Macroamylasaemia and selective IgA deficiency

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SUMMARY Macroamylasaemia and selective IgA deficiency were diagnosed in a 2 year old child who presented with persistent hyperamylasaemia. Macroamylasaemia is an isolated biochemical abnormality caused by aggregation of serum amylase activity with immunoglobulins. Early recognition of macroamylasaemia is important to avoid diagnosing pancreatic disease.

The occurrence of isolated hyperamylasaemia, in the absence of disease in the pancreas or in other organs, is well documented in adults. This biochemical abnormality is defined as macroamylasaemia.

Only two cases of this condition have so far been reported in the paediatric age group.[1 2] We think that it is worth while to report details of a case of macroamylasaemia in a child aged 29 months who also had a selective IgA deficiency.

Case report

A white girl aged 29 months was referred to our department with suspected chronic pancreatitis.

The child had been healthy until the age of 2 years. She then experienced recurrent abdominal pains, occasionally associated with vomiting, mostly localised in the periumbilical region. There had been no recent trauma to the abdomen. Weight loss, fever, and other organic symptoms were all absent. Routine blood tests were carried out after some such episodes. These showed only a higher than normal serum amylase activity (370 U/l compared with a normal of 10–50). The child was then admitted to a paediatric surgical ward as she was suspected of having acute pancreatitis. She was well on admission and remained so during this first stay in hospital. Body temperature, blood pressure, and intestinal movements were normal. Abdominal distension, tenderness, or localised swelling were not noted. The patient continued to complain of transient abdominal pains. Various tests were performed (including serum lipase activity, plain abdominal *x* ray film, and liver and pancreas ultrasonography), and results were within normal limits, except for the serum amylase activity, which remained persistently high. Given the provisional diagnosis of acute pancreatitis the following treatment was begun: (a) total parenteral nutrition; (b) continuous nasogastric aspiration; and (c) oral ranitidine (100 mg daily). After one month this treatment was stopped and the child was discharged in a generally good condition with a diagnosis of suspected acute pancreatitis of viral origin. The serum amylase activity was still abnormally high. She was then referred to us.

On admission her weight and height were at the 50th and 75th centiles, respectively. Her general condition was good and she seemed to have no abnormalities on physical examination. The abdomen was not painful on palpation and there were no abdominal masses. A free oral diet was begun, and the child did not show any more abdominal pains or other symptoms. The tests we performed can be grouped as follows:

(1) Routine haematological investigations: blood red cell count; haemoglobin; packed cell volume; white blood cell count; erythrocyte sedimentation rate; serum glutamic pyruvic and oxaloacetic transaminase activities; blood sugar, blood urea nitrogen, serum creatinine, total protein, electrolyte, bilirubin, triglyceride, cholesterol, and lipoprotein concentrations; and sweat test. All these yielded normal results.

(2) Examinations performed to investigate the origin of the hyperamylasaemia: basal serum amylase activity 636 U/l (normal 0–130); serum amylase activity after stimulation by intravenous secretin and pancreozymin (2 U/kg of body weight) 702 U/l; serum lipase activity 25 U/l (normal 0–190); urine amylase activity 36 U/l (lower than normal); Cam/Ccr ratio(urine amylase÷serum amylase)×(serum creatinine÷urine creatinine)=0·085 (normal 1–4); serum amylase analysis by electrophoresis on cellulose acetate, in which the serum amylase activity spread to one broad band with a reduced mobility compared with salivary amylase activity; immunoelectrophoresis of the amylase containing serum macrocomplex according to the method described by Harada *et al*,[3] which showed aggregates consisting of amylases and immunoglobulins belonging to class G (Figure).

(3) Immunological investigations (a selective IgA deficiency was occasionally found): serum IgA undetectable (by radial immunodiffusion), IgG 1190

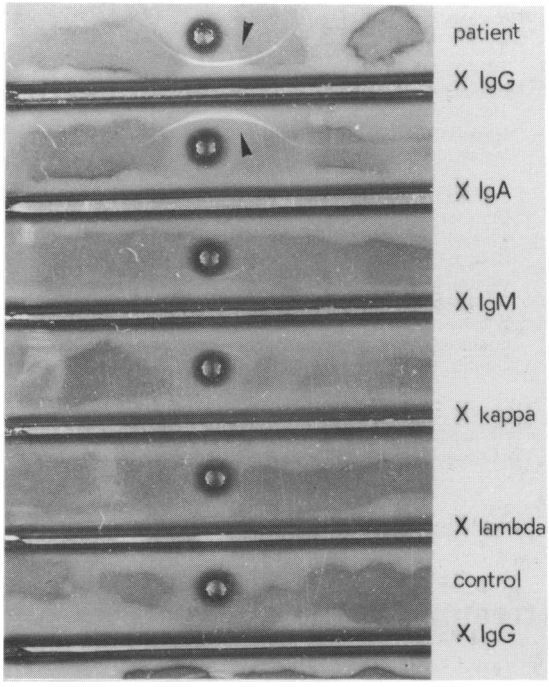

Figure *Characterisation of the macroamylasaemia by immunoelectrophoresis: the aggregates in the serum of the patient consist of amylase and immunoglobulins belonging to class G. The precipitation lines (arrows) are unstained due to the activity of amylase on a amylose treated plate.*

mg/100ml (normal 462–1710), IgM 271 mg/100ml (normal 62–257); salivary IgA undetectable; anti-organ autoantibodies and antinuclear factors absent; T lymphocytes percentage and T4:T8 ratio in the normal range.

