Arq Neuropsiquiatr 1994, 52(1): 103-105

FAMILIAL DYSAUTONOMIA

(RILEY-DAY SYNDROME)

EDWARD R. TONHOLO-SILVA, SETSUKO IKEDA TAKAHASHI**, LUCIA YOSHINAGA****

SUMMARY - Familial dysautonomia, also known as Riley-Day syndrome, is a disorder of autonomic nervous system with an autosomal recessive mode of inheritance. Reduction and/or loss of unmyelinated and small myelinated fibers is found, as reduction of dopamine beta-hydroxylase in blood. The diagnosis is based on clinical features: diminished lacrimation, insensitivity to pain, poor temperature control, abolished deep tendon reflexes, postural hypotension, vomiting attacks, poor motor coordenation, and mental retardation. The treatment is symptomatic and many children die during the first years of life, usually as a result of repeated aspiration pneumonia. We report the case of a 1 year-old child with familial dysautonomia.

KEY WORDS: familial dysautonomia, neuropathy, autonomic nervous system.

Disautonomia familial (síndrome de Riley-Day)

RESUMO - A disautonomia familial, também conhecida por síndrome de Riley-Day, é desordem do sistema nervoso autônomo com herança autossômica recessiva. Redução e/ou perda de fibras pouco mielinizadas e não mielinizadas é encontrada, bem como redução da dopamina beta-hidroxilase no sangue. O diagnóstico é clínico: diminuição do lacrimejamento, insensibilidade à dor, distúrbio do controle térmico, reflexos profundos abolidos ou hipoativos, hipotensão postural, vômitos, pobre coordenação motora e retardo mental. O tratamento é sintomático e a maioria das crianças morre nos primeiros anos de vida, geralmente por pneumonias aspirativas de repetição. Relatamos o caso de uma criança de 1 ano de idade com disautonomia familial.

PALAVRAS-CHAVE: disautonomia familial, neuropatia, sistema nervoso autônomo.

Familial dysautonomia (FD), first described in 1949 under the title "central autonomic dysfunction with defective lacrimation"[5], is a disorder of autonomic nervous system with an autosomal recessive mode of inheritance. Anatomic studies revealed a reduction and/or loss of unmyelinated and small myelinated fibers in autonomic and peripheral nervous system[4], focal demyelination of dorsal roots and posterior columns of the spinal cord, noted in necropsy of cases known to have FD[3]. Plasma levels of dopamine beta-hydroxylase, the enzyme that converts dopamine to norepinephrine, are lower in patients with FD than in control subjects[8]. The excretion rates of vanillyl mandelic acid (VMA) and homovanillic acid (HVA) are respectively decreased and increased in dysautonomic subjects. The elevated ratio HVA/VMA may reflect failure of cathecolamine precursors to be converted normally to norepinephrine and epinephrine[7]. The diagnosis is based on clinical features. In this report we present the clinical and laboratory findings of a child with FD.

Division of Child Neurology, Department of Pediatrics, Faculdade de Medicina de Marília (FMM): *Assistant Professor of Neurology; ** Assistant Professor of Pediatrics; *** Student of Medicine. Aceite: 24-junho-1993.

Dr. Edward Roberto Tonholo Silva - Rua Julio Mesquita,295 - 17515-320 Marília SP - Brasil.

CASE REPORT

JAL, a 1 year-old male child has been seen intermittently at FMM Hospital de Clínicas since 6 months of age. His greatest problem is that he has unexplained febrile episodes and deglutition difficulty with weight loss. He has presented insensitivity to pain, diminished lacrimation, poor muscular tone, poor coordenation, vomiting attacks, auto-mutilation and neuropsychomotor retardation. Pregnancy was uncomplicated and delivery was normal. There is no known Jewish ancestry and no known consanguinity. Family history revealed a paternal aunt with mental retardation and muscular weakness who died at 8 years-old without a defined diagnosis. At 5 months, he developed what was called pneumonia. He sustained his head at 6 months and sat at 11 months; he has not yet crawled. On physical examination: he is small for his age, with low-weight; temperature 38.5C; his skin is thick and with several scars resulting from cutaneous infections; his tongue is smooth without fungiform papillae; his right hand is swelled with an ulcer on the index finger caused by auto-mutilation. He presents indifference to pain, abolished deep tendon reflexes and poor muscular tone. Moreover, he has had diminished lacrimation, but corneal reflex is normal. Complementary Tests - 1. Electroencephalogram showed no abnormalities; 2. Electroneuromyography revealed a sensory neuropathy; 3. Plasma calcium and phosphate were normal; 4. Urinary HVA is elevated; 5. Urinary HVA/VMA ratio is elevated. Radiological Findings - 1. CT-scan showed no abnormalities; 2. Right hand X-Ray has shown a reduction in bone density and increased index finger soft tissue; 3. Barium examination of upper gastrintestinal tract has shown a gastroesophageal reflux; 4. Chest X-Ray showed no abnormalities.

