Lipodystrophy in Patients with Juvenile Dermatomyositis — Evaluation of Clinical and Metabolic Abnormalities

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ABSTRACT. ***Objective.*** Lipodystrophy and associated metabolic abnormalities are being increasingly recognized as complications of juvenile dermatomyositis (JDM). We investigated the prevalence of lipodystrophy and the extent of metabolic abnormalities related to lipoatrophic diabetes mellitus in patients with JDM.

Methods. Twenty patients with JDM were evaluated for evidence of lipodystrophy and associated lipoatrophic diabetes mellitus. All patients underwent clinical assessment, laboratory investigations, and metabolic studies (oral glucose tolerance test, lipid studies, insulin antibodies).

Results. We found clinical evidence of lipodystrophy and lipoatrophic diabetes mellitus in 4 of 20 patients with JDM and metabolic abnormalities known to be associated with lipodystrophy in another 8 patients. The 20 patients with JDM were categorized as follows: Group 1 (Patients 1–4) consisted of patients with lipodystrophy and either diabetes mellitus (2 patients) or impaired glucose tolerance (2 patients); Group 2 (Patients 5–12): no lipodystrophy but abnormal glucose and/or lipid studies; Group 3 (Patients 13–20): no lipodystrophy and no abnormalities of glucose and lipid studies.

Conclusion. We found 25% of patients with JDM have lipodystrophy, and 50% present with hypertriglyceridemia and insulin resistance. Screening for metabolic abnormalities in JDM should be included in routine followup because of the effect of lipodystrophy on longterm prognosis. (J Rheumatol 2001;28:610–5)

Key Indexing Terms:
JUVENILE DERMATOMYOSITIS LIPODYSTROPHY LIPOATROPHIC DIABETES

Juvenile dermatomyositis (JDM) is an inflammatory myopathy of unknown origin. Clinical manifestations include proximal muscle weakness and characteristic skin changes. Laboratory findings usually include elevated serum levels of muscle enzymes and electromyographic (EMG) abnormalities consistent with an inflammatory myopathy[1-3]. Muscle biopsies reveal perivascular infiltrates of mononuclear cells and perifascicular atrophy of muscle fibers[2,3].

An associated finding that may have considerable prognostic influence in patients with JDM is the syndrome of lipodystrophy and lipoatrophic diabetes mellitus[4-7]. Lipodystrophy describes a clinical condition characterized by either generalized or localized partial loss of subcutaneous fat, hirsutism, and acanthosis nigricans that is associated with hepatomegaly, insulin resistant diabetes mellitus, and hyperlipidemia[8]. We evaluated a clinic population of children with JDM for evidence of lipodystrophy and lipoatrophic diabetes mellitus to determine its prevalence. The results indicate a surprisingly high prevalence of lipodystrophy and metabolic abnormalities that may precede lipoatrophic diabetes mellitus in patients with JDM.

MATERIALS AND METHODS

Patients. Twenty patients with JDM (12 girls, 8 boys) who were referred to the Pediatric Rheumatology Clinic at British Columbia's Children's Hospital (BCCH) in Vancouver between January 1, 1981, and June 30, 1996, were enrolled in the study. The diagnosis of JDM was made on clinical grounds, with typical rash, proximal muscle weakness, and raised muscle enzymes in all patients. EMG studies and muscle biopsies in several patients were compatible with the diagnosis. BCCH is the only tertiary care children's hospital for British Columbia. From 1981 to 1996, 27 patients with JDM were seen in the clinic. According to recent census data[9] for the population at risk (roughly 800,000 children from age 0 to 16 yrs) and according to incidence data[10] for JDM in Canada the 27 children should represent all expected cases of JDM in the province. Seven patients were not available for study because they had moved or were lost to followup.

