Case Report

ISSN: 1735-0344 *Tanaffos 2013; 12(1): 74-77*

TANAFFOS

Upper Respiratory System Involvement as the Only Manifestation of Granulomatosis with Polyangiitis in a Child with Marfan Phenotype

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Received: 9 June 2012
Accepted: 19 September 2012

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We report a 9-year old girl with an unusual presentation of granulomatosis with polyangiitis in association with Marfan phenotype. The patient presented with recurrent sinusitis, epistaxis, hearing loss and hyperplastic gingivitis, without any signs or symptoms of major organ involvement.

Key words: Granulomatosis with Polyangiitis, Marfan Syndrome, Sinusitis, Epistaxis, Hyperplastic gingivitis

INTRODUCTION

Diagnosis of vasculitis is a challenge, because it has heterogeneous presentations in terms of severity and organ distribution, and there is a lack of diagnostic criteria; yet, the consequences of a missed or delayed diagnosis are potentially severe (1).

Granulomatosis with polyangiitis is an autoimmune inflammatory small-vessel vasculitis. Due to disease rarity, little awareness about its pediatric manifestations exists, compared to adults. As symptoms are vague or unique, children typically remain undiagnosed until deteriorating clinically (2).

This article represents a 9-year-old girl who had recurrent bouts of upper respiratory infections associated with fever, weight loss and an elevated erythrocyte sedimentation rate throughout the course of her disease. She also had some features of Marfan phenotype. However, there has been no association between granulomatosis with polyangiitis and Marfan syndrome in the literature.

CASE SUMMARIES

A 9-year-old girl was admitted with a past medical history of epistaxis, recurrent upper respiratory tract infections, fever and weight loss for 5 months, which all were initiated after an upper respiratory tract infection.

On arrival, she reported recurrent episodes of epistaxis, ear infections accompanied with otorrhea, hearing loss and sinusitis for five months but denied cough, dyspnea or chest pain. For the past three months, she had recurrent admissions to different hospitals with no definite diagnosis. There was also no history of any urinary tract symptoms.

Her physical examination revealed normal vital signs except fever. There were no skin lesions. But oral lesions as gingival hypertrophy and bleeding gums were evident (Figure 1).

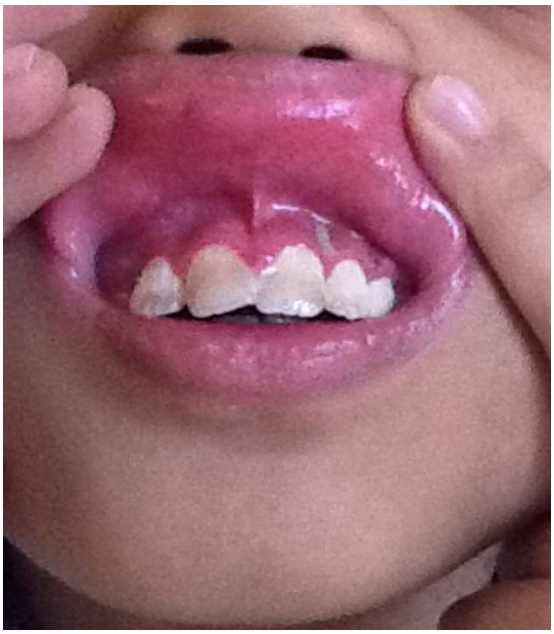

Figure 1. Gingival hypertrophy in the patient after treatment.

Saddle nose was present. She had also a phenotype compatible with Marfan syndrome, with her arm span>1.05 times the height. Wrist sign and thumb sign were both positive. She was thin with long slender fingers and thumbs. She did not have any vision problems (confirmed by an ophthalmologist). In echocardiographic evaluation a mitral valve prolapse was detected. She had a positive family history of the same phenotype in her uncle. Chest X ray was normal. CT-scan of the chest illustrated a linear opacity, indicative of fibrotic change or a subsegmental atelectasis in anteroinferior part of the lung. Sinus CT-scan revealed pansinusitis.

The initial laboratory work-up identified a normal CBC, urinalysis, basic chemistry panel and liver function tests, except hemoglobin level of 6.5 g/dl and platelet counts of 786000/cc. Reticulocyte count ,serum creatinine level ,total complement level ,serum Iron and TIBC were all normal but serum ferritin was significantly high. A 24 hr urine collection was done and the results were normal (total volume 1010cc, Prot=82.5mg, Creat=400mg).

