IgA and IgM were normal, and IgE was raised at 550 kU/l. Autoantibodies were negative. C3 and C4 were 1·5 and 0·19 g/l. She was treated with fluid restriction, vitamin K, cinetidine, albumin and, three days after admission, prednisolone 1 mg/kg/24 hours. Four days after admission grade III hepatic encephalopathy developed and prothrombin time lengthened to 70 seconds. Despite further deterioration, orthotopic liver transplantation was performed 24 hours later when prothrombin time was 120 seconds. The excised liver was shrunken with evidence of submassive necrosis. On histology there was widespread inflammation comprised of lymphocytes, pigmented macrophages, neutrophils, and fewer plasma cells (fig 1B). The child died of infectious complications three months after transplant.

In both cases hepatitis A and B, cytomegalovirus, Epstein-Barr, measles, and leptospira infections were excluded; α1 antitrypsin phenotype and caeruloplasmin, plasma and urine copper, serum potassium, calcium, phosphate, glucose, cholesterol, creatinine, and urea concentrations, and urinalysis were normal.

Discussion

The diagnosis of liver injury induced by drugs rests on the exclusion of other aetiological factors. In the two children described no other cause of liver damage or drug exposure could be identified.

Hepatic side effects of carbamazepine are very rare. Among them, changes in results of liver function tests, jaundice, and granulomatous or cholestatic hepatitis are the most common. In a study of children, a clinically insignificant rise in results of liver function tests was found in 6% of 220 patients. We have identified only three reported cases of fatal acute liver failure directly attributable to carbamazepine, one being a child. Recently four children with fatal fulminant hepatitis while on carbamazepine were reported. All were taking several drugs, with three receiving other potentially hepatotoxic drugs, such as phenytoin and primidone. The mechanism of liver injury in carbamazepine hepatitis remains poorly understood, although it is presumed to be an idiosyncratic hypersensitivity, possibly deriving from genetically determined inability to inactivate toxic metabolites. Consistent with reports from other authors, we found that clinical presentation and laboratory tests in our two patients suggest an immunoinflammatory mechanism. Thus both had onset of symptoms four weeks after starting treatment, fever, rash, arthralgia, and raised IgE with carbamazepine concentrations within the therapeutic range. In addition, case 1 had a heavy plasma cell infiltrate found on histology, decreased complement concentration with increased IgG and IgM, and her recovery has been aided by the administration of steroids. In case 2 these features were absent and no response to steroid was observed, possibly suggesting another mode of hepatocyte injury.

Liver function tests performed routinely in the first weeks of carbamazepine treatment, and in the presence of other idiosyncratic reactions to the drug, may help to detect patients at risk of developing this rare complication.

Addendum

Since this paper was accepted we have admitted and successfully transplanted a 3 year old child who had fulminant hepatic failure due to carbamazepine toxicity.

Contractural arachnodactyly with mitral regurgitation and iridodonesis

I C Hugon, J P Burke, J F Talbot

Paediatric Unit, Northern General Hospital
I C Hugon
Department of Ophthalmology, Royal Hallamshire Hospital, Sheffield
J P Burke
J F Talbot

Abstract
An infant girl with arachnodactyly, spontaneously resolving contractures, dolichostenomelia, and mitral and tricuspid incompetence died in cardiac failure. We confirm that congenital contractural arachnodactyly may exhibit serious cardiovascular and ophthalmic complications like Marfan's syndrome. The presence of iridodonesis further obscures the differentiation between classical Marfan's syndrome and congenital contractural arachnodactyly.

We thank Dr TK Hanid and Dr DM Cook for referring the patients. NH is a British Council Research Fellow, GMV is supported by the M McGough Foundation Against Liver Disease in Children.


Beals and Hecht described an autosomal dominant syndrome of congenital contractural arachnodactyly distinct from classical Marfan’s syndrome. It is characterised by multiple contractures at birth that resolve spontaneously (in 94%), dolichostenomelia, arachnodactyly (in 85%), abnormalities of the external ears (in 65%), and the absence of the eye and cardiovascular abnormalities typical of Marfan’s syndrome. Since then, however, serious eye and cardiac abnormalities that lessen the distinction from Marfan’s syndrome have been described.1–5
We report a case of congenital contractual arachnodactyly complicated by iridodonesis (shimmering iris) and anterior megalophthalmos (enlarged anterior segment).