Clinical and laboratory variables. Twenty patients underwent clinical evaluation by a pediatric rheumatologist and a pediatric endocrinologist. Examination included measurement of weight (for age) and height (for age)

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expressed as sex-specific centiles. The current medications of all patients were noted. Disease activity was assessed according to a physician's global assessment as inactive, mild, moderate, or severe. The disease course was defined as monocyclic or recurrent/continuous[11]. Muscle and skin disease were assessed according to clinical and laboratory variables of disease activity[1,3]. Remission of disease was defined as absence of muscle weakness or rash with normal muscle enzyme levels, and taking no medication.

Laboratory investigations included total and differential white blood cell count, erythrocyte sedimentation rate (ESR), creatine kinase (CK), factor VIII related antigen, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), gammaglutamyl transferase (GGT), the third component of complement (C3), blood urea nitrogen (BUN), creatinine, and urinalysis. Investigations to assess glucose and lipid status included measurement of venous plasma insulin (Pharmacia Insulin RIA 100), measurement of serum insulin antibodies by qualitative ELISA (Isletest kit, Biomerica), detection of serum insulin receptor antibodies by radioimmunoassay (Nichols Institute), and quantitation of fasting total serum cholesterol, HDL and LDL cholesterol and triglycerides. All patients underwent a 3 h oral glucose tolerance test (OGTT) as follows: a normal carbohydrate intake for 2 days was followed by 12 h overnight fast. An oral glucose load of 1.75 g/kg (maximum 75 g) was given at 8:00 AM and plasma glucose and insulin levels measured at half-hour intervals for 3 hours. Using the Diagnostic Criteria of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus[12], patients were grouped as having normal glucose tolerance (fasting plasma glucose < 6.1 mmol/l, and/or 2 h postload glucose < 7.8 mmol/l); or impaired glucose tolerance (fasting plasma glucose ≥ 6.1 but < 7.0 mmol/l, and/or 2 h postload glucose ≥ 7.8 but < 11.1 mmol/l; or diabetic (fasting plasma glucose > 7.8 mmol/l, and/or 2 h postload glucose > 11.1 mmol/l). Insulin resistance was defined as a fasting glucose to insulin ratio (fasting G:I ratio) < 7 mg/10^{-4} U (= 65 10×6 in SI units)[13,14].

RESULTS

The patients' characteristics are shown in Table 1. The 20 patients (12 girls, 8 boys) are grouped according to their clinical and laboratory findings: Group 1 (Patients 1–4): lipodystrophy and associated abnormalities of glucose and lipid studies; Group 2 (Patients 5–12): no lipodystrophy but abnormal glucose and lipid studies; and Group 3 (Patients 13–20): no lipodystrophy and normal glucose and lipid studies.

Patient characteristics. All patients had documented evidence of classical skin and muscle involvement. The most prominent findings were proximal symmetric muscle weakness (20 patients), facial rash (15 patients), peripheral rash (10 patients), Gottron's papules (11 patients), and generalized fatigue (6 patients). Nine patients with facial rash showed evidence of atypical heliotrope rash. Mean age at diagnosis was 8.3 ± 4.5 (mean ± standard deviation) years and mean interval from first symptoms of JDM to diagnosis was 3.4 ± 2.3 months.

All patients had initially been treated with high dose (30 mg/kg) intravenous methylprednisolone pulse therapy (IVMP). Subsequent treatment included oral prednisone (17 patients), intravenous gammaglobulin (IVIG, 6 patients), methotrexate (MTX, 3 patients), hydroxychloroquine (one patient), and cyclosporine A (CyA, one patient).

Table 1. Clinical characteristics of patients.

