LETTERS TO THE EDITOR

Polymyositis and pregnancy: report of a case with three pregnancies

Reports of polymyositis and dermatomyositis during pregnancy are uncommon and the available data referring to the possibility of recurrence as well as to the risks for the pregnant woman and the fetus are limited.

The association of polymyositis-dermatomyositis and pregnancy is very rare, and this has been attributed to the low percentage (14%) of cases in which the disease begins during the reproductive period of a woman's life¹; it is also probable that family planning policy after the clinical manifestation of the disease lowers the association of polymyositis-dermatomyositis and pregnancy.

A 35 year old woman was admitted to our neurological department (May 1992) after 16 weeks of pregnancy, with a six week history of fatigue, myalgia, and proximal muscle weakness of all four limbs which was progressively worsening.

At the age of 17 years she had been investigated (blood biochemistry, EMG, and muscle biopsy) at the University Department of Neurology in Athens where the diagnosis of polymyositis (first episode) was established. After three years of steroid treatment she recovered completely and five years later, when already married, she had a normal male baby without any relapse of her illness during gestation or postpartum. On admission to our department neurological examination showed bilateral weakness of the sternocleidomastoid and proximal muscle weakness of all four limbs (grade 3-4 of MRC scale). The rest of the cranial nerves were normal, there was no dermal rash or Reynaud's phenomenon and her general physical examination was normal. Laboratory investigations showed an erythrocyte sedimentation rate of 25 mm/hour, creatine kinase 3760 IU/l (normal value <190 IU/l), lactate dehydrogenase 415 (normal 80-260 IU/l), serum glutamic oxalacetic transaminase 115 IU/l (normal 5-35 IU/l), serum glutamic pyruvic transaminase 103 IU/l (normal 5-35 IU/l); antinuclear antibodies were negative and thyroid function tests were normal. Electromyography of deltoid, biceps, and quadriceps muscles showed myopathic changes (short duration, low amplitude, and polyphasic motor unit potentials) and a few neuropathic findings (spontaneous fibrillation potentials and positive sharp waves). Conduction velocity studies of the upper and lower limbs were normal. Muscle biopsy of the left deltoid (paraffin and cryostat sections) showed muscle fibre necrosis, phagocytosis, regeneration, diameter variation, interstitial fibrosis, mild infiltrates of chronic inflammatory cells which were mainly perivascular, and occasional perifascicular muscle fibre atrophy. The diagnosis of polymyositis was confirmed according to the criteria of Swash and Schwartz and the patient was started on steroid treatment (62.5 mg prednisone/day). A few days later, her muscle weakness deteriorated rapidly. At this stage both her husband and the patient became very anxious about the probable

complications and the decision was taken for an emergency termination of pregnancy by caesarian section at the end of 16 weeks. Three weeks after the termination of pregnancy she was discharged home with considerable improvement. The steroid treatment was continued on a schedule of reducing doses (every other day) for the next two years when it was discontinued due to her complete recovery. Thirty months after the last pregnancy and without any clinical or laboratory evidence of relapse she had her second normal baby (female) by caesarian section. She has remained in remission.

Polymyositis-dermatomyositis is rarely a life threatening disease for pregnant women and there is only one case report of maternal death which was attributed to severe exacerbation of the disease.² Women in remission at the time of conception tend to have a more favourable outcome and exacerbations can usually be controlled with corticosteroids.²

In active polymyositis-dermatomyositis associated with pregnancy healthy infants resulted only in 30% of cases, premature babies in 30%, and fetal death or abortion in 40%, whereas during inactive or improved polymyositis-dermatomyositis the figures were 57%, 21.5%, and 21.5% of cases respectively.³ Most authors who have reviewed the literature on the association of polymyositis-dermatomyositis and pregnancy advocate, when this is clinically required, steroid treatment.⁴ The criteria for initiation and discontinuation of steroids as well as steroid dosage should be identical during pregnancy and in the non-pregnant state.³ The risk to the fetus of steroid administration seems very low, as placental enzymes inactivating prednisolone decrease the fetal steroid blood concentration to 10% of the mother's blood concentrations.⁴ Finally for patients on steroids at the time of delivery, additional hydrocortisone is recommended to prevent acute adrenal insufficiency.⁵

In our present case it is not clear whether the improvement was due to the pregnancy termination or was a slightly delayed response to treatment. If it was the termination which had the positive effect on the patient's condition this might be of interest from an immunological point of view.

In conclusion the present case report shows that the occurrence of polymyositis during one pregnancy does not necessarily dictate its recurrence with subsequent pregnancies. Women should be discouraged to become pregnant during the active phase of the disease and if pregnancy does occur during remission a close follow up is necessary by frequent creatine kinase estimations.

