SHORT REPORTS

Aflatoxins in breast milk, neonatal cord blood, and serum of pregnant women

Aflatoxins are fungal metabolites commonly found as toxic contaminants of food commodities in the tropics.[1] Aflatoxins have been detected in breast milk from mothers in the Sudan.[2] A study in the United States has shown that aflatoxins cross the complex porcine placenta and exert adverse biological effects on neonatal pigs.[3] Investigations conducted in Accra, Ghana, and Jos, Nigeria, therefore, sought to confirm the presence of aflatoxins in human breast milk and explored the possibility that aflatoxins cross the human placental membrane.

Subjects, methods, and results

In Accra 142 breast milk samples were collected in the mid-dry season and a further 122 samples at the onset of the wet season. Cord blood samples were obtained from 188 infants at birth. In Nigeria venous blood was collected from 77 mothers during pregnancy and cord blood samples from their infants after complete delivery of the placenta. All specimens were transported frozen to Liverpool for aflatoxin analysis by high performance liquid chromatography using fluorescence detection after extraction and partition.[4,5] Concentrations of aflatoxins B_1, B_2, G_1, G_2, M_1, and M_2 and aflatoxicol were determined.

Aflatoxins were detected in 90 (34%) of the 264 breast milk samples. The frequency of detection was higher in the wet season (50 samples; 41%) than in the dry season (40; 28%) (exact $p=0{\cdot}039$). Aflatoxin M_1 was detected most frequently (59 specimens), in concentrations ranging from 20 to 1816 ng/l. The mean concentration was higher in the wet season (445 (SD 442) ng/l) than in the dry season (293 (281) ng/l). Aflatoxin M_2 was detected in 18 milk samples (16-2075 ng/l), aflatoxin B_1 in 17 (130-8218 ng/l), and aflatoxin B_2 in two (49 and 50 ng/l) and aflatoxicol in three (64, 128, and 270 ng/l).

Aflatoxins were detected in 63 (34%) of the 188 Ghanaian cord blood specimens. Aflatoxins M_1 and M_2 were each detected in 21 specimens in concentrations ranging from 34 to 7320 ng/l and 30 to 572 ng/l respectively. Aflatoxins B_1 and B_2 were each detected in 17 specimens (concentrations 185-43 822 ng/l and 11-925 ng/l respectively). Aflatoxin G_1 was detected thrice (611, 1354, and 354 ng/l), aflatoxin G_2 once (37 ng/l), and aflatoxicol once (117 ng/l).

Blood samples from Nigeria showed aflatoxins in 16 (21%) of 77 maternal samples and 9 (12%) of 78 cord blood samples (including a set of twins). Aflatoxins were found in maternal and cord blood in seven instances (see table). One stillbirth was recorded in the study. The maternal blood contained aflatoxin B_1 553 ng/l.

Nigerian aflatoxin concentrations (ng/l) detected at delivery

Study No	Maternal blood	Cord blood	Study No	Maternal blood	Cord blood
1	M_2 175	M_2 245	50	M_1 483	B_2 10
8	B_1 553	Negative	51	B_1 5005	Negative
12	B_1 4880	Negative	56	Negative	M_2 378
26	B_1 540	Negative	101	M_1 265	M_1 8942
27	B_1 878	M_1 25	102	M_2 48	M_2 330
33	B_2 33	Negative	104	Negative	M_2 208
37	M_1 38	Negative	106	B_2 28	Negative
42	B_1 10 390	M_1 593	111	M_2 90	M_2 155
45	M_2 3480	Negative			

Comment

The frequency of detection of aflatoxin in breast milk in Ghana was similar to that reported in Sudan[2]; concentrations, however, were considerably higher in this series, and the presence of aflatoxin B_1 in 17 samples in concentrations up to 8218 ng/l was surprising. These findings confirm that newborn infants in Africa are frequently exposed to aflatoxins in breast milk and that there are seasonal fluctuations in the level of exposure.

Finding aflatoxins in 34% of Ghanaian and 12% of Nigerian cord blood samples provides firm proof that aflatoxins cross the human placental barrier. The very high concentrations in some Ghanaian specimens and the higher concentrations of aflatoxins in some cord blood than maternal blood samples collected simultaneously in Nigeria suggest that aflatoxins may accumulate in the fetus when exposed to these toxins in utero.

These studies and findings in Kenya reported separately show that a high proportion of infants in tropical Africa have prenatal and continuing postnatal exposure to aflatoxins. Given the adverse effects of such exposure on immunity, liver function, nutrition, and overall survival in controlled experiments on pigs,[3] we should be concerned about the possible consequences of aflatoxin exposure for the human fetus and infant.

