Correlation coefficients (r) between HbA_1 concentrations at each period of gestation and at delivery and total skinfold thickness, birth weight, and birthweight ratio

	Weeks of gestation						Delivery	
	≤14		15-27		≥28			
	No	r	No	r	No	r	No	r
Total skinfold thickness	17	0·38	14	0·26	38	0·52†	25	0·46*
Birth weight	19	0·28	15	−0·12	42	0·25	28	0·17
Birthweight ratio	19	0·26	15	−0·09	42	0·28	28	0·20
Mean ±SD HbA_1 (%)	9·6±2·0		8·8±1·5		7·9±1·3		8·1±1·1	

†$p<0·001$.
*$p<0·05$.

$p<0·001$) and at delivery ($r=0·46$, $p<0·05$) (table), and with the mean inpatient blood glucose concentration ($r=0·42$, $p<0·01$).

The mean inpatient blood glucose concentration but not the HbA_1 concentration correlated with the birthweight ratio ($r=0·30$, $p<0·05$). Neither HbA_1 nor mean inpatient blood glucose concentrations correlated with the birth weight. There was no correlation between the HbA_1 or the mean outpatient blood glucose concentrations in the first and second trimesters and the total skinfold thickness, birth weight, or birthweight ratio.

Comment

Maternal diabetic control in the third trimester, whether estimated by HbA_1 or mean blood glucose concentrations, was related to the amount of neonatal subcutaneous fat. No relation was found between diabetic control in the first and second trimesters and skinfold thickness, birthweight ratio, or birth weight. These observations suggest that subcutaneous fat in the infants of diabetic mothers is determined by control of maternal blood glucose in the third trimester.

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Pulmonary eosinophilia and asthma associated with carbamazepine

Carbamazepine (Tegretol) is the medical treatment of choice for trigeminal neuralgia and is used in many cases of temporal lobe epilepsy. Although phenytoin has often been associated with pulmonary abnormalities, pulmonary complications with carbamazepine are rarely recognised. We describe a case of pulmonary eosinophilia and asthma believed to have been caused by carbamazepine.

Case report

A 52-year-old man presented with a two-month history of an itchy rash on his legs and a month's history of asthma, which had been partially relieved with antihistamines. He had also suffered from trigeminal neuralgia for nine months, for which he was taking carbamazepine 200 mg three times daily. On examination he was mildly feverish, wheezy, and had discoid eczema on his limbs. He had moderate airflow obstruction, forced expiratory volume in 1 second was 1·0 l (predicted 3·2 l), forced vital capacity was 2·0 l (4·2 l), and forced expiratory ratio was 50% (76%) with a normal carbon monoxide transfer coefficient. Chest *x*-ray examination showed a left apical segmental shadow, a blood count showed a 20% eosinophilia ($1·9\times10^9$/l), and erythrocyte sedimentation rate was 40 mm in first hour. There were eosinophils in his sputum but renal and liver function were normal. Repeated examinations of his sputum, stools, and blood showed no bacterial, fungal, or parasitic infection. Prick tests to common allergens, aspergillus and candida were negative despite a positive histamine control. Tests using precipitins to aspergillus and candida were negative. The concentration of serum IgE was raised at 250 U/ml (normal: <122 U/ml) but other immunoglobulin concentrations were normal.

His asthma deteriorated considerably over 48 hours when his antihistamines were stopped, and these were reinstituted with nebulised salbutamol before there was clinical improvement. Carbamazepine was stopped and within 72 hours his peripheral eosinophil count, erythrocyte sedimentation rate, and chest radiograph were normal. The rash disappeared within three days but his asthma remained troublesome for six months before complete recovery, despite a good initial response to a short course of prednisolone.

Unfortunately his trigeminal neuralgia was poorly controlled with phenytoin, so to prove that he did have carbamazepine sensitivity, he was challenged with 200 mg carbamazepine. A mild eczematous rash appeared after six hours but there was no airflow obstruction or radiological abnormalities, although there was a slight increase in his eosinophil count from 3% to 5% over this time. Carbamazepine was continued under close supervision and over the next two weeks cusum analysis[1] showed that his asthma had gradually deteriorated. This improved again when the drug was discontinued. A positive lymphocyte stimulation assay (stimulation index >2) to carbamazepine was maximal at 1 mg/l of the drug in the presence of autologous serum; the stimulation index was 3·26 (index of positive control to 10 mg/l purified protein derivative was 14·4). Such a pronounced response on lymphocyte stimulation supported the role of carbamazepine as the cause of his symptoms.

Comment

Unlike our case, two previous cases of acute pulmonary reactions associated with carbamazepine treatment[2,3] were complicated by tuberculosis[2] and *Mycoplasma pneumoniae* infection. Nevertheless, their clinical pictures suggested that carbamazepine hypersensitivity was indeed a problem. The presymptomatic exposure to carbamazepine varied; the patients had been taking the drug for five weeks, three months, and, in our case, nine months before presentation. All patients presented with a rash and eosinophilia with their pulmonary disease. The total duration of their illnesses also varied greatly and, although one patient recovered within nine days,[3] the other took five weeks,[2] and our patient took six months to recover completely. The treatment is supportive but the drug must be stopped. The use of corticosteroids is dictated by the patient's condition, although the patient would probably recover without them.

The mechanism for this complication is unknown and the pronounced deterioration of our patient's asthma after the withdrawal of antihistamines is interesting. Lymphocyte transformation in the presence of carbamazepine has been reported[2,4] and is similar to that found in nitrofurantoin sensitivity, which is better documented as a cause of pulmonary eosinophilia. The pathogenesis of the pulmonary eosinophilia in nitrofurantoin sensitivity is thought to include not only T-lymphocytes but also immune complexes formed between the drug and antibody.[5]

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