Blood and urine cultures were negative. Mantoux test for tuberculosis was negative. Gastric lavage was performed for her in 3 occasions in early morning and fasting state to detect acid fast bacilli which were all negative for tuberculosis. Bronchoscopy was also performed and bronchoalveolar lavage was evaluated for TB bacilli and the result was negative.

Immunodeficiency work-up (including Ig level, specific antibody titer and flowcytometry) and bone marrow aspiration were normal.

The serological evaluation looking for an autoimmune process initially identified an elevated erythrocyte sedimentation rate (at 93) and CRP was positive. ANA and p-ANCA were negative, but c-ANCA was positive (c-ANCA titer of 1/10 in the patient with a control of up to 1/8 in two separate occasions and different laboratories with a time interval of two weeks and the third one performed after a month the result of which was 12 with a control of up to 12) but mildly elevated. A pulmonary function test was performed, and the following results were obtained which all were within the normal range: FVC=1.62 (with a predicted of 1.81), FEV1=1.25 (with a predicted of 1.48), FEV1/FVC=71.74 (with a predicted of 84.4), and PEF=3.31 (with a predicted of 3.66). A sinus biopsy was done. Pathology report was as follows:

"Multiple granulomas, necrosis and eosinophils are present. PAS stain was negative for fungi. Wegener's Granulomatosis should be considered."

DISCUSSION

Childhood vasculitis encompasses a broad spectrum of diseases that share a common denominator, inflammation of blood vessels. The distribution of vascular injury includes small vessels, medium vessels and large vessels. Additionally, some forms of small vessel vasculitis are characterized by the presence of antineutrophil cytoplasmic antibodies (ANCAs), whereas others are associated with immune complex depositions in affected tissues (3).

In addition to Henoch-Schonlein purpura and Kawasaki disease, etiologies of vasculitis in children can include granulomatosis with polyangiitis, childhood polyarteritis nodosa, microscopic polyangiitis, Takayasu's

arteritis, primary angiitis of the CNS, Churg-Strauss syndrome and unclassified vasculitis (4).

Granulomatosis with polyangiitis is the most common pulmonary vasculitis and classically involves the triad of the upper respiratory tract, lower respiratory tract and kidneys(5).Population studies from 1970s to 1990s,all describe an increasing incidence of granulomatosis with polyangiitis rising from 0.2 to 1.2 per 100,000 persons per year(6).

The numerous disease manifestations of granulomatosis with polyangiitis in the respiratory tract have long engendered suspicion that the disease results from interactions between an inhaled microbial pathogen and a susceptible host (as was seen in our case) (7).

There is also a more limited form of disease that seems to primarily affect the upper respiratory tract (8).This limited form with clinical findings isolated to the upper respiratory tract and/or the lungs at diagnosis, occurs in approximately one-fourth of cases. Patients with limited disease (like our patient) have the following characteristics compared to those with systemic involvement:

-they are younger at disease onset and more likely to be female.

-they are less likely to be ANCA positive.

-they are more likely to have chronic recurring disease and destructive upper respiratory tract disease (saddle-nose deformity) (9).

In addition, many patients present with non-specific symptoms, which can make a definitive diagnosis difficult. Oral manifestations of granulomatosis with polyangiitis occur in approximately 10% of patients (10,11). Our patient exhibited the most common oral lesion, hyperplastic gingivitis which is known as “strawberry gingivitis”, although it is a rare event for granulomatosis with polyangiitis in the literature, especially during childhood.

Based on the presence of some manifestations of Marfan syndrome in the patient, a thorough search was done in the literature but no association between these two entities was found. Thus, we explained this condition as a co-existence only in this patient with no meaningful relationship between these two disorders and just as an unusual presentation.

CONCLUSION

It should be considered that acute vasculitis may mimic other disorders such as infections. A detailed history and examination is important in making the diagnosis. Even, despite effective management of the acute vasculitic phase, patients may be left with end organ damage (deafness, nasal destruction) that may need specific investigation and therapy. Granulomatosis with polyangiitis is a rare disease in children.

Upper and lower respiratory involvement, even if asymptomatic, is a common occurrence in granulomatosis with polyangiitis.

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