Maternal serum and amniotic fluid concentrations of alphafetoprotein in epidermolysis bullosa simplex

Maternal serum and amniotic fluid alphafetoprotein (AFP) concentrations have been used since 1972 in diagnosing neural tube defects in the fetus. These concentrations are raised in congenital abnormalities of the gastrointestinal tract, kidney, and other sites.1 We report here, for the first time, a case of epidermolysis bullosa simplex, an autosomal dominant condition, in which the AFP concentrations were raised.

Case report

A 21-year-old primigravida with no significant medical or family history was first examined at 16 weeks gestation. The date of conception was uncertain, so the gestational age was assessed by clinical examination and measuring the fetal biparietal diameter and the head/abdominal circumference. The maternal serum AFP concentrations at 16, 17, and 18 weeks gestation were 150, 165, and 160 µg/l—well above the upper limit of normal (90, 100, and 124 µg/l respectively). The AFP concentration in the amniotic fluid at 20 weeks gestation was 26-5 mg/l, which was within the normal range (upper limit 28 mg/l). A live female infant weighing 2-4 kg was born after 39 weeks after an uncomplicated spontaneous labour. She had blistering and superficial skin loss over the long, wrists, and abdomen affecting 20% of the total skin area. No bullae were present on the head, neck, back, soles, or palms. The pattern of the lesions suggested epidermolysis dystrophica of the autosomal dominant type, and healing was associated with superficial scarring. Epidermolysis bullosa simplex was diagnosed by electron microscopy. The basal lamina remained intact. Cleavage occurred at the level of the basal epidermal cells, which showed varying stages of disintegration.1

The widespread lesions on the limbs presenting at birth are an unusual but recognised feature of epidermolysis bullosa simplex. Healing may be associated with scarring.1 There were no other congenital abnormalities and the karyotype was normal. During the neonatal period the lesions improved with topical corticosteroid treatment only and the baby was discharged home after 21 days. AFP concentrations in the bullous fluid and neonatal serum were 6-0 and 5-6 mg/l respectively, indicating transudation of serum.

Comment

This is the first report of raised serum AFP concentrations in a case of epidermolysis bullosa simplex. Raised concentrations have been described in a patient with skin necrosis and duodenal atresia of the fetus,1 but the atresia could have accounted for the rise in this case. The raised AFP concentration in maternal serum probably resulted from transudation of fetal serum into the bullae and subsequent rupture thereof into the amniotic fluid cavity. Transudation from amniotic fluid would account for the raised serum levels at around 17 weeks gestation. The amniotic fluid concentration three weeks later, however, was near the upper limit of normal. The explanation for this could be that there had been no recent rupture of bullae. Our case suggests that AFP assay might be of value in patients who have already had an infant with epidermolysis bullosa. They could be screened at around 17 weeks gestation and the diagnosis confirmed by fetoscopy.

We thank Dr R A J Eady for the electron microscopy report.


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Rupture of spleen at colonoscopy

Colonoscopy is now a routine procedure in many hospitals. Complications on the whole are few and consist mainly of perforation of the bowel and haemorrhage after polypectomy. Injuries to other viscera seem to be very rare. We report a case in which both spleen and liver were damaged.

Case report

A 33-year-old woman presented with an 18-month history of diarrhoea accompanied by sharp central abdominal pain and a feeling of distension. She was passing 10 to 15 stools daily with mucus and occasionally fresh blood. She was tender in the umbilical region, and at sigmoidoscopy a nodular area was seen in the upper rectum. Biopsy showed active chronic colitis affecting the mucosa and superficial submucosa, possibly of the Crohn's type. A barium enema was normal. The patient was admitted for colonoscopy.

The preoperative haemoglobin level was 13.2 g/dl. The bowel was prepared with 4 litres of 5% mannitol by mouth. On examination under light sedation with diazepam and pentazocine there was obvious colitis in the sigmoid colon and descending colon with some scattered ulcers and oedema in the transverse colon. The cecum was reached without undue difficulty and was normal. Samples of tissue were taken for biopsy. Four hours later the patient complained of severe abdominal pain, predominantly in the left hypochondrium. On examination she had a tender, silent abdomen. Plain radiographs showed no evidence of pneumoperitoneum. Initial management was conservative, with analgesics and intravenous fluids. Her condition remained stable over the next two days and she passed a loose stool. On the third day her pain increased, with radiation to the left shoulder-tip. She appeared pale, although not shocked. The haemoglobin level had fallen to 4.5 g/dl. She was therefore transfused and prepared for surgery.
Benign gastric ulceration with pernicious anaemia

Since 1910 Schwartz's dictum "no acid—no ulcer" has only rarely been found to be false and it continues to be of clinical value. Indeed, the absence of peptic ulceration in pernicious anaemia has been regarded as evidence that acid is necessary for the development of gastric ulcers. Rare examples of achlorhydric peptic ulceration have been reported but there has been doubt about the adequacy of the maximal stimulus. A patient with a peptic ulcer associated with long-standing pernicious anaemia, hypothyroidism, and insulin-dependent diabetes has also been reported. We describe a further case in which pernicious anaemia presented with symptoms of anaemia and pyloric obstruction from a benign gastric ulcer.