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Spontaneous recovery of opsoclonus-myoclonus syndrome caused by enterovirus infection

Opsoclonus-myoclonus syndrome is a well recognised disease in children. The aetiology, except for neuroblastoma accounting for a few patients, remains unknown.¹ Viral infection is one of the presumed pathophysiological mechanisms. We report a case of opsoclonus-myoclonus syndrome due to enterovirus infection with spontaneous remission, no recurrence, and full recovery after 36 months follow up.

A two year old girl, with a previously normal development, exhibited acute ataxia after a two day history of fever and vomiting. One day later, she developed myoclonic jerks and opsoclonus. Initially, she was febrile (39°C), irritable, and unable to sit or to stand because of truncal ataxia. There was resistance to neck flexion. Rapid irregular and oscillatory eye movements were seen with continual myoclonus of the neck and limbs. Enterovirus RNA was detected in CSF at day 3 by polymerase chain reaction (PCR).² The CSF, on day 3, contained 113 leucocytes/mm³ (98% lymphocytes and 2% polymorphonuclear leucocytes), 25 mg/dl protein, and normal glucose concentrations. The interferon- α titre in CSF was raised (3 U/ml). At day 15, the CSF contained 20 leucocytes/mm³. The interferon- α titre was normal in both CSF and blood. EEG and brain MRI were normal. A chest radiograph, abdominal ultrasound examination, and urine titres of homovanillic acid and vanillylmandelic acid were normal. Viral culture from CSF was negative. Treatment with clobazam (1mg/kg/day) led to resolution of the myoclonus over 15 days. Developmental and neurological examinations were normal 36 months later (Denver developmental screening test).

We report a child with opsoclonus-myoclonus syndrome associated with enterovirus infection. Enterovirus infection associated with this syndrome has been rarely reported but could be underestimated.³ In fact, a diagnostic method with a high sensitivity was only recently provided by PCR, whereas the previous diagnostic test—namely, viral culture and serological assay, had a low diagnosis yield. Development of enterovirus RNA detection by PCR in blood and CSF should be more systematically performed in opsoclonus-myoclonus syndrome to better define the place of this infection as a cause of this syndrome. The relation between enterovirus infection and opsoclonus myoclonus syndrome could have some therapeutic implications. Interestingly, this patient and the two other similar cases reported in the literature had a spontaneous recovery in less than 15 days.³ Despite the lack of a well designed therapeutic trial, corticosteroid treatment is commonly used in patients with opsoclonus-myoclonus syndrome whatever the aetiology. Most of the patients given this treatment have shown a resolution of ataxic and myoclonic symptoms. However, long term follow up shows nearly constant mental sequelae and a high rate of myoclonic relapse.¹ There is clear experimental evidence

that corticosteroids potentiate coxsackie virus infection leading some authors to recommend avoidance of this treatment in enterovirus related disease.⁴ Thus in our opinion corticosteroid treatment should be considered cautiously before the results of virological investigations and avoided during acute enterovirus infection associated with opsoelonus-myoclonus syndrome.

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Postpartum manifestation of a necrotising lipid storage myopathy associated with muscle carnitine deficiency

Carnitine deficiency as a cause of lipid storage myopathy originates from a defect of carnitine transport into muscle cells.¹ Secondary carnitine deficiency with lipid storage myopathy² can be a result of genetic defects of intermediary metabolism, especially mitochondrial respiratory chain defects, defects of β -oxidation enzymes, or drug therapy—for example, valproate or pivampicillin. A transient systemic carnitine deficiency regularly occurs during pregnancy even in healthy women. At delivery, decreased plasma carnitine concentrations are in the same range as in patients with inborn carnitine deficiency.³

We report a 24 year old woman in good health without any previous episodes of muscle weakness or metabolic crises who experi-

enced a slowly progressive weakness of proximal muscles after delivery. The pregnancy and delivery had been uneventful other than the necessity for a caesarean section due to placental insufficiency. She did not receive any medication during pregnancy or after delivery with the exception of the nitrous oxide-oxygen-isoflurane anaesthesia in combination with vecuronium bromide, suxamethonium chloride, codeine, and fentanyl. Atropine and theophylline were given during the first hours after the section.

The muscular weakness was first noticed three months after delivery and increased to a so far stable deficit with only slight fluctuations within the next six months. The weakness of her proximal arm and leg muscles prevented her lifting her arm above her head and impaired stair climbing. There was no muscle pain, no myoglobinuria, and no sensory deficits.