**Case report**
An infant girl was delivered normally at term after an uneventful pregnancy with normal liquor volume. She was the fourth child of healthy 25 year old unrelated parents and the other siblings (age 8, 5, and 4 years) were normal. Her birth weight was 3750 g (>50th and <75th percentile) and length was 57 cm (3 cm >97th percentile). She had gross arachnodactyly (fig 1), doliocostenomelia, prominent symmetrical flexion contractures of the knees, hips, elbows, and ankles, and appreciable enophthalmos. The ears were unremarkable. A loud pansystolic murmur and click were present and cardiac ultrasound demonstrated mitral and tricuspid regurgitation; skeletal survey showed arachnodactyly. Chromosome studies and urinary homocystine concentrations were normal.

From the age of 6 weeks she required diuretic treatment for cardiac failure. There was failure to thrive, but her developmental milestones were not significantly delayed. She was noted to have iridodonesis. Ophthalmic examination at this time and at 4 months confirmed iridodonesis in association with anterior megalophthalmos, alternating divergent squint (fig 2), myopic astigmatism, normal fundoscopy, and no evidence of lens subluxation on slit lamp biomicroscopy. She fixed and followed objects with each eye.

There was a gradual spontaneous improvement in all her joint contractures with time. Hospital admissions with persisting vomiting or exacerbations of cardiac failure were frequent and she died aged 4 months.

Permission for necropsy was limited to examination of the heart. This confirmed incompetence of the mitral and tricuspid valves. The chordae tendineae attached to the posterior leaflet of the mitral value had ruptured permitting prolapse into the left atrium, which was thought to be the immediate cause of death.

**Discussion**
The condition of this 4 month old infant with resolving congenital contractures, arachnodactyly, fatal mitral regurgitation, and iridodonesis presumably arose as a spontaneous mutation. In the original description of congenital contractual arachnodactyly the authors argued that the absence of severe cardiac and ophthalmic abnormalities helped to distinguish congenital contractual arachnodactyly from Marfan’s syndrome and indicated a better prognosis in the former.1 Subsequent reports of congenital contractual arachnodactyly in patients with mitral valve prolapse5 and regurgitation,4 keratoconus,7 and myopia5 have blurred this distinction. The presence of congenital symmetrical contractures at birth maximally involving the knees and enophthalmos, as in our case, favours the diagnosis of congenital contractual arachnodactyly.

The concept that congenital contractual arachnodactyly and Marfan’s syndrome are separate entities is challenged by the kindred described by Bass et al, where one family member appeared to satisfy better the criteria for Marfan’s syndrome while the remainder had congenital contractual arachnodactyly.3 Until specific biochemical or genetic abnormalities,
or both, are identified that differentiate these syndromes their separate existence based on clinical criteria alone will be disputed by some.

Before this report, iridodonesis, which is usually associated with lens subluxation, has only been described in cases with Marfan’s syndrome. The iridodonesis in our patient appeared secondary to anterior megalophthalmos, rather than to isolated lens subluxation. Anterior megalophthalmos has occurred rarely in Marfan’s syndrome, but has not been previously described in congenital contractural arachnodactyly. Slit lamp biomicroscopy is helpful in distinguishing these abnormalities.

Although patients with congenital contractural arachnodactyly are less likely than those with Marfan’s syndrome to develop serious ocular and cardiovascular complications, the case we describe emphasises the importance of serial cardiovascular and ophthalmic assessment of all these patients and further blurs their clinical separation.

We wish to thank Dr B A M Smith for permitting us to write this report on his patient.

Contractural arachnodactyly with mitral regurgitation and iridodonesis.

I C Huggon, J P Burke and J F Talbot

Arch Dis Child 1990 65: 317-319
doi: 10.1136/adc.65.3.317

Updated information and services can be found at:
http://adc.bmj.com/content/65/3/317

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/