Case report

A 63-year-old housewife presented with a four-month history of fatigue, breathlessness, anorexia, weight loss of 10 kg, and intermittent vomiting of food taken several hours earlier. Her father had died from anaemia treated with liver extract. She denied taking alcohol or analgesics. Her general practitioner had found an anaemia with a low serum vitamin B12 concentration, an intrinsic factor antibody, and a low serum ferritin, for which she was referred to us for endoscopy and haematological examination. On examination she was anaemic. A gastric succession splash could be elicited. Endoscopy confirmed superficial and chronic ulceration in the prepyloric region with deformity. The instrument could not be passed through the pylorus.

Investigations showed a haemoglobin of 7.2 g/dl with mean corpuscular volume (MCV) 84 fl and mean corpuscular haemoglobin (MCH) 24.7 pg and platelets of 258 × 10^9/l (258 000/mm^3). The blood film was dacrocrine and the serum B12 concentration 106 ng/l (normal 170-1000 ng/l). Serum iron concentration was 4 μmol/l (22.3 μg/100 ml) (normal 14-22 μmol/l (78-2-123 μg/100 ml)) with a total iron binding capacity of 76 μmol/l (424 μg/100 ml) (normal 50-64 μmol/l (279-357 μg/100 ml)). The serum folate concentration was twice estimated at 1.4 and 2.2 μg/l (normal >2.0 μg/l) and the red cell folate concentration was only slightly reduced at 141 μg/l (normal 160-640 μg/l). Bone marrow examination confirmed megaloblastic erythropoiesis with absence of stainable iron. Stool was positive for occult blood. Serum was positive for parietal cell antibody but negative for intrinsic factor antibody.

Blood urea and electrolyte concentration, and the results of routine liver function tests were all normal. The results of gastric secretion studies are shown in the table. Except for the first Schilling test with intrinsic factor, performed 10 days after surgery, the postoperative studies were done after three months of vitamin B12 and iron treatment, when the haemoglobin was 13 g/dl. Biopsy specimens of tissue taken during two endoscopies showed only inflammatory changes but it was felt that malignancy could not be excluded. Polya gastrectomy was therefore performed. Macroscopically, the specimen showed a 0.5-cm diameter peptic ulcer, but extensive sectioning showed only superficial gastritis and intestinal metaplasia without malignant change. One year later the patient was well on vitamin B12 injections. Endoscopy of the gastric remnant showed pronounced atrophic gastritis confirmed by histological examination of a biopsy specimen. A further Schilling test produced a urine recovery of 1-1/3% of the administered vitamin B12.

Comment

Although the anaemia seems to have been partly due to iron deficiency secondary to bleeding from the ulcer, the abnormal Schilling test corrected by intrinsic factor administration, in the presence of achlorhydria to pentagastrin, substantiates the diagnosis of "Addisonian" pernicious anaemia. The postoperative secretary studies confirm that these were not transient abnormalities related to the ulceration and gastritis or to iron deficiency, since a Polya gastrectomy alone would not reduce secretions to such levels. It has been suggested that previous cases of benign ulceration in the absence of demonstrable acid secretion might reflect methods not sufficiently sensitive to stimulate or detect acid secretion. The presence of pernicious anaemia in our case seems to resolve this issue, since even the strongest of stimuli will fail to produce any acid secretion in pernicious anaemia. In the absence of alcohol or drugs bile reflux was probably cause of the ulceration. Seemingly, therefore, our case and others weaken Schwartz's dictum. But in practice we agree with Isenberg, that gastric ulceration with achlorhydria should be managed as gastric carcinoma, since a possible intramucosal carcinoma might be detected only on examining the resected specimen.

We thank Drs N C Allan and Anne Ferguson for their advice and permission to report this case.

1 Schwartz, K, Beitrage zur klinischen Chirurgie, 1910, 67, 96.

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<tr>
<th>Investigation</th>
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<tr>
<td>(3) 300-mg dose</td>
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*No intrinsic factor detected on analysis of aspirated secretions. Hcg intrinsic factor, Armour Pharmaceuticals.

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