The patient was first seen in our department six months after the onset of weakness. She had pronounced symmetric weakness of proximal muscles of the arms, legs, and neck without muscle pain and sensory deficits. Muscle enzymes were still greatly increased: creatine phosphokinase 720 U/l (normal <70 U/l), lactic dehydrogenase 543 U/l (normal <240 U/l), glutamic oxaloacetic transaminase 32 U/l (normal <15 U/l). Erythrocyte sedimentation rate was normal (6 mm in the first hour). Needle EMG showed spontaneous fibrillation in the deltoid and rectus femoris muscle. Motor units were of short duration, small amplitude, polyphasic, and showed a dense interference pattern on submaximal effort. Her ECG, chest radiography, and echocardiogram were normal. In her family history neither her parents nor her two brothers nor any other member of the family had muscle weakness.

A biopsy of the left deltoid muscle disclosed severe necrotising myopathy with pronounced atrophy predominantly of type 2 fibres, widespread regenerating fibres, scattered fibre necroses undergoing phagocytosis, single ghost fibres, and few ragged-red-fibres. There was pronounced endomysial fibrosis reflecting the chronicity of the disease. Signs of inflammation were not present. Histochemical stains disclosed prominent storage of lipid droplets in the muscle fibres. In addition, single fibres showed slightly reduced activity of cytochrome c oxidase. The lipid storage myopathy was confirmed by electron microscopy; the mitochondria were ultrastructurally normal.

Biochemical studies of muscle tissue showed a reduction of total carnitine to 15.1 μ mol/g of non-collagenous protein (NCP, reference value 21.0-43.1 μ mol/g NCP) and free carnitine to 11.9 μ mol/g NCP (reference value 19.5-35.1 μ mol/g NCP). Acylcarnitine

was normal (3.2 μ mol/g NCP, reference value 0.5-13.4 μ mol/g NCP) as well as mitochondrial enzymes (carnitine palmitoyl transferase, NADH coenzyme Q reductase, cytochrome c oxidase, succinate/cytochrome c oxidoreductase). Southern blot analysis of mitochondrial DNA showed a single population of mitochondrial DNA molecules. Point mutations typical for MELAS, MERRF, and Leigh disease could be excluded. Plasma carnitine concentrations were normal: 35.1 μ mol/l (normal 25-64 μ mol/l).

After diagnosis of muscular carnitine deficiency a treatment was started with 4 g carnitine/day orally. After 11 months of therapy, there was no increase in muscle strength and no decrease in the high plasma concentrations of muscle enzymes but her condition was stable.

Carnitine contributes to muscular energy supply by controlling the influx of long chain fatty acids into mitochondria and a carnitine deficiency myopathy is often secondary to mitochondrial enzyme defects.

Lipid storage is the predominant histological manifestation in carnitine deficiency.¹⁻⁴ In our case additional and unusual features such as severe muscle fibre necrosis and a few ragged-red-fibres were seen. Necrotic and regenerating muscle fibres have occasionally been described after acute phases of deterioration in carnitine deficiency.² Lipid storage in combination with ragged-red fibres is suggestive of a respiratory chain defect with secondary carnitine deficiency.⁵ Although few ragged-red fibres were present in the muscle biopsy of our patient further biochemical analysis excluded a respiratory chain defect. Moreover, mutations for MELAS and Leigh's disease as well as drug therapy causing carnitine deficiency could be excluded. Defects of β -oxidation enzymes which can mimic primary carnitine deficiency² seems to be unlikely as there were no episodes of metabolic crisis or hepatic dysfunction.

The myopathy in our patient occurred after her first pregnancy. To our knowledge, the clinical course of lipid storage myopathies during and after pregnancy has been reported in only three cases (table). Two patients showed a deterioration of a prediagnosed myopathy⁶ whereas one woman experienced the manifestation of a lipid storage myopathy with decreased concentrations of muscle and plasma carnitine after delivery.⁷ The muscle weakness started some weeks after delivery and reached a peak within several months (table). Two other patients with mitochondrial myopathies (one with an unidentified enzyme defect,⁸ one with carnitine palmitoyl transferase deficiency⁹) were asymptomatic during pregnancy and after delivery.

Course of lipid storage myopathies during pregnancy and after delivery

No	Age*	Myopathy*	Muscle biopsy	Time delivery to peak of weakness	Carnitine†		Therapy and outcome	Reference
					Plasma	Muscle		
1	19	Deterioration after delivery	LSM	5 months	ND	4%	No therapy Death within 1 year	Boudin et al 1976 ⁶
2	26	Deterioration after delivery	LSM	NG	ND	25%	No therapy Death within 2 years	Cornelio et al 1977 ⁴
3	16	Manifestation after delivery	LSM	6 months	50%	15%	Carnitine supplementation Improvement of weakness	Angelini et al 1978 ⁷
4	24	Manifestation after delivery	LSM	9 months	Normal	47%	Carnitine supplementation No effect	Case reported here

* At pregnancy.

† Compared with healthy controls as given by the authors.

ND=not determined; NG=not given; LSM=lipid storage myopathy.