this family have all presented over the age of 35. Because of this uncertainty, angiography, an invasive procedure with a definite morbidity, should perhaps be reserved for people with symptoms and older relatives who request the investigation. Computerised axial tomography with contrast enhancement is an alternative investigation for such cases. It must be emphasised, however, that, though less hazardous, this is not an accurate method of diagnosing aneurysms and that negative investigation does not rule out the condition.

The benefits of surgery for symptomatic cases of berry aneurysm are well established. The long-term results of major surgery for the treatment of asymptomatic people are not known. In experienced hands the surgery of operable unruptured aneurysms should carry a mortality and morbidity of well below five per cent. The technical difficulties in such cases are much less, making the procedure safer and simpler. The alternative is to reserve surgery for symptomatic cases or for those in whom precipitating factors such as hypertension develop. When a choice is made, it should be remembered that the first haemorrhage from an aneurysm carries an appreciable immediate mortality. The asymptomatic proposita in this family, because of the rapid death of so many of her relatives, had no doubts that she wanted elective surgery.

We suggest that a detailed family history should always be taken in cases of berry aneurysm. If other cases are found or strongly suspected in the family, angiography should be considered but due attention given to the relative risks of angiography compared with simple observation. If berry aneurysms are found, however, surgical intervention may have to be offered.

Pope *et al*[5] recently showed type III collagen deficiencies in skin biopsy preparations from some patients with congenital cerebral aneurysms. In future collagen patterns may be helpful in identifying individuals at risk in families where cerebral aneurysm appears to be segregating as a dominant trait.

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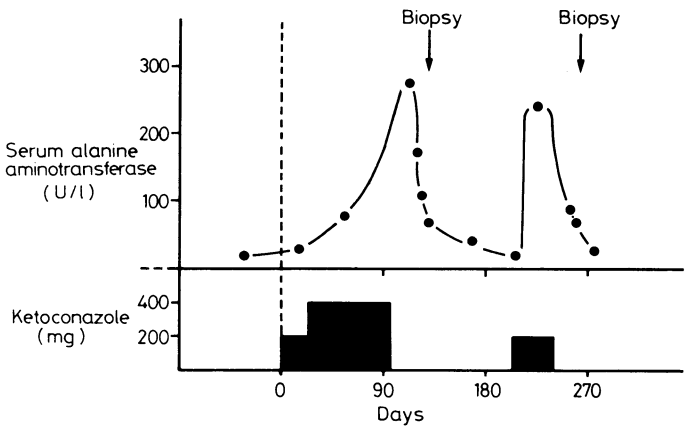
Toxic hepatitis during ketoconazole treatment

Ketoconazole, a synthetic imidazole-piperazine compound, is a new oral broad-spectrum antimycotic drug for the treatment of superficial and systemic fungal infections. The side effects reported have been minor and mostly subjective, such as nausea, itching, headache, and dizziness. Liver toxicity as shown by raised serum enzyme activities has been reported in a few cases.[1] We report a case of hepatotoxicity with clinical symptoms associated with ketoconazole.

Case report

A 68-year-old woman who had had severe recalcitrant dermatophytosis (*Trichophyton rubrum*) of feet and toe-nails for 35 years was admitted to a multicentre study of ketoconazole. She underwent clinical investigation including liver function and blood tests every three weeks. Treatment was started with 200 mg ketoconazole daily, which she received for 12 weeks, after which the dose was increased to 400 mg owing to lack of improvement. After two weeks on this dose she developed pruritus and rhinorrhoea and felt tired and dizzy. Three days later dark urine and pale faeces were observed, and she was admitted to a regional surgical department. Intravenous cholecystography showed no abnormality. Results of liver function tests, including serum alanine aminotransferase and serum alkaline phosphatase activities and serum bilirubin concentration, were compatible with parenchymal liver damage (see figure). A liver biopsy specimen showed preserved lobular architecture. The portal tracts were enlarged, with slight bile duct proliferation and moderate infiltration with mononuclear cells. Focal necroses were seen in the parenchyma. The centrilobular area showed condensation of the reticulin and increased amounts of seroid in Kupffer's cells, indicating recent necroses. Proliferation of Kupffer's cells was pronounced.



Serum alanine aminotransferase activity during two periods of ketoconazole treatment with different doses.
Normal range of serum alanine aminotransferase activity is 10-40 u/l.

Ketoconazole treatment was stopped and her symptoms disappeared. Results of liver function tests returned to normal. Seventeen weeks later ketoconazole treatment with 200 mg daily was restarted. After two weeks of treatment the symptoms reappeared and results of the liver function tests were again abnormal. A liver biopsy specimen showed enlarged portal tracts, but the parenchymal changes were less prominent. Necroses were rare and Kupffer's cell proliferation was absent. After ketoconazole treatment was stopped her symptoms again disappeared and the results of liver function tests returned to normal, and have remained normal now for eight months.

Results of tests for hepatitis B surface antigen and antibodies to hepatitis B virus and to hepatitis A virus were negative. Haematological values remained normal, and eosinophilia was not found. She did not receive other drugs. A third liver biopsy specimen six months after ketoconazole was withdrawn showed only rather enlarged portal tracts with moderate mononuclear infiltration.

