Short report

Myelopathy in neonatal and infantile lupus erythematosus

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SUMMARY Two children with lupus erythematosus and myelopathy were studied. The first child developed the neonatal lupus erythematosus syndrome associated with transplacentally acquired anti-Ro/SSA antibodies. The cutaneous manifestations of neonatal lupus erythematosus disappeared but a residual myelopathy was confirmed at 16 months of age. The second child developed cutaneous lupus erythematosus at 3 months of age associated with a total deficiency of the C1r component of complement. A myelopathy and mesangial glomerulonephritis developed at 2 years of age which required treatment with corticosteroids. These two children with CNS lupus erythematosus, one associated with transplacentally acquired antibodies and the other associated with a complement deficiency, may suggest an immune-mediated mechanism for the pathogenesis of myelopathy in childhood lupus erythematosus.

Neonatal lupus erythematosus is a rare disorder which consists of skin lesions, primarily facial, occurring at birth or shortly thereafter.1-6 The disease has been associated with congenital heart block and the presence of passively acquired maternal anti-Ro/SSA and occasionally anti-La/SSB antibodies.1-6 Systemic symptoms do not usually develop in these children during the neonatal period6 although several children have subsequently developed systemic lupus erythematosus in the second decade of life.2-4 The neonatal lupus erythematosus syndrome is thought to be a benign, self-limited disease and neurological problems such as myelopathy have not been previously described.

Lupus erythematosus is also unusual in infancy but may occur when predisposing factors such as familial lupus erythematosus or hereditary complement deficiencies are present.7 8 Central nervous system involvement in children with lupus erythematosus may mimic adult onset disease with such symptoms as seizures, psychosis, cranial nerve palsies and chorea.9-11 Myelopathy has been uncommonly reported in the first two decades of life, especially during the first few years1-2 and has not been reported in patients with C1r complement deficiency.

Two children are described, one with neonatal onset and the other with infantile onset lupus erythematosus, who developed a clinically similar myelopathy.

Case 1

The patient was a full term black female infant born to a 19 year old mother. Portions of the dermatologic and immunologic data from this mother and child have been previously reported.5 6 At birth the child was well and weighed 3.2 kg. A red and scaly butterfly distribution rash was noted about the face at the time of birth but cultures and serologic studies for herpes simplex were negative. There was no evidence of congenital heart block. At 2 months of age, serologic studies demonstrated the presence of anti-Ro/SSA antibodies which could no longer be detected at 8 months of age. Anti-La/SSB antibodies could not be detected. The skin lesions gradually faded leaving residual atrophy and hypopigmentation. Development progressed normally except for delays in standing and walking. At 16 months of age, the child was neurologically evaluated because of the delayed walking. The lower extremities showed spasticity, increased reflexes, extensor plantar responses and contractures at the ankles. A flexed posture was noted with toe walking and

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circumduction of the right leg. The upper extremities were normal and sensory abnormalities could not be detected. At 24 months, a computed tomographic (CT) brain scan, electroencephalogram, somatosensory evoked potentials, cerebrospinal fluid (CSF) studies (including oligoclonal bands, myelin basic protein, immunoglobulins and anti-neuronal antibodies) and myelogram were normal.

The mother had no clinical evidence of lupus erythematosus at the time of delivery. She did have, however, a positive ANA (speckled), Ro/SSA antibody, rheumatoid factor and anti-Sm but a negative anti-RNP. Subsequently, the mother developed fever, polyarthritis, Coombs' positive autoimmune haemolytic anaemia, hypocomplementaemia and antibodies to native DNA and nRNP. Anti-Ro remained positive.

Case 2

The patient was a 3 kg black male infant born following an uneventful pregnancy, labour and delivery. The infant was normal until 3 months of age when a scaly rash developed over the cheeks. At 19 months, a skin biopsy demonstrated deposits of C3 at the dermal-epidermal junctions consistent with a discoid form of lupus erythematosus. Serum complement levels of C3 and C4 were elevated at 227 and 116 mg/dl and the ANA was negative. The child was treated with hydroxychloroquine.

At 2 years of age a generalised seizure occurred. Although his initial motor development was normal, a scissoring gait with toe walking, spasticity and weakness of the legs began at 2 years, 4 months. The discoid facial lesions worsened and the gait deteriorated to the point that the child could no longer walk. High doses of intravenous and oral corticosteroids were administered until the rash and gait improved. Antinuclear antibody was detected in the serum at a titre of 1:80 (speckled). Antibodies to ssDNA, dsDNA, and anti-SM were present in the serum. CT of the brain and a myelogram were normal although a mild elevation of the CSF myelin basic protein was observed. An electrocardiogram, electroencephalogram, visual, somatosensory and brainstem evoked potentials and electromyogram were all normal. Microscopic haematuria was detected and a renal biopsy showed mesangial glomerulonephritis with focal proliferative changes and C3 and IgA deposits in the mesangium.

