The syndrome of diabetes insipidus, diabetes mellitus and optic atrophy (DIDMOA) with diabetic cheiroarthropathy

G. A. FITZGERALD*†
M.R.C.P.I., M.R.C.P.

J. F. GREALLY**
M.D., M.Sc.

M. I. DRURY†
M.D., F.R.C.P.I.

†The Department of Diabetes/Endocrinology, Mater Misericordiae Hospital, Dublin 7, and

**The Department of Immunology, School of Pathology, Trinity College, Dublin 2, Ireland

Summary

Two sisters with diabetes mellitus and optic atrophy are described. One of them also has vasopressin responsive diabetes insipidus. Both have diabetic cheiroarthropathy, an unusual deformity of the hands.

Introduction

The coexistence of diabetes mellitus with diabetes insipidus and optic atrophy was first described by de Lawther in 1949 and has been termed the DIDMOA syndrome. Since then nerve deafness, ataxia and renal anomalies have been added (Page, Asmal and Edwards, 1976). Two siblings are described who display additional features.

Patients

The eldest sibling is a 23-year-old female who had a classical onset of diabetes mellitus at the age of 5 years. Despite adequate control of hyperglycaemia with a twice daily insulin regimen, polyuria remained troublesome. An IVP performed at the age of 12 years showed bilateral hydronephrosis. A transurethral resection produced symptomatic benefit. Bilateral optic atrophy and Argyll-Robertson pupils were noted but diabetes insipidus was not suspected.

At 22 years of age vision was limited to light perception. Although the patient did not have symptomatic polyuria, an 8-hr water deprivation test (Dashe *et al.*, 1963) confirmed vasopressin responsive diabetes insipidus. A repeat IVP was normal. Bilateral high tone deafness was detected on pure tone audiometry. Additional clinical features were noted at this time. There was a fixed flexion deformity of all interphalangeal joints (Fig. 1). This was unassociated with any palpable fascial mass, clinical myopathy or neuropathy. The patient's IQ

FIG. 1. The hands of the eldest sibling.

was 69 (WISC) and she worked in a sheltered workshop. She had cerebellar ataxia and nystagmus.

The second sibling is an 18-year-old female who had a classical onset of diabetes mellitus at the age of 12 years. She is poorly controlled on a twice daily insulin regimen. Bilateral optic atrophy and Argyll-Robertson pupils are present but functional vision is retained ($R=6/60$, $L=6/30$). She displays hand deformities identical with those of her sister but does not have diabetes insipidus. An IVP shows a duplex collecting system on the right side.

Both sisters have normal ulnar, radial and median nerve conduction, electromyograms and hand X-rays. Rheumatoid factor and antibodies to nuclear factor, smooth muscle, mitochondria and

* Present address: Department of Clinical Pharmacology, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12.

TABLE 1. Red cell antigens

Patients	ABO	Rh	MN	P	S	s	Lu ^a	K	k	Fy ^a	Fy ^b	JK ^a	JK ^b
♂	A	CcDee	MN	+	-	+	-	-	+	+	+	+	-
♀	A	ccdde	NN	-	-	+	-	-	+	+	+	+	+
C1	A	ccdde	NN	-	-	+	-	-	+	+	-	+	-
C2	A	CcDee	NN	-	+	-	-	+	+	+	+	+	+
C3	A	ccdde	NN	+	-	+	-	-	+	+	-	+	+
C4	A	CcDee	NN	+	-	+	-	-	+	-	+	+	+

Parents are denoted as ♂, ♀; siblings C1, C2, etc.

TABLE 2. HLA types: serological and mixed lymphocyte culture determinants

Patients	Serological† haplotyping	♂	♀	Stimulating cells C1	C2	C3	C4
♂	a/b	/	++	+	+	+	+
♀	c/d	+	/	±	+	+	+
C1	a/c	±	+	/	±	+	+
C2*	a/c	+	+	+	/	+	+
C3*	b/c	+	++	+	+	/	±
C4	b/d	+	+	+	+	±	/

* Denotes affected sibling, C2 being the eldest

† Serological haplotypes: a=A1, B8, b=A28, x
c=A2 B12, d=Aw29 Bw40.

thyroidal colloid and microsomes are negative. In addition, thyroxine, cortisol, urea and electrolytes are normal. Skull X-rays and pituitary tomography are normal. The second sibling has a selective increase in urinary alanine but other indices of renal tubular function are normal.