Patient	Sex	Age at Diagnosis, yrs	Age at Study, yrs	Course of Disease	Active Muscle Disease at Study	Active Skin Disease at Study	Duration of Prednisone Treatment, mo	Prednisone Dose at Study, mg/kg/day	Weight for Age, percentile	Height for age, percentile
Group 1										
1	F	8.3	13.5	REC	No	GLD, CAL, HIR,	59	0.17	< 5th	< 5th
2	M	4.2	15.1	REC	No	PLD, A	23	0.37	25th	75th
3	M	10.8	13	REC	Yes	PLD, CAL, A	27	0.22	25th	< 5th
4	F	10.7	16.7	REC	Yes	PLD, HIR, A	65	0	50th	< 5th
Group 2										
5	F	11.2	12.5	MC	Yes	R	17	0.24	10th	< 5th
6	M	10	14.5	REC	Yes	R, CAL	60	0.21	75th	< 5th
7	F	4.9	5	NEW	Yes	R	1	i.v. 3× 30	50th	10th
8	M	12.9	14	MC	Yes	R	13	0.24	75th	< 5th
9	F	7.4	10.2	REC	Yes	R	34	0.47	75th	< 5th
10	F	6.2	10	MC, REM	No	No	1	0	95th	> 95th
11	F	14	14	NEW	Yes	R, GP	1	1.0	50th	50th
12	F	15.7	15.7	NEW	Yes	R	1	0.9	50th	10th
Group 3										
13	F	3.5	7.9	MC	No	R	1	0	50th	50th
14	M	12.2	18.1	REC	No	R	2	0	10th	25th
15	M	1.7	4	MC	Yes	R	22	0.36	< 5th	< 5th
16	F	14.7	26.2	REC, REM	No	No	73	0	ND	ND
17	M	1.2	3.1	REC	No	GP	23	0.06	95th	90th
18	F	9	10.3	REC	Yes	R, CAL	38	0.43	10th	10th
19	F	3.7	4	MC	Yes	R	1	0.9	90th	95th
20	M	3.2	8.1	MC, REM	No	No	20	0	25th	10th

MC: monocyclic course of disease, REC: recurrent or continuous course of disease, NEW: newly diagnosed, REM: remission, GLD: generalized lipodystrophy, PLD: partial lipodystrophy, CAL: calcifications, HIR: hirsutism, R: JDM rash, GP: Gottron's papules, A: acanthosis nigricans, ND: not done.

Mean interval from diagnosis of JDM to study entry was 3.9 ± 3.2 years overall, 6.1 ± 3.6 years in Group 1, 1.7 ± 1.8 years in Group 2, and 4.1 ± 3.6 years in Group 3.

At entry into the study only 3 patients were in full remission and taking no medication. One patient was receiving intermittent IVMP treatment and 13 patients (70%) were receiving oral prednisone in a dose range from 0.06 to 1 mg/kg/day. Mean duration of prednisone treatment was 24.1 ± 23.8 months overall. Height for age was less than the 5th centile in 7 of 12 children in Groups 1 and 2 and in only one of 8 in Group 3 ($p = 0.028$, Fisher's exact test).

Comparing the groups separately or in combination (Group 1 and 2 versus 3), there was no difference between sex distribution, age at diagnosis and/or at study entry (Group 1 was too small to include this group in individual comparisons). Duration of prednisone treatment was considerably shorter in Group 2 (compared with Group 1 and Group 3, see Table 1), as there were 4 patients in Group 2 with newly diagnosed disease, who had just received IVMP treatment.

Clinical symptoms and metabolic investigations (Tables 1 and 2). Group 1 (Patients 1–4). Patient 1, the index case, is a representative example of evolution of lipodystrophy in JDM: a diagnosis of JDM was made in this girl in 1987 at the age of 8 years, when she presented with a 4 month history of muscle weakness. She had typical erythematous rash of the face, Gottron's rash on her fingers, and proximal muscle weakness. She was treated with IV methylprednisolone followed by oral prednisone and physiotherapy, and showed initial improvement. Prednisone taper was followed by exacerbation of symptoms and the disease pursued an unrelenting course. Trials of IVIG, MTX, CyA, and continued glucocorticoids failed to prevent the progression of disease, and she became wheelchair dependent.

