Department, Hospital Professor Doutor Fernando Fonseca, Portugal*
[2]*Clinical Immunology Consultant, Pediatric Department, Hospital Professor Doutor Fernando Fonseca, Portugal*
[3]*Infectious Diseases Consultant, Pediatric Department, Hospital Professor Doutor Fernando Fonseca, Portugal*

Corresponding author
Andreia Martins, Pediatric Department of Hospital Professor Doutor Fernando Fonseca, E.P.E, IC 19, 2720-276 Amadora, Lisbon, Portugal; Tel: 351 214 348 287; Fax: 351 214 348 292; Email: andreialuismartins@gmail.com

Submitted: 23 November 2014

Accepted: 22 January 2015

Published: 24 January 2015

Keywords
- Vasculitis
- Group A Streptococcus
- Post-streptococcal syndrome

Abstract

Post-streptococcal vasculitis is not awell-recognized non-suppurative complication of Group A streptococcal infections. Seventeen-year-old male was admitted with palpable purpura in the limbs, ankle swelling, microscopic hematuria and elevated inflammation markers. After short remission period, an extensive exudative pleural effusion was identified. High anti-streptococcal antibodies titers were found. This report illustrates an atypical and rare presentation of a post-streptococcal syndrome.

ABBREVIATIONS

GAS: Group A streptococci; ARF: Acute Rheumatic Fever; PT: Prothrombin; PTT: Partial Thromboplastin Time; CRP: C Reactive Protein; LDH: Lactate Dehydrogenase; ESR: Erythrocyte Sedimentation Rate; HSP: Henoch-Schönlein Purpura

INTRODUCTION

Group A streptococci are Gram-positive cocci that appear in chains and pairs and demonstrate fully lysis (beta-hemolysis) on blood agar. These cocci, particularly *Streptococcus pyogenes* tend to colonize the pharynx and skin. Nonetheless GAS is also responsible for several infections in the humans such as pharyngitis, pyoderma, cellulitis, necrotizing fasciitis, osteomyelitis, septic arthritis, bacteremia and pneumonia. Complications may arise after GAS infections and can be of suppurative or non-suppurative nature (post-streptococcal syndromes) [1].

GAS has an extensive array of virulent factors. Several types (over 100) of GAS have been described on basis of the serologically distinct M proteins on the surface of the cell that oppose phagocytosis [1]. Distinct M protein serotypes cause infections in distinct sites. These proteins are often divided into nephrogenic and rheumatogenic serotypes as well. However, some serotypes are associated withboth syndromes.

Although the pathophysiology of post-streptococcal syndromes is not fully understood it is widely accepted that there exists an immune-mediated basis. Indeed, antigenic mimicry is known to be the triggering factor. Several studies have shown cross-reactions with autoantibody responses between different serotypes of M protein of GAS and several human tissues such as cardiac (myosin), joint (collagens I and IV) or neuronal tissues (gangliosides), which may explain the diversity of post-streptococcal immunologic syndromes [1,2]. Besides M protein serotypes, a host susceptibility seems to exist regarding GAS immune complications, namely acute rheumatic fever (ARF), as reviewed by Bryant *et al* [3]. However other immune mechanisms operable in post streptococcal syndromes have been described such as super antigen stimulation of T cells in ARF, guttate psoriasis and Kawasaki disease [4].

Post-streptococcal syndromes usually occur 1 to 3 weeks after a pharyngitis or skin infection. Early treatment with systemic antibiotic prevents acute rheumatic fever [5]. However the same is not true for post-streptococcal glomerulonephritis [6]. There are no known studies that support this evidence for other SGA immune-mediated complications.

Post-streptococcal vasculitis is not a well-recognized condition. That is why a high degree of suspicion is required for the diagnosis of less frequent post-streptococcal syndromes.

CASE PRESENTATION

We present a 17-year-old caucasian boy with unremarkable past medical history other than vitiligo, that presented to the hospital emergency care with a two-day left thoracic pain with pleuritic features and fever (38.8°C). No cough or other respiratory symptoms were reported. Chest radiograph revealed a bilateral

interstitial pattern and a five-day course of azithromycin was prescribed with remission of the symptoms.

A week later, he was admitted due to the sudden appearance of an erythematous rash characterized for maculo-papular urticarial-like patches coexisting with palpable non-blanching purpuric plaques symmetrically spread over lower limbs, feet and dorsal hand surface associated with ankle and hand swelling. Laboratory findings showed a moderate normocytic anemia (Hb 10.9 g/dL), leukocytosis 16500/µL with 81.2% neutrophilia, thrombocytosis of 561 000 platelets/µL, normal PT and PTT, elevated D-Dimer 15926µg/L and fibrinogen 521g/L values, CRP of 21 mg/dL. There was a slight increase in serum creatinine (1.3mg/dL) and blood urea (54mg/dL). Urine analysis revealed microscopic hematuria (2 erythrocytes/field) with no proteinuria. No dysmorphicerythrocites were found (Table 1).