Comment

In clinical trials of more than 2000 patients ketoconazole was shown to be effective and reliable in the treatment of candida, dermatophytes, and fungi causing deep mycoses.[2 3] It was also effective compared with other systemic antimycotics—for example, griseofulvin.[3 4]

Imidazole-piperazine compounds either stimulate or inhibit liver enzyme production[5] and therefore the side effect reported here is not surprising. The liver histology was like that seen in methyldopa-induced hepatitis—that is, enlarged portal tracts with mononuclear cell infiltration and piecemeal necrosis as seen in chronic active hepatitis. The fact that the liver impairment reappeared shortly after ketoconazole treatment was restarted strongly supports the evidence for ketoconazole-induced liver damage. In animal experiments liver toxicity has not been found.[2] So the type of hepatotoxicity seen in our case must be classified as a type II reaction (National Institutes of Health classification)—that is, the hepatotoxicity of ketoconazole cannot be predicted from animal experiments, it is rare in humans, and it is dose-independent.

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Abdominal hernias in patients receiving continuous ambulatory peritoneal dialysis

Continuous ambulatory peritoneal dialysis[1] is gaining wider acceptance as an alternative to haemodialysis in the treatment of end-stage renal failure. We report six cases of abdominal hernias encountered in 61 patients treated with continuous ambulatory peritoneal dialysis.

Case reports

The table summarises the pertinent features of the patients. The first case is described in detail.

Case 1—A 52-year-old man whose original kidney disease defied diagnosis despite extensive investigations including renal arteriography and renal biopsy was transferred to our unit in end-stage renal failure in April 1979. Peritoneal dialysis was started in May 1979 and after eight weeks in hospital, including an initial three weeks undergoing intermittent peritoneal dialysis to ensure adequate healing of the subcutaneous tunnel made during the insertion of the single-cuffed Teckenhoff silastic catheter, he was discharged receiving continuous ambulatory peritoneal dialysis with four exchanges of two litres isotonic solutions a day. Blood chemical values were quite acceptable and the patient's general condition satisfactory despite five episodes of peritonitis, which was cleared by continuous peritoneal lavage with antibiotics. On 24 December 1980 he was readmitted with fever and abdominal pain. Peritoneal fluid was clear and examination showed an irreducible umbilical hernia. Radiography of the abdomen showed multiple fluid levels. Strangulated hernia was diagnosed and he underwent laparotomy, at which 18 cm of gangrenous small bowel were resected. The hernia was repaired and the peritoneum carefully stitched. Immediately after operation peritoneal dialysis was continued using exchange volumes of 200-250 ml with zero dwell time. Flucloxacillin and ampicillin were given intraperitoneally and metronidazole rectally. He recovered uneventfully and continued with intermittent peritoneal dialysis for three weeks before returning to continuous ambulatory peritoneal dialysis. He was well when reviewed three months after discharge from hospital.

Comment

The incidence of hernias in patients receiving continuous ambulatory peritoneal dialysis (9·8%) was not appreciably different from that in patients receiving intermittent peritoneal dialysis (8%) at the same centre (unpublished observations). Of the five hernias observed in 64 patients receiving intermittent peritoneal dialysis, however, two were incisional hernias at the site of failed renal allografts and were probably not directly attributable to intermittent peritoneal dialysis. Moreover, the hernias in patients receiving continuous ambulatory peritoneal dialysis occurred within a short time (less than two years) of starting treatment. Undoubtedly the constant presence of two litres of dialysis solution will encourage the development of hernias through any sites of weakness in the abdominal wall—for example, catheter sites in case 2, umbilical hernias in cases 1 and 3, and a patent processus vaginalis in case 4. While the first differential diagnosis of abdominal pain in a patient undergoing peritoneal dialysis is peritonitis, the possibility of intestinal obstruction must not be forgotten. Our experience of abdominal hernias in patients receiving continuous ambulatory peritoneal dialysis is similar to that reported by the Toronto group.[2] In addition we have shown that careful repair of the hernia by surgeons familiar with the use of peritoneal dialysis catheters rendered it possible to continue dialysis immediately after operation. To avoid leakage of peritoneal fluid and dehiscence of the wound, intermittent dialysis with small volumes (125-250 ml) was used.

The true incidence of hernias in patients receiving continuous ambulatory peritoneal dialysis may be determined only when more experience with this technique has accumulated. Nevertheless, case 3 serves as a reminder that such a complication could ultimately lead to the failure of the technique in some patients.

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Clinical features of patients receiving continuous ambulatory peritoneal dialysis with abdominal hernias

Case No	Sex	Age (years)	Original kidney disease	Other important medical condition	Hernial site	Presenting symptoms	Interval*	Operation	Outcome
1	M	52	Unknown	Ischaemic heart disease	Umbilical	Fever, abdominal pain	19 months	Resection of gangrenous bowel. Hernia repair	Continuing continuous ambulatory peritoneal dialysis
2	M	19	Vesicoureteric reflux with dysplastic kidneys	Two failed renal allografts	Catheter site	Sudden "collapse" with abdominal pain	10 months	Hernia repair	Continuing continuous ambulatory peritoneal dialysis
3	M	42	Hypertensive nephrosclerosis	—	Umbilical	Abdominal pain, cloudy peritoneal fluid	11 months	Hernia repair	Continuous ambulatory peritoneal dialysis abandoned owing to unexplained persistent abdominal pain after the operation
4	F	13	Vesicoureteric reflux with dysplastic kidneys	Annular pancreas	Inguinal	Inguinal swelling on instilling dialysis solution	2 months	Resection of patent process vaginalis. Hernia repair	Continuing continuous ambulatory peritoneal dialysis
5	M	62	Polycystic kidneys	Poor nutritional state	Incisional	Swelling related to catheter site	2 months	—	Catheter leak has sealed. Continuing continuous ambulatory peritoneal dialysis
6	M	65	Unknown	Gastric carcinoma	Inguinal	Inguinal swelling	10 months	—	Currently undergoing haemodialysis for reason unrelated to the hernia

*Time between initiation of treatment of end-stage renal failure with continuous ambulatory peritoneal dialysis and the diagnosis of hernia.