Table 2. Laboratory investigations and metabolic studies at time of study.

Patient	CK	F-VIII Rel AG	AST	ALT	LDH	GGT	Fasting Serum Triglyc	HDL Chol	LDL Chol	OGTT, Fasting Glucose/ 2 h Glucose	OGTT, Base Insulin/ Peak Insulin	Fasting Glucose/ Insulin Ratio	Comment
	U/l 50–295	U/l 0.5–1.5	U/l 10–30	U/l 10–30	U/l 380–640	U/l 14–26	mmol/l†	mcmol/l†	mmol/l†	mmol/l*	pmol/l*	10 × 6**	
Group 1													
1	< 20	0.84	120	198	693	59	1.98	0.66	4.66	5.8/9.2	607/2356	9.6	Impaired GT, IR, HTG
2	367	1.8	94	172	676	67	9.12	0.68	4.32	8.1/17.7	672/2452	12.0	Diabetic GT, IR, HTG
3	41	1.8	77	109	830	175	2.91	0.5	4.23	4.9/9.7	233/2020	21.0	Impaired GT, IR, HTG
4	200	ND	77	136	500	72	1.84	ND	4.26	6.3/15.8	2156/3388	2.9	Diabetic GT, IR, HTG
Group 2													
5	32	0.72	14	24	732	22	1.37	1.25	5.17	4.6/9.4	152/2970	30.2	Impaired GT, IR
6	86	1.28	32	33	858	45	1.5	0.93	ND	4.5/7.0	148/1315	30.4	IR
7	131	1.2	43	43	397	15	2.54	0.81	3.3	4.5/4.8	104/599	43.2	IR, HTG
8	< 20	0.47	21	33	519	25	2.08	1.35	4.8	4.6/7.1	158/2480	29.11	IR, HTG
9	< 20	1.61	45	24	523	36	2.03	0.8	5.07	4.3/5.9	144/2346	29.9	IR, HTG
10	64	0.98	36	26	ND	ND	1.89	0.62	3.66	5.2/6.7	192/2494	27.1	IR, HTG
11	515	2.15	114	144	1090	ND	1.73	0.75	4.57	5.5/6.4	208/1432	26.4	IR, HTG
12	< 20	2.93	47	55	912	56	2.07	ND	4.42	4.3/6.2	54/1360	79.6	HTG
Group 3													
13	44	1.29	25	28	551	18	0.48	1.09	3.43	4.9/6.6	72/806	68.0	Normal
14	1058	ND	68	59	392	18	1.09	0.99	ND	5.0/6.3	71/354	69.4	Normal
15	35	1.23	57	20	828	16	1.09	ND	3.47	4.0/5.9	42/254	95.2	Normal
16	34	ND	11	23	ND	ND	ND	ND	ND	5.4/6.3	84/866	64.2	Normal
17	103	0.76	31	21	701	20	0.56	1.07	3.25	4.6/5.6	42/247	109.5	Normal
18	80	1.04	28	17	666	17	ND	1.28	3.48	4.7/6.0	ND		Normal
19	822	1.21	129	72	1313	19	1.11	0.99	4.14	4.8/6.8	31/278	154.8	Normal
20	39	0.75	21	11	ND	14	0.56	1.14	2.75	5.1/6.1	42/161	121.4	Normal

F-VIII Rel AG: Factor VIII related antigen, CK: creatin kinase, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, GGT: gamma glutamyl transferase, Triglyc: triglyceride, Chol: cholesterol, Impaired GT: impaired glucose tolerance, IR: insulin resistance, HTG: hypertriglyceridemia, ND: not done.

†Reference values according to Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents, National Cholesterol Education Program, 1991, US Department of Health and Human Services.

*Impaired glucose tolerance: fasting ≥ 6.1–7.0 mmol/l, 2 h ≥ 7.8–11.1 mmol/l. Diabetic glucose tolerance: fasting ≥ 7.0 mmol/l or 2 h ≥ 11.1 mmol/l.