During the two-day stay in the ward there was as pontaneous near complete remission of the purpuric rash, with maintenance of apyrexia and normal blood pressure. There was also a normalization of urine analysis and decrease in inflammation parameters (CRP 13.1mg/dL).

Three days after discharge, he was admitted for reassessment. There was clinical and radiological evidence of an extensive pleural effusion in the left hemithorax as well as a slight liver enlargement. Thoracocentesis was performed with an outlet of exudative pleural effusion (2727 cells/uL with polymorphonuclear predominance, proteins 6.9g/dL (serum proteins 9,53g/dL), LDH 307 UI/L). Cultural examination of the pleural fluid was negative and for acid-fast bacteria as well. Further laboratorial evaluation revealed a new elevation of inflammation parameters (CRP 20mg/dL; ESR 86 mm/h) and of D-Dimer (25714 µg/L). Protein electrophoresis showed a hyper gammaglobulinemia (3.58 g/dL) with high immunoglobulin G and A determinations (IgG 3390 mg/dL and IgA 403 mg/dL) (see Table 1). High titers of ASO were found (5860 UI/mL) as well as of DNase-B (700U/mL), rising the suspicion of a previous recent streptococcal infection. Intramuscular benzathine penicillin was administered in order to prevent ARF. Cardiac and ophthalmologic evaluation was normal. Successive urine analyses were normal. The patient maintained apyrexia and hemodynamic stability during all the stay. No recrudescence of vasculiticcutaneous lesions was observed. At the day of discharge, inflammation (CRP 6.9mg/dL) and vasculitic parameters (D-dimer 4385 µg/L and fibrinogen 423g/L) were to normalize.

Two weeks after second discharge, the patient had no further symptoms with further rise in ASO titers (6000UI/mL), a slight decrease of gamaglobulinemia (2.87g/dL) and normalization of inflammation and vasculitic laboratorial findings. Nine months after discharge, the patient is asymptomatic.

Table 1: Laboratory searching for infectious and immune diseases in the first and second admission.

First admission		
Infectious diseases	**Results**	**Reference**
EBV-VCA IgM/ VCA IgG /EBNA IgG	Negative/Positive/Positive	
Parvovírus B19, CMV IgM/IgG	Negative/ Positive	
HIV 1 and 2	Negative	
HBs antigen, HBc antibody	Negative	
Mycoplasma IgM/IgG	Negative	
Blood culture	Negative	
Immune diseases		
ANA	Negative	
C3 fraction	74 mg/dL	(77-125)
C4 fraction	19.2 mg/dL	(21-39)
CH50	47.7 U/mL	(23-46)
Second admission		
Infectious diseases	**Results**	**Reference**
ASO titer	5860 UI/mL	(<200)
DNase-B	700 U/mL	(<200)
Borrelia burgdorferi, *Coxiella burnetti* serology	Negative	
IgG	3390 mg/dL	(70 - 1600)
IgA	403 mg/dL	(89 - 314)
IgM	56 mg/dL	(59 - 261)
Tuberculin sensitivity test	Energy	
Immune diseases		
ANA, anti-dsDNA, c and p-ANCA	Negative	
Rheumatoid factor	Negative	
Angiotensin converting enzyme	Normal	

Abbreviations: EBV: Epstein-Barr Virus; VCA: Viral Capsid Antigen; EBNA: Epstein-Barr Nuclear Antigen; CMV: Cytomegalovirus; HIV: Human Immunodeficiency Virus; HBs: Hepatitis B surface Antigen; HBVc: Hepatitis B core antibody; ANA: Anti Nuclerar Antibody; Anti-dsDNA; Antibody Anti- double strand DNA; c and p-ANCA: cytoplasmic and perinuclear Antineutrophil Cytoplasmic Antibody

DISCUSSION

The patient first presented symptoms of a lower respiratory infection, which was promptly treated with a five-day macrolide antibiotic. Nevertheless he gradually developed a metapneumonic exudative pleural effusion only noticed in the second admission meaning two weeks after the first symptoms. No blood or pleural fluid cultures were able to identify the infectious agent. A GAS infection was endorsed by the high ASO titers three weeks after the beginning of respiratory symptoms. DNase-B titers were also elevated which supports GAS infection, with a sensibility of 95% and specificity of 98% [7,8].

A week after the respiratory first symptoms, the patient developed palpable purpura in the extremities, ankle swelling and transient microhematuria, with no proteinuria or renal dysfunction. If we consider this isolated urinary finding this case meets the criteria for Henoch-Schönlein purpura (HSP). [9] There have been some reports of HSP occurring after a GAS infection. Indeed HSP is preceded by an upper respiratory infection, mostly viral, but there are reports of SGA pharyngitis, in up to a third of cases. Kalyoncu presented a 13-year old boy with HSP with pulmonary hemorrhage and active carditistwo weeks after GAS pharyngitis [10]. In another report, HSP with nephritis and a GAS antigen in glomeruli was studied [11]. Kawasaki disease and GSA pleural effusion have been also reported in the literature as a rare association of this agent in a vasculitic disease [12]. Polyarteritisnodosa has also been

associated to GAS infection in some reports occurring in isolated or recurrent cutaneous and systemic form [13-16]. Other forms of post-streptococcal vasculitis have been described such as cutaneous leucocytoclasticvasculitis, vasculitic neuropathy or granulomatous polyangiitis [17].

