Acute renal failure after eating raw fish gall bladder

Various fishes are poisonous, the most commonly recognised being ciguatera and scombroid poisoning.¹ The raw gall bladder of the grass carp (*Ctenopharyngodon idellus*) has both nephrotoxic and hepatotoxic properties, which are less known.

Case reports

Case 1—A 37 year old housewife ate the raw gall bladder of a grass carp and six hours later had central colicky abdominal pain, vomiting, and watery diarrhoea for several hours. She was admitted to hospital three days later because of oliguria. Physical examination showed nothing abnormal except for jaundice. There was no dehydration. Results of investigations were: serum urea concentration 37.5 mmol/l (226 mg/100 ml), creatinine 1350 μ mol/l (15.3 mg/100 ml), bilirubin 75 μ mol/l (4.4 mg/100 ml) (direct 56 μ mol/l; 3.3 mg/100 ml), aspartate aminotransferase (AST) activity 114 μ mol/min/l (normal 8-32), alanine aminotransferase (ALT) activity 1178 μ mol/min/l (normal 3-34). Total urine output was below 500 ml for seven days but gradually increased to 1200 ml by the twelfth day, reaching 4750 ml on the fourteenth day. Her serum creatinine concentration peaked on the tenth day and then improved. Dialysis was not performed. AST activity decreased to 43 μ mol/min/l and ALT activity to 180 μ mol/min/l after three days (table). Renal biopsy at four weeks showed evidence of recent interstitial oedema with interstitial fibrosis and features of acute tubular necrosis with regeneration. Immunofluorescence results for IgG, IgM, IgA, and fibrin were negative. Both renal and liver function returned to normal on discharge.

Case 2—A 32 year old man was admitted because of central abdominal pain with vomiting and watery diarrhoea five hours after eating the raw gall bladder of a grass carp. Physical examination showed nothing abnormal. On admission the serum urea concentration was 5.4 mmol/l (32.5 mg/100 ml), creatinine concentration 60 μ mol/l (0.7 mg/100 ml), AST activity 12 330 μ mol/min/l (normal 11-35) and ALT activity 5730 μ mol/min/l (normal 5-48). After admission his urine output decreased and he became anuric with a serum urea concentration rising to 34.5 mmol/l (208 mg/100 ml) on the third day. Haemodialysis was performed. Diuresis occurred 17 days later, after a total of eight sessions of haemodialysis, and renal function gradually returned to normal. Liver function improved spontaneously, AST activity falling to 53 μ mol/min/l and ALT activity falling to 1060 μ mol/min/l on the third day (table). Renal biopsy showed acute tubular necrosis with swelling and degeneration of epithelial cells, mainly of the proximal convoluted tubules.

Laboratory and clinical findings in the three patients

	Case 1	Case 2	Case 3
Red blood cell count/high power field	—	—	8-10
White blood cell count/high power field	5-6	10-20	2-8
Casts	—	Epithelial +	Granular +
Bilirubin	Negative	Negative	Negative
Urobilinogen	Not raised	Not raised	Not raised
24 hour urinary protein (g)	0.12	0.18	0.19, 0.3
Maximum blood urea (mmol/l)	36.4	34.5	25.9
Maximum serum creatinine (μ mol/l)	1850	1930	964
AST on admission and 3 days later (μ mol/min/l)	114, 43	12 330, 53	7380, 17
ALT on admission and 3 days later (μ mol/min/l)	1178, 180	5730, 1060	5130, 478
Time to onset of symptoms (hours)	6	5	18
Time to onset of oliguria/anuria (hours)	48	72	—
Time to onset of diuresis (days)	14	17	—

Conversion: SI to traditional units—Blood urea: 1 mmol/l $\approx$ 6 mg/100 ml. Serum creatinine: 1 μ mol/l $\approx$ 0.01 mg/100 ml. AST: 1 μ mol/min/l = 1 IU/l. ALT: 1 μ mol/min/l = 1 IU/l.