**Insulin resistance: fasting G:I ratio < 7 mg/10^{-4}U (= < 65 10 × 6).

Table 3. Spearman correlation coefficients between metabolic variables and measures of disease or treatment in patients with JDM.

	Disease					Treatment	
	ALT	AST	CK	F-VIII Rel Antigen	LDH	Dose of Prednisone	Duration of Prednisone Treatment
Triglycerides	0.6039*	0.3169	–0.1246	0.1472	–0.0235	0.2288	0.4921
HDL Cholesterol	–0.6057	–0.6745	–0.0634	–0.6237	–0.2200	–0.0200	–0.0313
LDL Cholesterol	0.4426	0.1877	–0.3859	0.0956	0.0642	0.2642	0.1554
Peak Insulin	0.4249	0.0860	–0.2440	–0.0397	–0.2147	0.0080	0.1907
G:I Ratio	–0.6148	–0.3153	0.057	–0.2135	0.2546	0.0075	–0.3522

*$p < 0.05$.

Hirsutism noted one year after onset was ascribed to steroid use. In 1991 she became increasingly anorectic with marked weight loss and amenorrhea despite normal onset of puberty. CK, ALT, and GGT were normal; AST was elevated. Random glucose was < 7.8 mmol/l. She had diminished subcutaneous fat, which was thought to reflect her anorexia. Continued weight loss led to introduction of nasogastric tube feeding. Abdominal ultrasound revealed enlarged hyperechogenic liver consistent with fatty infiltration, and serum levels of liver enzymes (ALT, GGT) were then elevated. In September 1992, at age 13 years, the diagnosis of lipodystrophy with insulin resistant diabetes was first entertained. Retrospectively, a number of features had been more longstanding and present since age 12 years, but were ascribed to other causes: raised glucose, high liver enzymes, generalized loss of subcutaneous fat, acanthosis nigricans, hirsutism, hepatomegaly, and primary amenorrhea. Further investigations showed that cholesterol was 4.66 mmol/l (normal range 3.11–5.18) with HDL cholesterol 0.66 mmol/l (0.93–2.15) and triglycerides 1.98 mmol/l (0.42–1.47). OGTT showed diabetic glucose tolerance and G:I ratio of 1.2 (abnormal: < 7 mg/10^{-4} U) indicated insulin resistance. The luteinizing hormone/follicle stimulating hormone (LH/FSH) ratio was 7.3:4.1 IU/l (LH 2–14, FSH 3–15), and testosterone was 8.8 nmol/l (normal adult value 10–30).

In addition to Patient 1, 3 other patients were found to have evidence of partial lipodystrophy involving their extremities. Patient 3 also developed lipoatrophic facial changes. The first documented lipodystrophic changes occurred 4 years after the diagnosis in Patient 1 and 12, 3, and 6 years after diagnosis in Patients 2–4. All 4 patients had acanthosis nigricans, and 2 patients had hepatomegaly. Both female patients (Patients 1 and 4) had elevations of LH/FSH ratio, elevated testosterone levels, and hirsutism consistent with hyperandrogenism. Patients 1, 3, and 4 had chronic recurrent JDM with severe flexion deformities (Patients 1, 3), calcinosis (Patients 1, 3), and growth failure. Patient 2 presented with lipodystrophy and diabetes mellitus when the JDM, which had been quiescent for more than 12 years, flared (indicated by CK, AST, and ALT elevations) prior to study entry. Progression of disease and steroid dependence led to introduction of MTX (one patient), IVIG (2 patients), and CyA (one patient). All patients showed marked elevation of triglycerides and GGT in addition to elevated AST, ALT, and LDH levels indicating liver disease, but probably also reflecting ongoing myositis. Liver ultrasound tests of all patients showed no specific morphologic abnormalities. OGTT results revealed insulin resistant diabetes in 2 patients and impaired glucose tolerance in 2 patients (Table 2). Insulin antibodies were detected by ELISA in Patient 1 but were absent in Patients 2 and 3; insulin receptor antibodies were measured by radioimmunoassay in Patients 1, 2, and 3 and were negative. Three patients (Patients 1–3) had a family history of diabetes in 1st degree (Patient 2) and 2nd degree (Patients 1–3) relatives. C3a level was only measured in Patient 1 and showed marked elevation (463 µmol/l). Patients 1–3 had microalbuminuria at time of the study, with albumin excretion rates ranging from 37 to 67 µg/min. All patients of Group 1 received dietary counselling and 2 patients started alpha-glucosidase inhibitor treatment (acarbose) in an attempt to decrease postprandial blood glucose levels. Unfortunately, acarbose treatment had to be discontinued due to nausea and dizziness in both patients.