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Department of Tropical Paediatrics, School of Tropical Medicine, Liverpool L3 5QA
S M LAMPLUGH, PHD, research assistant
R G HENDRICKSE, MD, FRCP, professor

Military Hospital, Accra, Ghana
F APEAGYEI, MB, CHB, public health specialist

Vom Christian Hospital, Vom, Nigeria
D D MWANMUT, MB, BS, senior medical officer

Correspondence to: Dr Lamplugh.

Plastic material from a syringe causing fatal bowel necrosis in a neonate

Plastic particles from syringes have been reported to enter the circulation through intravenous lines.[1] We report on a neonate in whom this caused ischaemia of the bowel with a fatal outcome.

Case report

A male infant weighing 860 g was born vaginally at 25 weeks' gestation. He had Apgar scores of 3 at one minute and 9 at five minutes. He was ventilated from birth because of the respiratory distress syndrome, and an umbilical artery catheter was inserted at 1 hour of age. Injections were given into this catheter with polypropylene syringes (Omniflex 2 ml, Braun Melsungen). Ventilatory requirements decreased, and by day 4 ventilator pressures were 16/3 cm water at five breaths per minute in 35% oxygen. An ultrasound scan of the central nervous system was normal. The umbilical artery catheter was removed, but within an hour his abdomen became distended and the abdominal wall turned black. Meconium peritonitis was diagnosed. Radiography of the abdomen showed distended loops of small bowel but no gas in the bowel wall.

Nasogastric feeds were stopped, and he was given intravenous nutrition, penicillin, gentamicin, and metronidazole. His condition was static until day 12, when his abdomen became more distended owing to scrotal crepitus and a mass in the right iliac fossa. An abdominal radiograph showed free gas. By day 15 he had not passed further stools and his abdominal signs were unchanged. An enema of sodium and meglumine diatrizoates (Gastrografin) showed that contrast did not pass beyond the hepatic flexure. At laparotomy an inflammatory mass consisting of caecum, gall bladder, and distal ileum was found; the ileum contained a stricture and perforation. The remainder of the small bowel looked viable, and there was no evidence of necrotising enterocolitis. The stricture was resected and an end to end anastomosis made.

For the next 19 days the infant required ventilation; his abdominal signs were unchanged. Rectal washouts and enemas of iopamidol resulted in the passage of only small amounts of meconium. Serial plasma concentrations of immunoreactive trypsin were normal. At laparotomy the small bowel was limp, showed scattered necrotic areas, and contained plugs of inspissated meconium. An ileal stoma was formed, but despite washouts with acetylcysteine no stool was passed and he eventually died at 52 days of age.

On histopathological examination the resected part of the small bowel showed signs of acute infarction. The mesenteric arteries were thrombosed. The thrombus contained irregular fragments of plastic 50-200 μm long, which were identified by laser raman spectroscopy as polypropylene. At postmortem examination there was no evidence of any residual infarction of viscera. Sections

of small bowel showed several serosal granulomas containing fragments of refractile plastic, which were also identified as polypropylene. Granulomas containing identical polypropylene material were also present in the hepatic capsule. Starch granules, possibly derived from glove powder, were found in the granulomas at both sites. No granulomas were found in sections from other organs.

Comment

This child died from the sequelae of small bowel infarction. There was unequivocal histopathological evidence of embolism caused by plastic splinters restricted to tissue supplied by the coeliac axis. Furthermore, the syringe used to perfuse the umbilical artery catheter was made from material identical with that found in the emboli, showing a causal association. This is supported by the finding that after insertion of umbilical artery catheters neonates who died of necrotising enterocolitis had higher levels of plasticiser in their bowels than similar infants dying from other causes.[2] If a repetition of this tragedy is to be avoided manufacturers must make greater efforts to minimise particulate contamination and the use of filters in intravenous lines should be considered.

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Royal Sussex County Hospital, Brighton BN2 5BE
A J CANT MD, MRCP, paediatric registrar, Trevor Mann Baby Unit
W LENNEY, MD, MRCP, consultant paediatrician, Trevor Mann Baby Unit
N KIRKHAM, MRCPATH, consultant pathologist

Cranial diabetes insipidus after upper gastrointestinal haemorrhage

Isolated impairment of posterior pituitary function with normal anterior pituitary function after haemorrhagic shock is most unusual but has been reported in obstetric patients. We describe a patient who developed cranial diabetes insipidus after a profound gastrointestinal haemorrhage.

Case report

A previously well, asymptomatic 65 year old man was admitted with haematemesis of acute onset after two days of melaena. He was not taking any drugs and denied taking alcohol. He was drowsy, pale, and shocked with a pulse of 120/min and systolic blood pressure of 80 mm Hg. Haemoglobin concentration was 54 g/l, but blood urea and glucose and serum electrolyte and calcium concentrations were normal. He was given three units of whole blood and 4% dextrose-saline one litre 12 hourly. Two hours after admission his systolic blood pressure was 100 mm Hg; thereafter it was maintained above 100 mm Hg. Gastroscopy showed a gastric ulcer, which was shown to be benign on histological examination of mucosal biopsy specimens.