At 3 years, while on a low alternate day dosage of prednisone, the child developed increasing difficulty with walking and flexion contractures of the hips, knees and ankles (fig). Examination showed facial scarring, spasticity of the legs with increased reflexes and extensor plantar responses. The upper extremities were normal. A total deficiency of serum Clr component of complement was demonstrated. Complement levels were normal in the mother and her ANA was negative.

Discussion

Myelopathy is one of many neurological abnormalities observed in systemic lupus erythematosus. Although central nervous system symptoms may occur within the first decade, spinal cord involvement due to lupus erythematosus has only rarely been documented. Central nervous system disabilities such as myelopathy have not been previously described in the neonatal lupus erythematosus syndrome or in Clr complement deficiency states.

The pathogenesis of CNS lupus erythematosus, including myelopathy, is poorly understood. A true vasculitis, represented by inflammatory cells within the vessel walls, is uncommon in neurologically affected patients with lupus erythematosus although on occasions vasculitis may explain the neurological symptoms. The vasculopathy of CNS lupus erythematosus consists of proliferative changes in small arterioles and capillaries with surrounding gliosis and occasional perivascular collections of mononuclear cells suggesting an autoimmune basis. The autoimmune theory for CNS lupus erythematosus has been strengthened with the discovery of choroid plexus and CSF immune deposits and
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brain reactive (anti-neuronal) antibodies in CSF and plasma.20–23

In the neonatal lupus erythematosus syndrome, passage of maternal anti-Ro/SSA and anti-La/SSB antibodies to the child is associated with transient cutaneous manifestations and heart block. Immunoglobulin and complement deposits were noted on the atrial appendage of a three day old infant with this syndrome and suggested a causal relationship between the passively transferred antibodies and cardiac symptoms.24 Ro(SSA) antigen has been found in fetal and adult cardiac tissues and anti-Ro/(SSA) antibody binding in serum was noted to be decreased in a child with congenital heart block compared to an unaffected twin.25 Anti-Ro antibodies were also found in mothers of infants with isolated congenital heart block.26 Antibodies to the Ro(SSA) antigen can occur rarely in polymyositis and myotonic dystrophy which may have associated cardiac conduction defects.27 These antibodies may also be associated with neurological disabilities and mothers of dyslexic children have a higher incidence of anti-Ro antibodies.28 It is known that cardiac and neural tissues contain the largest quantities of the Ro antigen within the body.28 Thus in the neonatal lupus erythematosus syndrome, transplacentally acquired anti-Ro antibodies could cause neurological injury such as myelopathy, as well as cardiac conduction defects, through a direct immunopathological effect. It is also possible that anti-Ro(SSA) antibodies may cross-react with other antigens causing damage to selected tissues.29 Thus the pathogenesis of neonatal lupus erythematosus could be similar to other neonatal diseases such as transient myasthenia gravis, hyperthyroidism, and isoimmune thrombocytopenia in which transplacental factors are important.29

Lupus erythematosus is unusual in the first year of life unless it is inherited or associated with complement deficiencies.7,8 Our second patient developed systemic lupus erythematosus and myelopathy associated with a total C1r complement deficiency. C1r complement deficiency has been associated with recurrent infections, nephritis and systemic lupus erythematosus30,31 but neurologic disease has not been recorded. The associated immune defect may have predisposed this young child to develop CNS lupus erythematosus. Anti-Ro/SSA antibodies have been reported to be elevated in other complement deficiencies associated with systemic lupus erythematosus.32 Further, myelopathy has been noted in patients with anti-Ro/SSA antibodies and connective tissue disease.33 It is possible that anti-Ro/SSA antibodies may be significant in infantile onset hypocomplementaemic lupus erythematosus but unfortunately these antibodies were not measured in this second case during the active phase of the lupus erythematosus.

Myelopathy in very young children may be seen as a rare complication of lupus erythematosus. The transplacental passage of antibodies (anti-Ro/SSA) in neonatal lupus erythematosus is associated with transient symptoms but, as observed in our first case, these antibodies may also be associated with permanent neurological sequelae. The pathogenesis for the neurological damage in neonatal lupus erythematosus may be similar to the proposed immune mediated mechanisms causing congenital heart block. In addition, the myelopathy of infantile lupus erythematosus associated with a complement deficiency may suggest a similar autoimmune basis for the neurological disorder. Lupus erythematosus should be considered in the differential diagnosis of early onset myelopathy and anti-Ro(SSA) antibodies measured in neonates and infants presenting with an unexplained myelopathy.

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References

12. Gold AP, Yahru MR. Childhood lupus erythematosus: a clinical


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