Group 2 (Patients 5–12). Seven of the 8 patients in Group 2 had active muscle disease or cutaneous changes of JDM (rash in all 7 patients, calcinosis in Patient 6), but there were no clinical features of lipodystrophy. Patients 7, 11, and 12 had disease of less than 6 weeks' duration and were receiving moderate to high doses of steroids when enrolled in the study. Laboratory investigations in Group 2 revealed normal LDL cholesterol levels but marked hypertriglyceridemia and depressed HDL cholesterol levels in all patients. OGTT revealed impaired glucose tolerance only in Patient 5; fasting G:I ratios were abnormal in Patients 5–11, indicating insulin resistance[12].

Group 3 (Patients 13–20). Six of 8 patients in Group 3 had evidence of active myositis (3 patients) or dermatitis (6

patients), but had no clinical signs of lipodystrophy. Lipid studies as well as OGTT results and fasting G:I ratios were all normal.

Characteristics of 7 female patients who were not enrolled in the study. Six patients (age 10–19 years) were lost to followup; at their most recent assessments (2–16 years after diagnosis) 5 were in full remission and one was in partial remission. One patient, age 19 years, who was diagnosed at age 3 years and had a poor response to therapy (multiple courses of IVMP and CyA) has been followed closely by a pediatric rheumatologist outside BCCH. At her most recent followup (1999) she had generalized lipoatrophy and was severely disabled by flexion deformities and calcifications. Metabolic studies were not available for this patient.

DISCUSSION

The coexistence of JDM and lipodystrophy, with or without diabetes (but always with hyperinsulinemia, when measured, has been documented in several case reports[5-8], but we are not aware of any studies investigating the prevalence and etiological factors of this association. Our study summarizes a 16 year, single center experience and characterizes lipodystrophy and the associated abnormalities of glucose and lipid metabolism in patients with JDM. Lipodystrophic changes of patients in our study included acquired generalized lipodystrophy in one patient and partial lipodystrophy of upper extremities in another 3 patients; all 4 patients also had acanthosis nigricans and marked abnormalities of glucose and lipid metabolism. None of these patients had a history indicating preceding panniculitis, but skin biopsies were not performed. The most notable finding in our patients with JDM is the high prevalence of hypertriglyceridemia, OGTT abnormalities, and abnormal fasting G:I ratios; 5 of 20 patients (25%) had impaired or diabetic glucose tolerance. During our study one patient in Group 1 (Patient 3) had OGTT abnormalities 6 months prior to development of partial lipodystrophy of the extremities. This is probably the first documented OGTT abnormality in a patient with JDM that preceded lipoatrophic changes. In our followup assessments no patient in Group 2 has yet developed clinical features of lipodystrophy (mean total followup for all patients 5.7 ± 2.7 years, mean followup for patients of Group 2 since study 2.8 ± 0.9 years). We have identified the 7 patients in whom followup was not possible. It is possible that they could have influenced the frequency with which lipodystrophy or abnormalities of glucose metabolism were identified. One patient, although well known to us, was not available for studies of glucose metabolism and was therefore not included, although she had severe lipodystrophic features. No others had clinically evident lipodystrophy at last followup, but they were not available for OGTT.