The patient was discharged with a diagnosis of macroamylasaemia and selective IgA deficiency. She has now been well for 20 months. Her serum amylase activities are persistently high.

Discussion

In this child with persistent raised serum amylase activities the final diagnosis of macroamylasaemia was made on the basis of the reduced concentration of urine amylase activity and a clearance amylase: clearance creatinine ratio lower than normal. Confirmation of the diagnosis came from electrophoresis of the amylase isoenzymes and further analysis of the amylase aggregates by immunoelectrophoresis. Macroamylasaemia, which was first described by Wilding in 1964,[4] is the result of aggregation of serum amylase activity with immunoglobulins, usually of classes A or G. These aggregates have a molecular weight between 150 000 and 1 000 000 as against a weight of 55 000 for amylase alone. The large dimension of these macrocomplexes leads to a reduction in renal filtration and in elimination of serum amylase activity through the urine, leading to hyperamylasaemia.[5] The prevalence of macroamylasaemia in the adult population varies from 0·4 to 2%. As far as we know there have only been two reports of macroamylasaemia in children, one of them concerning a 12 year old boy who was also affected with recurrent abdominal pain.[2]

The pathogenesis of macroamylasaemia is unknown. There are no family studies either to confirm or to reject a hypothesis of genetic transmission. The fact that the amylase aggregates contain immunoglobulins could suggest that this biochemical abnormality has an autoimmune origin. In our case these immunoglobulins were of the IgG class, as shown by immunoelectrophoresis (Figure). The discovery of macroamylasaemia in patients with other autoimmune disorders—for example, systemic lupus erythematosus—supports the autoimmune hypothesis. It is interesting to note that our patient presented, along with the macroamylasaemia, a selective deficiency of serum IgA, a primary immunodeficiency notoriously associated with higher incidence of autoimmune phenomena.

No distinct clinical feature accompanies macroamylasaemia, which is sometimes found in subjects who are otherwise healthy. A higher than normal incidence of macroamylasaemia has been reported, however, in patients suffering from malabsorption states or recurrent abdominal pains, but this could be due to the fact that these patients are far more likely to undergo a serum amylase test. It has been suggested that the abdominal pains encountered in some cases of macroamylasaemia may be caused by the precipitation of immunocomplexes, consisting of amylase and immunoglobulins, in the pancreas.[6] In our patient the recurrent abdominal pain was the factor that directed the investigations and led to the discovery of the macroamylasaemia. Several months after the disappearance of the abdominal pains our subject still has macroamylasaemia, which suggests that there is no cause-effect relation between macroamylasaemia and abdominal pain.

Early recognition of macroamylasaemia is important to avoid diagnostic mistakes. The child described in this case report was given a variety of needless and potentially harmful treatments, such as total parenteral nutrition, because she was suspected of having a disorder of the pancreas. When a subject has a high serum amylase activity, especially if there is neither clinical nor haematological evi-

dence for active pancreas disease, it would seem to be correct practice to investigate the urine amylase activity and the Cam/Ccr ratio, especially as these tests are both easy to carry out and minimally invasive. Given a good renal function the Cam/Ccr ratio is significantly decreased in subjects with macroamylasaemia (as in our case) while it is normal or increased in subjects with diseases of the pancreas or other organs containing amylase—that is, salivary glands. The electrophoresis of serum amylase activity should confirm a diagnosis of macroamylasaemia by producing the typical broad band.

The interpretation of laboratory results has become an important aspect of medical practice. Macroamylasaemia is a condition that does not require any treatment, and a correct diagnosis can mean that a patient can be spared unnecessary pharmacological or dietetic treatments.

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Use of human growth hormone in treatment of nesidioblastosis in a neonate

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SUMMARY Growth hormone was effective in reducing the glucose requirement in an infant with nesidioblastosis. He was suffering from fluid overload secondary to glucose and water infusions necessary to maintain blood glucose. Early pancreatectomy is the preferred treatment in severe cases, but human growth hormone has a place in preoperative management.

A neonate with hyperinsulinism was referred to us. He was being treated with intravenous dextrose and diazoxide but was oedematous and in heart failure. Water overload may arise from the treatment of hyperinsulinism with dextrose solutions. Diazoxide is known to cause sodium retention,[1] and this compounds the problem. To reduce his glucose requirement we treated him with human growth hormone.

Case report

The boy was the third full term child of Asian parents who are first cousins. At delivery he weighed 3900 g and looked like the baby of a mother with gestational diabetes. He became symptomatically hypoglycaemic at four hours and was treated with intravenous glucose. To maintain his blood glucose concentration above 2 mmol/l (36 mg/100ml) he was treated with increasing amounts of intravenous glucose and oral feeds. Hydrocortisone 4 mg/kg/day intravenously and on four separate occasions glucagon 100 μg/kg did not have any apparent effect. By the sixth day his carbohydrate requirement (oral feeds plus intravenous) had risen to 23 mg/kg/min, but he was still having periods of symptomatic hypoglycaemia (Figure). He was subsequently found to have an insulin concentration of 38 IU/l, with a blood glucose concentration of 2·3 mmol/l (41·5 mg/100ml).

He was referred to Birmingham Children's Hospital on the sixth day. He was in heart failure with pulmonary oedema, a patent ductus arteriosus, and some peripheral oedema. The liver was two and a half centimetres below the costal margin. During the previous 12 hours he had received 260 ml/kg/day of fluid. Treatment with hydrocortisone was stopped. His heart failure was treated with frusemide for 24 hours, and he was started on human growth hor-