COMMENTS

The clinical course of this child fulfils the criteria outlined by Riley and Moore[6], which they considered essential for diagnosis, as well as others which may be helpful. The essential criteria for diagnosis were: a) history suggesting feeding difficulty from birth; b) regular failure in producing overflow tears; c) absent or hypoactive deep tendon reflexes; d) absent corneal reflex; e) postural hypotension; f) emotional lability; g) relative indifference to pain; h) absence of fungiform papillae on tongue. Other helpful criteria not essential for diagnosis were: a) Jewish progeny; b) blotching of skin with eating and/or excitement; c) abnormal temperature control; d) excessive sweating; e) abnormal esophageal motility; f) elevated urinary HVA/VMA ratio. Our patient has presented many features which are found in FD, such as: feeding difficulty, diminished lacrimation, absent deep tendon reflexes, indifference to pain, absence of fungiform papillae on tongue, abnormal temperature control, abnormal esophageal motility and elevated urinary HVA/VMA ratio.

Analysing the laboratory features, patients with FD have been reported to have low levels of plasma dopamine beta-hydroxylase (about half of that in normal subjects), enzyme that converts dopamine to norepinephrine and is released from sympathetic nerve endings. In those patients with FD an elevated urinary HVA/VMA ratio was found, reflecting failure of cathecolamine precursors to be normally converted to norepinephrine and epinephrine[7,8]. Our patient presented elevated urinary HVA/VMA ratio.

Brown and Johns[1] evidenced a defect of peripheral nerve conduction in 7 of 10 patients with FD. Dyck has proposed a classification of hereditary autonomic sensory neuropathies (HASN) in five groups: HASN-I, dominant inheritance; HASN-II, recessive inheritance; HASN-III, familial dysautonomia (Riley-Day syndrome); HASN-IV, congenital indifference to pain; HASN-V, congenital indifference to pain with neuropathic pattern[2].

There is no specific treatment, and prognosis is poor. Many children die during the first years of life, usually as a result of repeated aspiration pneunomia. The management of our patient is concentrated on prevention of complications.

REFERENCES

1. Brown JC, Johns RJ. Nerve conduction in familial dysautonomia (Riley-Day syndrome). JAMA 1967, 201: 118-121.
2. Dyck, PJ. Inherited neuronal degeneration and atrophy affecting peripheral motor, sensory and autonomic neurons. In: Dyck PJ, Thomas PK, Lambert H, Bunge R (eds). Peripheral Neuropathy. Ed.2 Philadelphia: Saunders 1984, p. 1600-1655.

3. Fogelson MH, Rorke LB, Kaye R. Spinal cord changes in familial dysautonomia. Arch Neurol 1967, 17: 103-108.
4. Pearson J, Budzilovich G , Finegold MJ. Sensory, motor and autonomic dysfunction: the nervous system in familial dysautonomia. Neurology 1971, 21:486-493.
5. Riley CM, Day RL, Greeley DM, Langford WS. Central autonomic dysfunction with defective lacrimation: I. Report of five cases. Pediatrics 1949, 3:468-478.
6. Riley CM, Moore RH. Familial dysautonomia differentiated from related disorders. Pediatrics 1966, 37: 435-446.
7. Smith AA, Taylor R, Wortis SB. Abnormal cathecolamine metabolism in familial dysautonomia. N. Engl J Med 1963, 268:705-707.
8. Weinshilboum RM, Axelrod J. Reduced plasma dopamine beta-hydroxylase activity in familial dysautonomia. N Engl J Med 1971, 285: 938-942.