Systemic Lupus Erythematosus, Sjögren Syndrome, and Mixed Connective Tissue Disease in Children and Adolescents

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KEYWORDS

• Juvenile systemic lupus erythematosus • Juvenile mixed connective tissue disease
• Juvenile Sjögren syndrome • Autoantibodies • Lupus nephritis
• Antinuclear antibodies

KEY POINTS

- Juvenile systemic lupus erythematosus (jSLE) is a multisystem inflammatory disease with autoantibodies to nuclear antigens and complement consumption. It causes rapidly progressive damage if not recognized and treated promptly.
- Juvenile mixed connective tissue disease (jMCTD) presents with features similar to jSLE, with higher likelihood of prominent Raynaud phenomenon and high antibodies to ribonucleoprotein. Many children develop systemic scleroderma features over time.
- Juvenile Sjögren syndrome (jSS) usually presents with recurrent sialadenitis and causes dry eyes and mouth, arthralgia, arthritis, and systemic symptoms. Rarely it predisposes to lymphoma.
- Outcomes for jSLE, jMCTD, and jSS depend on early recognition and referral to rheumatology and other specialists depending on the organ system affected. Treatments involve control of inflammation and autoimmunity to minimize the risk for morbidity and mortality.

INTRODUCTION

Systemic lupus erythematous (SLE), mixed connective tissue disease (MCTD), and Sjögren syndrome (SS) are lifelong autoimmune diseases that present special challenges in the pediatric population because they are rare (<1 in 2000 children), and often associated with severe morbidity including mortality. These diseases are characterized by immune dysregulation and chronic multisystem inflammation

Disclosure: The authors have no relevant disclosures.

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Pediatr Clin N Am 65 (2018) 711–737
https://doi.org/10.1016/j.pcl.2018.04.001
pediatric.theclinics.com

leading to a myriad of clinical features of varying severity. Optimal care requires ongoing evaluation and management by a pediatric rheumatologist. This article discusses common disease characteristics, provides an overview of diagnosis and principles of treatment, outlines common mechanisms in pathogenesis, and highlights distinctions between juvenile SLE (jSLE), juvenile MCTD (jMCTD), and juvenile SS (jSS).

INCIDENCE AND PREVALENCE OF JUVENILE SYSTEMIC LUPUS ERYTHEMATOUS, JUVENILE MIXED CONNECTIVE TISSUE DISEASE, AND JUVENILE SJÖGREN SYNDROME

Children account for 20% of all cases of SLE.[1]

- SLE yearly incidence: 2.22 per 100,000 children in the United States.[2]
- SLE prevalence: 9.73 per 100,000 children ages 3 to 18 years.[2]
- jMCTD and jSS incidence and prevalence are not known. Based on small case series, MCTD is approximately 5-fold to 10-fold less common than jSLE, and jSS is less common still.[3,4]

DEMOGRAPHICS

Age

- jSLE mean age of diagnosis is 13 years.[5]
- jMCTD mean age of diagnosis is 13 years[3]
- jSS: median age at diagnosis is 10 years.[4]

Gender

- jSLE female/male ratio is 4:3 before age 10 years, increasing to 9:1 at puberty.[2]
- jMCTD and jSS: female predominance, similar to jSLE

Race and Ethnicity

- jSLE higher incidence rate in children of African, Asian, or Native American descent; these genetic groups also have high severity.[6]
- jMCTD and jSS: not known.

MAJOR DIFFERENCES FROM ADULT DISEASE

Compared with adults with SLE, children generally have more aggressive disease and worse outcomes.[7] Onset in childhood carries a higher risk of nephritis, malar rash, anti–double-stranded DNA (anti-dsDNA) antibodies, and hemolytic anemia compared with adults with SLE.[8] Pulmonary hypertension, a common cause of morbidity and death in adults with MCTD, is rarer and less severe in children with jMCTD.[9] Children with jSS present with recurrent parotitis and less commonly with sicca symptoms, although adults are more likely to have sicca symptoms.[4,10]

DELAYS IN DIAGNOSIS ARE COMMON FOR JUVENILE MIXED CONNECTIVE TISSUE DISEASE AND JUVENILE SJÖGREN SYNDROME

jMCTD can confuse diagnosticians because symptoms change during the development of the disease.[9] However, data on time to diagnosis are not known. The diagnosis of jSS is often delayed (mean, 3 years). The swelling of cheeks and lymph nodes in jSS are often attributed to obstructive sialadenitis or infection until recurrences happen. The autoantibodies associated with jSS, anti–Sjögren syndrome A (anti-SSA) (Ro) and anti–Sjögren syndrome B (anti-SSB) (La), are often detectable before overt glandular dysfunction is detected.[11,12]