Primary Sjogren’s Syndrome in a Child

Abstract

Sjogren’s syndrome is an autoimmune exocrinopathy of unknown aetiology characterized by xerostomia and xerophtalmia or keratoconjunctivitis sicca. It might be a primary condition, which is rare during infancy. It is usually secondary, in most cases due to autoimmunity (systemic lupus erythematosus, rheumatoid arthritis and others). There is a polyclonal reaction with positive antinuclear antibodies, anti-Ro/SS-A and anti-La/SS-B due to B cell hyperstimulation. This case is of a 16-year-old female with autoimmune thrombocytopenia as initial manifestation, and a serology that suggests recent Epstein-Barr virus infection as a possible trigger. She has had recurrent parotiditis, multiple dental cavities and keratoconjuntivitis with positive antinuclear antibody, positive anti-Ro/SS-A and hypocomplementemia. She was diagnosed as a primary Sjogren’s syndrome and received a short course of steroids and hydroxychloroquine with a good clinical response.

Keywords: Sjogren syndrome; Autoimmunity; Exocrinopathy; Immunoglobulin; Auto antibodies

Introduction

Sjogren’s syndrome (SS) is infrequent in childhood. It is a slowly progressive, chronic autoimmune (organ specific) exocrinopathy of unknown aetiology characterized by a decrease in the secretion of saliva and tears, with xerostomia and xerophthalmia or keratoconjunctivitis sicca [1,2]. There is a secondary polyclonal expansion exhibiting auto antibodies in most of the cases: antinuclear antibodies (95%), anti-Ro/SS-A (95%) and anti-La/SS-B (85%) [2].

Case Presentation

A 16-year-old female presented to our department with a history of tonsillectomy and adenoidectomy at 4 years of age. There was no relevant family history. She started at age 10 with thrombocytopenia (107,000/mm³), and ecchymosis. Her serology suggested recent Epstein-Barr virus infection (ITP). She had positive anti-nuclear antibody (ANA: 1/80) and positive anti SS-A. She had a history of recurrent parotiditis. During our follow-up, parotid ultrasound shows gland enlargement, conduct ectasia and increased flow uptake, without masses or calcifications. One year later, she associated recurrent conjunctivitis with an ANA persistently positive (variable dilutions up to 1/1280), negative anti-DNA, positive anti-SSA, negative anti-SSB, negative anti-Smith, negative RNP and non-reactive VDRL (venereal disease reactive laboratory). She had complement C3 levels in 93.6 mg / dl and C4 levels in 10.8 mg / dl. Her erythrosedimentation rates (ESR) were always high (up to 55mm/hr). Blood count showed no anaemia nor leucopenia and the platelets were normal after spontaneous remission of her ITP. In addition, she had a normal echocardiogram and multiple consultations in Dentistry for deep cavities that were treated with amalgams.

When she consulted to our department, her history of recurrent parotiditis, chronic conjunctivitis due to xerophthalmia and some positive auto antibodies, after other causes were ruled out; these findings were compatible with a diagnosis of primary Sjogren’s syndrome (SS). To alleviate her ocular discomfort and active right parotiditis, she received prednisone (50 mg per day for 5 days) and hydroxychloroquine (300 mg per day). Three months later she was asymptomatic: with ocular improvement, free of parotiditis, ESR 9 mm/hr and considerably improvement in her quality of life.

Discussion

SS is usually secondary and part of other autoimmune disease such a systemic lupus erythematosus, rheumatoid arthritis or mixed connective tissue disease. It can also be secondary to chronic graft versus host disease or human immunodeficiency virus infection [2,3]. When isolated, it is called primary SS. It is a rare condition in children [3,4]. finding less than 200 reported cases in the literature. It is 9 times more frequent in women than in men [3]. Its onset in children is reported between 9.3 and 12.4 years of age (mean 10.7 years of age) [2]. This patient started with keratoconjunctivitis sicca at around 12 years of age and her recurrent parotiditis presented some months after that.