The characteristic metabolic abnormality in patients with total or partial lipodystrophy is insulin resistance and abnormal glucose tolerance[15-19]. The mechanism responsible for insulin resistance is not known, but the heterogeneity of insulin dysfunction in patients with lipodystrophy, illustrated by reports of prereceptor, receptor, and postreceptor abnormalities, suggests that lipodystrophy may be associated with several different disorders involving altered insulin action. Several studies have also revealed that muscle disease may be a major contributor to insulin resistance in patients with non-insulin dependent diabetes[19-23]. Skeletal muscle is the principal site of insulin mediated glucose disposal, and variations in the rate of insulin stimulated glycogen synthesis in muscle account for most of the variance in insulin sensitivity among healthy subjects[20]. Borkman, *et al*[22] demonstrated that changes in the fatty acid composition of muscles modulate the action of insulin and thus contribute to altered insulin sensitivity. It may therefore be hypothesized that inflammatory muscle disease itself may represent the link to insulin resistance in patients with JDM. Accumulation of hepatic triglycerides interferes with the liver's capacity to convert fatty acids to VLDL, leading to steatosis and hepatomegaly[23].

A high C3a level was found in the one patient in whom it was measured. C3a is identical to adipsin-acylation stimulating protein (ASP), which is more potent than insulin at stimulating esterification of fatty acids into triglycerides in human fibroblasts and adipocytes[24]. High triglyceride levels have been shown to correlate with high C3a levels[25]. This association requires further exploration.

Whether any patient of Group 2 presenting with metabolic abnormalities has an increased risk of developing lipodystrophy and lipoatrophic diabetes in the future remains unknown. Some of our patients' metabolic abnormalities such as the dyslipoproteinemia and hyperinsulinemia may be caused by corticosteroid treatment. Ilowite, *et al*[26] differentiated between characteristic patterns of dyslipoproteinemia caused by corticosteroid treatment and a pattern attributable to disease activity in patients with pediatric systemic lupus erythematosus. Longterm use of corticosteroids results in elevated HDL cholesterol, VLDL cholesterol, and triglycerides, whereas disease activity causes a depression in HDL cholesterol, while VLDL and triglycerides are elevated. If an analogous argument can be made for JDM, then the finding of low levels of HDL cholesterol suggests that the dyslipoproteinemia is on the basis of disease activity rather than corticosteroid use.

Longterm use of CyA, also known to be associated with hyperinsulinemia and lipid abnormalities, has never to our knowledge been observed to contribute to the occurrence of lipodystrophic changes in patients with JDM.

As shown in Table 3, Spearman correlation coefficients were calculated to define possible relationships between metabolic variables (triglycerides, HDL cholesterol, LDL cholesterol, peak insulin levels, G:I ratio) and measures of

disease (ALT, AST, CK, factor VIII related antigen, and LDH) or treatment (duration and dose of prednisone): no significant relationship could be observed between steroid treatment and metabolic abnormalities.

Our study revealed a surprisingly high prevalence of lipodystrophy or associated biochemical abnormalities in patients with juvenile dermatomyositis. We identified one subgroup of patients with abnormalities of glucose and lipid metabolism who may represent patients at risk of progressing to lipodystrophy. We were not able to identify predictors for the development of lipodystrophy in those patients. We hypothesize that insulin resistance in JDM is closely related to muscle disease and that the metabolic abnormalities may be primarily associated with disease activity. The recognition of the association between JDM and lipoatrophic diabetes will undoubtedly lead to recognition of many more cases. Where unrecognized diabetes and hypertriglyceridemia are found, this may provide the opportunity for early intervention and greater understanding of pathogenesis and clinical course.

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