Twenty four hours later he was haemodynamically stable but confused and dehydrated; nasogastric aspirate was free of blood. Urine output was more than three litres in the first 24 hours and six litres in the next 12 hours. He complained of severe thirst. His serum sodium concentration had risen to 170 mmol/l and chloride concentration to 115 mmol/l. Blood urea concentration was 6·5 mmol/l, potassium 4·9 mmol/l, and glucose 5·9 mmol/l and serum calcium 2·1 mmol/l. Serum osmolality was 340 mmol/kg and urine osmolality 150 mmol/kg. Diabetes insipidus was diagnosed, and desmopressin 20 μg administered intranasally caused a prompt reduction in urine output with a sharp rise in urine osmolality to 620 mmol/kg. With continued use of desmopressin 10 μg twice daily, all his symptoms, including complaints of thirst subsided, serum electrolyte concentrations and osmolality returned to normal. Repeat endoscopy six weeks later showed that the ulcer had healed completely. Radiographs of the chest and skull, results of visual perimetry, and computed tomograms of the head were normal. Anterior pituitary function was normal: serum free thyroxine concentration 12 pmol/l (normal range 8·2-24·0 pmol/l), serum prolactin 172-300 mIU/l (normal range <460 mIU/l), plasma cortisol 395 nmol/l at 0900 and 200 nmol/l at 2400, urinary free cortisol 210 nmol/24 h (normal range 100-370 nmol), and random growth hormone 4·2-19 mU/l (normal stimulated value >15 mU/l). Stimulation of the anterior pituitary gland by thyrotrophin releasing hormone and luteinising hormone releasing hormone yielded normal responses.

The patient continued taking desmopressin and remained symptomatic with normal serum electrolyte concentrations. Two years later anterior pituitary function was normal, but an eight hour water deprivation test showed failure to concentrate urine: urine osmolality was 289 mmol/kg and serum osmolality 299 mmol/kg, associated with a weight loss of 1·6 kg (2·9% of body weight). Plasma immunoactive vasopressin was undetectable (<0·3 pmol/l) after eight hours.[1] Administration of desmopressin 2 μg intramuscularly caused a prompt rise of urine osmolality to 795 mmol/kg, confirming the diagnosis of cranial diabetes insipidus.

Comment

This patient showed persistent partial cranial diabetes insipidus without any clinical or biochemical evidence of dysfunction of the anterior pituitary gland. The abnormality clearly developed immediately after his haematemesis, when he was hypotensive. We were unable to find any cause for the diabetes insipidus other than hypovolaemic hypotension. Cranial diabetes insipidus has been reported after postpartum haemorrhage, temporarily after coronary artery bypass surgery, and after cardiorespiratory arrest.[2-5] To our knowledge no case of persistent disease has been reported after haemorrhagic shock other than severe postpartum haemorrhage. Our patient's abnormality probably resulted from selective neuronal damage in the supraoptic and paraventricular areas of the hypothalamus while he was hypotensive. Hypernatraemia, polyuria, and intense thirst should alert clinicians to the possibility of cranial diabetes insipidus after haemorrhagic shock.

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Sunderland District General Hospital, Sunderland SR4 7TP
L S P WICKRAMASINGHE, MRCP, DGM, senior registrar, department of medicine for the elderly and general medicine
B I CHAZAN, MD, FRCP, consultant physician, department of medicine and endocrinology
A R MANDAL, FRCP, consultant physician, department of medicine for the elderly

Department of Medicine, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU
P H BAYLIS, MD, FRCP, reader in endocrinology

Department of Medicine for the Elderly, Ryhope General Hospital, Sunderland SR2 01Y
IAIN RUSSELL, MB, CHB, senior house officer

Correspondence to: Dr Wickramasinghe.

Increasing doses of naloxone hydrochloride by infusion to treat pain due to the thalamic syndrome

The opioid antagonist naloxone hydrochloride has been used for several years to treat pain resulting from the thalamic syndrome with variable results.[1] We describe two cases in which previous treatments had failed and a course of naloxone infusions at weekly intervals, during which the dose was steadily increased, successfully relieved pain for up to six months.

Patients, methods, and results

In this unit a series of weekly naloxone infusions was offered to outpatients with the thalamic syndrome. At each infusion the dose was increased by 0·4 mg or 0·8 mg until roughly 12 mg was reached, and this dose was given for a further two weeks. The naloxone was added to 500 ml of compound sodium lactate (Hartmann's solution) and given intravenous infusion over three hours into a peripheral vein. Electrocardiograms and blood pressure were monitored throughout,[1,2] although no exceptional changes have been observed in any patient in this district given naloxone for pain relief.