The pathogenesis is unknown without a clear trigger. There are possible triggers reported in the literature such as: environmental, constitutional, and infectious (especially viral) and autoimmune factors [1]. An aetiological hypothesis is that after an infection of the exocrine gland, in genetically susceptible individuals,
there is activation of the T lymphocytes that further activate the B lymphocyte, with loss of tolerance and local synthesis of antibodies such as rheumatoid factor, anti-Ro (SS-A) and anti-La (SS-B) [1]. In this case, the Epstein Barr virus could act as a trigger and as there are no family members with rheumatic diseases.

There are no diagnostic criteria in the paediatric population, but those used in adults are usually extrapolated. Table 1 summarizes the diagnostic criteria, with clinical findings and their possible pathogenic explanations [2,3,5].

Table 1: Diagnostic criteria, clinical and laboratory findings and pathophysiology [1,2,5,10].

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Clinical and Laboratory Findings</th>
<th>Pathophysiology</th>
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<tbody>
<tr>
<td>Keratoconjuntivitis</td>
<td>Positive Schimertest*</td>
<td>Abnormal local production of cytokines: BAFF/BLyS, IL-17 y TNF in the inflamed</td>
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<td></td>
<td>Superficial corneal erosions</td>
<td>salivary tissue</td>
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<td></td>
<td>Presents with photophobia</td>
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<tr>
<td>Xerosthomy</td>
<td>Difficulty to chew and swallow</td>
<td>Activated T lymphocytes secrete IL-2 and IFN-α</td>
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<td></td>
<td>Taste abnormalities</td>
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<td>Salivary gland biopsy with lymphocyte</td>
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<tr>
<td>infiltrate at least 2 sites of 4 mm².</td>
<td>Germinal follicle formation with secondary atrophy and acinus obliteration</td>
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<td></td>
<td>Ductal cell proliferation</td>
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<tr>
<td>Rheumatoid Factor³ ≥1:160, ANA³ 1: 160</td>
<td>-</td>
<td>Secondary polyclonal hypergammaglobulinaemia</td>
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</table>

*Deficiency in tear production (wat paper<5 mm in 15 minutes).

Symptoms that have frequently been described are: fever, arthralgia, arthritis and recurrent submandibular oedema [3,4]. Sicca syndrome is described in 37.5% of cases (dry mucous surfaces: nose, pharynx and vagina). Others are Raynaud’s phenomenon and lymphadenopathy. Laboratory findings are anaemia, leucopenia, lymphopenia, cryoglobulinaemia and vasculitis [3,4]. In this case, she started with ITP and other clinical findings, occurred later. Ramos Casals [6] and Rama Krishna [7] have previously reported cases of severe thrombocytopenia in patients with SS (<50,000 / mm³).

Early diagnosis is important to prevent complications, 25% of adults with primary SS develop systemic complications, such as renal tubular acidosis, vasculitis, cryoglobulinaemia, autoimmune hepatitis, interstitial pneumonia, interstitial nephritis, myositis, achalasia with achlorhydria, Hashimoto’s thyroiditis, central nervous system involvement and neuropathy associated with antiphospholipid antibodies [2,3]. It can present from a benign autoimmune disorder up to a malignant lymph proliferative process. In the later cases, it presents with a risk of developing lymphoma 20 to 40 times greater than the general population [1,2]. Our patient has not presented any further complications and she is still in biannual follow-ups.

Treatment is usually symptom-free and non-specific [8]. Sicca requires environmental humidification, artificial tears, saline nasal wash and acidic lemon drops to stimulate salivation [2]. Glucocorticoids and hydroxychloroquine have been successfully reported just like with our patient. In refractory cases, cyclosporine A and cyclophosphamide have been used [2,9]. There are very few studies with biological drugs that have proven to be effective such as: interferon, Rituximab and Epratizumab; being rituximab the one with the best results according to literature [10].

Acknowledgement

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References