Case 3—A 53 year old housewife was admitted complaining of dizziness preceded by flushing 18 hours after eating part of the raw gall bladder of a grass carp. There was no gastrointestinal upset. Physical examination showed no abnormality. Her symptoms subsided spontaneously after admission. On admission her serum urea concentration was 6.4 mmol/l (38.6 mg/100 ml) and creatinine concentration 118 μ mol/l (1.3 mg/100 ml), but these rose to peak values of 25.9 mmol/l (156 mg/100 ml) and 964 μ mol/l (10.9 mg/100 ml) respectively after five days. The patient, however, continued to have a daily urine output of 1500-2000 ml. Renal function returned to normal in three weeks. Liver function also showed improvement, AST activity decreasing from 7380 to 17 μ mol/min/l and ALT activity decreasing from 5130 to 478 μ mol/min/l after three days (table). Muscle enzyme activities (creatinine phosphokinase 39 μ mol/min/l and lactate dehydrogenase 230 μ mol/min/l) were normal.

Comment

The freshwater grass carp is commonly eaten in Asia. Swallowing its gall bladder raw is believed by some to be good for health, especially for rheumatism, and our patients did so for this reason. Cases of toxicity after eating raw gall bladder of grass carps have been reported only sporadically.²⁻⁴ All except one patient (our case 3) presented initially with gastrointestinal upset including abdominal pain, nausea, vomiting, and watery diarrhoea several hours after ingestion. In all patients hepatotoxicity and nephrotoxicity occurred. The hepatic picture, observed within hours of ingestion, was attributed to hepatotoxins rather than to an infective agent in the raw bile.² The putative toxin has not been identified; nevertheless, that such a toxin exists is supported by the fact that boiled raw bile of the grass carp is toxic in animals.⁵ This implies possible toxicity of cooked fish gall bladders, although no case has been reported.

Spontaneous resolution of hepatic dysfunction within a few days is usual. More serious is the nephrotoxicity, which culminates in either the oliguric or the non-oliguric form of acute renal failure, usually within 48-72 hours after ingestion while hepatic dysfunction is resolving. The biopsy findings of acute tubular necrosis are similar to that produced by other common nephrotoxins. In the one patient (case 3) in whom muscle enzyme activities were measured no evidence of rhabdomyolysis was obtained.

Our report should help alert physicians to such a possible but rare cause of acute renal failure.

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Respiratory arrest after solvent abuse

Roughly 80 deaths each year in the United Kingdom are associated with solvent abuse.¹ In about half the cases death is attributed to cardiac arrhythmias, a direct central nervous depressant effect, asphyxia, and hepatorenal failure.² Most cases of sudden death are thought to be caused by cardiac sensitisation with resultant ventricular fibrillation linked with hypercapnia, stress, or activity.³ Nevertheless, most deaths associated with solvent abuse occur outside hospital and the exact mechanism of sudden death is still not clear. Asphyxia has been proposed in cases where no other cause was found or seemed likely.² We report a case of reversible respiratory arrest after acute inhalation of adhesive containing toluene.

Case report

A previously fit 21 year old punk rocker was admitted to the casualty department after a six hour glue sniffing session, which resulted in severe behavioural disturbance. On the way to hospital by ambulance his level of consciousness deteriorated and respiration stopped for about two minutes. He was resuscitated with an airway and Ambu bag and spontaneous respiration restarted. On admission to the casualty department he was breathing normally with an airway in situ. He was drowsy, but had no focal neurological signs and normal sized pupils. He suffered a further respiratory arrest (again lasting about two minutes) while in the casualty department. His electrocardiogram, which was monitored continuously during this period of apnoea, showed sinus tachycardia only. He was resuscitated again with an Ambu bag and after an attempt at intubation began breathing spontaneously. He quickly regained full consciousness and made an uneventful recovery over the succeeding 24 hours. He was given no drugs.

He later gave a six year history of heavy solvent abuse (four litres of Evostick per week, which he inhaled from a plastic bag). He denied intravenous drug abuse and the consumption of any drugs or alcohol on the day of admission. Urine screen for toluene breakdown products was strongly positive (urine hippuric acid concentration = 2.5 g/l; normal range 0.1-0.2 g/l). A complete drug screen was otherwise negative. The results of routine blood tests and chest x ray examination were normal.

Comment

Considerable emphasis has been placed on cardiac arrhythmias as the major cause of sudden death in solvent abuse. We believe that reversible respiratory arrest, despite a normal electrocardiogram, has not been reported. Nevertheless, respiratory depression in solvent abusers might be expected, since studies in animals have shown that toxic concentrations for the central nervous system and cardiac sensitisation are similar. Depression of central nervous system function by solvents probably occurs in a similar manner to the depressant effects of most general anaesthetic agents. Central nervous system toxicity in rats evolved from tremor to narcosis, followed by shallow respiration and death from respiratory depression. Death was inevitable above a critical toxic concentration.⁴ For this reason patients who lose consciousness during or after solvent abuse should be closely monitored.