Besides the relevant laboratorial inflammatory syndrome verified during acute disease, analyzing the auto-limited evolution of this case without immunosuppressive therapy and the absence of immunological laboratory markers (see Table 1), render likely a post-infectious immune mechanism. However further follow-up is needed to exclude a rheumatologic disease, paying special attention to the fact that the patient has another immune disease (vitiligo). All things considered, we assume that our patient had two non-suppurative immune-mediated complications of a GAS infection, being vasculitis very rarely described in the literature.

Finally, this report highlights the importance of a high degree of suspicion of SGA complications even more if no evident previous symptoms pointing to a Streptococcus infection are reported. Further studies are needed in order to the precise the exact pathogenic role of GAS in less common immune-mediated complications.

REFERENCES

1. Ivory DM, Folzenlogen DD. Post Streptococcal Syndromes, a Rheumatologist Perspective. The Internet Journal of Rheumatology. 2010; 6: 2.
2. Martins TB, Veasy LG, Hill HR. Antibody responses to group A streptococcal infections in acute rheumatic fever. Pediatr Infect Dis J. 2006; 25: 832-837.
3. Bryant PA, Robins-Browne R, Carapetis JR, Curtis N. Some of the people, some of the time: susceptibility to acute rheumatic fever. Circulation. 2009; 119: 742-753.
4. Commons RJ, Smeesters PR, Proft T, Fraser JD, Robins-Browne R, Curtis N. Streptococcal superantigens: categorization and clinical associations. Trends Mol Med. 2014; 20: 1.
5. Shulman S, Bisno AL, Clegg HW, Kaplan EL, Lee G, Martin JM, et al. Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2012; 15; 55: 1279-1282.
6. Martin JM, Green M. Group A streptococcus. Semin Pediatr Infect Dis. 2006; 17: 140-148.
7. Johnson DR, Kurlan R, Leckman J, Kaplan EL. The human immune response to streptococcal extracellular antigens: clinical, diagnostic, and potential pathogenetic implications. Clin Infect Dis. 2010; 50: 481-490.
8. Blyth CC, Robertson PW. Anti-streptococcal antibodies in the diagnosis of acute and post-streptococcal disease: streptokinase versus streptolysin O and deoxyribonuclease B. Pathology. 2006; 38: 152-156.
9. Ozen S, Pistorio A, Iusan, SM, Bakkaloglu A, Herlin T, Brik R, et al. EULAR/PRINTO/PRES criteria for Henoch-Schönlein purpura, childhood polyarteritisnodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part II: Final classification criteria. Ann Rheum Dis 2010; 69: 798-806.
10. Kalyoncu M, Cakir M, Erduran E, Okten A. Henoch-Schönlein purpura: a case with atypical presentation. Rheumatol Int. 2006; 26: 669-671.
11. Masuda M, Nakanishi K, Yoshizawa N, Iijima K, Yoshikawa N. Group A streptococcal antigen in the glomeruli of children with Henoch-Schönlein nephritis. Am J Kidney Dis. 2003; 41: 366-370.
12. Alhammadi AH, Hendaus MA. Comorbidity of Kawasaki disease and group a streptococcal pleural effusion in a healthy child: a case report. Int J Gen Med. 2013; 6: 613-616.
13. Tonnelier JM, Ansart S, Tilly-Gentric A, Pennec YL. Juvenile relapsing periarteritis nodosa and streptococcal infection. Joint Bone Spine. 2000; 67: 346-348.
14. Hofer M, Rivier G, Guerne PA, Brunner J, Hanquinet S, Chesseaux JJ, et al. Post-streptococcal vasculitis in childhood presenting with fever and muscular pain. Ann Rheum Dis. 2000; 59: 746-748. Abstract 12.9.
15. Till SH, Amos RS. Long-term follow-up of juvenile-onset cutaneous polyarteritis nodosa associated with streptococcal infection. Br J Rheumatol. 1997; 36: 909-911.
16. David J, Ansell BM, Woo P. Polyarteritis nodosa associated with streptococcus. Arch Dis Child. 1993; 69: 685-688.
17. Watanabe T. Atypical Clinical Manifestations of Acute Poststreptococcal Glomerulonephritis. In: An Update on Glomerulopathies - Clinical and Treatment Aspects, Prof. Sharma Prabhakar, InTech. 2011.

Cite this article

Martins AL, Figueiredo AE, Brito MJ (2015) Vasculitis, a Rare Presentation of a Post-Streptococcal Syndrome. Clin Res Infect Dis 2(1): 1011.