The other family members, comprising two male siblings aged 17 and 26 years and the parents, are clinically normal and have normal glucose tolerance, urinary osmolarity and audiometry. There is no marital consanguinity, nor family history of endocrine or neurological disease and the mother's obstetric history is normal. A study of the HLA and ABO patterns (Tables 1 and 2) in the family did not suggest linkage between the genes for these surface antigens and for those of the syndrome. Chromosomal G banding of peripheral blood lymphocytes in the eldest daughter is normal.

Discussion

The association of 'double diabetes' with optic atrophy is rare. Piley and Thompson (1976) estimate that twenty-four cases have been described. The similarity of symptoms between poorly controlled diabetes mellitus and diabetes insipidus may delay the diagnosis of the latter condition. Thus diabetes mellitus and optic atrophy have tended to be detected before diabetes insipidus in most published cases (Marquardt and Loriaux, 1974; Page *et al.*, 1976). Nerve deafness is usually asymptomatic but detected on audiometry.

A deformity of the hands similar to that of these

patients has been termed diabetic cheiroarthropathy (Benedetti and Noacco, 1976) and has not previously been described in the DIDMOA syndrome. It occurs in long-standing juvenile onset diabetics who are poorly controlled with insulin (Rosenbloom and Frias, 1974; Grgic *et al.*, 1975). There is a progressive stiffness of the interphalangeal joints. Shortness of stature and hepatomegaly may be additional features. This condition differs from the 'diabetic hand syndrome' (Jung *et al.*, 1971) in that nerve conduction studies and electromyography are normal.

The DIDMOA syndrome is thought to be of autosomal recessive inheritance (Page *et al.*, 1976). Affected siblings of index cases usually incompletely express the syndrome. Parental consanguinity has been reported in some cases (Rose *et al.*, 1966).

Acknowledgment

This work was supported by a grant to Dr Fitzgerald from the Mater Misericordiae Hospital Diabetes Research Fund.

References

- BENEDETTI, A. & NOACCO, C. (1976) Cheiroarthropathy of juvenile diabetes. *Acta diabetica latina*, 13, 54.
- DASHE, A.M., CRAMM, R.E., CRIST, C.A., HOBNER, J.F. & SOLOMAN, D.H. (1963) A water deprivation test for the differential diagnosis of polyuria. *Journal of the American Medical Association*, 185, 699.
- DE LAWTHER, D.S. (1949) Coexistence of diabetes insipidus and diabetes mellitus. *Medical Annals of the District of Columbia*, 18, 398.

- GRGIC, A., ROSENBLOOM, A.L., WEBER, F.T. & GIORDANO, B. (1975) Joint contracture in childhood diabetes (Correspondence). *New England Journal of Medicine*, **292**, 372.
- JUNG, Y., HOHMANN, T.C., GERENTH, J.A., NOVAK, J., WASSERMANN, R.C., D'ANDREA, B.J., NEWTON, R.H. & DANOWSKI, T.S. (1971) Diabetic hand syndrome. *Metabolism*, **20**(11), 1008.
- MARQUARDT, J.L. & LORIAUX, D.L. (1974) Diabetes mellitus and optic atrophy. *Archives of Internal Medicine*, **134**, 32.
- PAGE, M.McB., ASMAL, A.C. & EDWARDS, C.R.W. (1976) Recessive inheritance of diabetes: The syndrome of diabetes insipidus, diabetes mellitus and optic atrophy and deafness. *Quarterly Journal of Medicine*, **45**, 505.
- PILEY, S.F.J. & THOMPSON, H.S. (1976) Familial syndrome of diabetes insipidus, diabetes mellitus, optic atrophy and deafness (didmoad) in childhood. *British Journal of Ophthalmology*, **60**, 294.
- ROSE, R.C., FRASER, G.R., FRIEDMANN, A.I. & KOHNER, E.M. (1966) The association of juvenile diabetes mellitus and optic atrophy: Clinical and genetic aspects. *Quarterly Journal of Medicine*, **35**, 385.
- ROSENBLOOM, A.L. & FRIAS, J.L. (1974) Diabetes mellitus, short stature and joint stiffness – a new syndrome. *Clinical Research*, **22**, 92A.