We believe that this case report supports the theory that respiratory depression alone may be an important cause of sudden death in solvent abusers. There may be no distinctive features at necropsy suggestive of the mode of death, and this probably accounts for the rarity of respiratory depression as a postmortem diagnosis in solvent abusers.

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Pregnancy after chemotherapy induced ovarian failure

Several groups have studied reproductive function after MVPP (mustine, vinblastine, procarbazine, and prednisolone) or MOPP (mustine, vincristine, procarbazine, and prednisolone) chemotherapy for Hodgkin's disease, and the incidence of amenorrhoea has ranged from 15% to 62%.¹⁻⁴ The cessation of menses is related to age and is accompanied by an increase of serum gonadotrophin concentrations and a decreased serum oestradiol value consistent with primary ovarian failure. Apart from age, there have been no clear differences noted between those women who become amenorrhoeic and those who do not. Schilsky *et al*, in their long term follow up of ovarian function in women treated with quadruple chemotherapy for Hodgkin's disease, concluded that if premature ovarian failure developed, then it was invariably permanent. We describe a patient in whom amenorrhoea was not permanent and in whom pregnancy occurred only because she disregarded the advice of her doctors concerning sex steroid replacement therapy.

Case history

In June 1978 a 23 year old woman presented with cervical lymphadenopathy and an enlarged liver and spleen. Histologically a biopsy sample of lymph node showed nodular sclerosing Hodgkin's disease. Between July 1978

and May 1979 she received eight courses of quadruple chemotherapy with MVPP. Subsequently she remained well and required no further treatment for Hodgkin's disease.

Up until early 1981 she had taken the oral contraceptive pill but this was stopped as she was interested in the possibility of fertility. By January 1982 she had seen only one period in the past nine months. Serum follicle stimulating hormone and luteinising hormone concentrations (>32 IU/l) and serum oestradiol concentration (104 pmol/l; 28 pg/ml) were consistent with primary ovarian failure. She was advised that the cause of her amenorrhoea was chemotherapy induced ovarian failure and that she required sex steroid replacement therapy. Treatment with ethinyloestradiol-levonorgestrel (Microgynon 30) was begun but she remained concerned about her chances of fertility. Thus in order to provide further information about her fertility prospects a laparoscopy and ovarian biopsy were performed in March 1983. The biopsy samples showed complete absence of ovarian follicles and she was advised to continue with Microgynon 30. She did not take her sex steroid replacement therapy. Between July and December 1983 she had five normal periods, and in January 1984 the progesterone concentration on day 21 was consistent with ovulation. In February pregnancy was confirmed, and at the end of September she delivered a healthy baby boy weighing 3400 g.

Comment

This young woman showed clinical and biochemical features of primary ovarian failure as a result of quadruple chemotherapy for Hodgkin's disease. The amenorrhoea was thought to be permanent in the light of the ovarian biopsy findings and the "known" course of chemotherapy induced ovarian failure.³

In young women with ovarian failure sex steroid replacement therapy is advised to prevent dyspareunia, loss of libido, and the risk of osteoporosis. During treatment it is impossible to determine if the ovarian failure is reversible and, of course, infertility is permanent.

Our patient's history indicates that cytotoxic induced ovarian failure may be reversible, and this poses a therapeutic dilemma in patients similarly treated who wish to conceive. It may be argued that we were unwise to assume an absence of residual primordial follicles from an ovarian biopsy sample obtained at laparoscopy.⁵ Thus to ensure that enough ovarian material has been obtained for adequate histological evaluation, laparotomy and ovarian wedge resection may be required in some of these young women; these procedures, however, are not without their own complications.⁵ Under similar circumstances, if an otherwise asymptomatic young woman who is desirous of a pregnancy prefers not to undergo a laparotomy and ovarian wedge resection she may choose not to take sex steroid replacement therapy despite the increased risk of osteoporosis.

The reproductive history of this patient illustrates that it is unwise to assume that amenorrhoea and infertility are inevitably permanent after chemotherapy induced ovarian damage.

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Correction

Blood group as a prognostic indicator in breast cancer

In the results section, third paragraph, third line, and in table III of the article by P J Holdsworth *et al*, published on 2 March (p 671) "M stage" should read "N stage."