Mistletoe hepatitis

JOHN HARVEY, D G COLIN-JONES

Abstract

A 49-year-old woman presented with nausea, general malaise, and a dull ache in the right hypochondrium. Liver biopsy showed slight inflammatory-cell infiltration, and results of liver function tests suggested hepatitis. Hepatitis B surface antigen was not detected, and a cholecystogram was normal. Two years later she presented with similar symptoms, and both illnesses were found to have occurred after ingestion of a herbal remedy containing kelp, motherwort, skullcap, and mistletoe. A challenge test established this to be the cause of the illness.

Mistletoe is the only constituent of the tablets known to contain any potential toxin and thus was probably the cause of the illness. Mistletoe is widely used in herbal remedies, whose ingestion may therefore cause hepatitis.

Introduction

We report a case of hepatitis caused by ingestion of a herbal remedy containing mistletoe. Thirty thousand mistletoe-containing pills are sold by one herbalist every week in Portsmouth, and until May 1978 a drug containing mistletoe extract (Felsol) was listed in MIMS.

This form of hepatitis may be much more common than is generally realised and may be implicated in the development of chronic liver disease.

Once again results of liver function tests were abnormal (table), and liver biopsy showed a light inflammatory-cell infiltrate with occasional foci of liver cell necrosis but preservation of architecture. Symptoms again settled with rest, liver function tests returning to normal within six weeks. Autoimmune antibodies were not detected on screening.

A formal challenge test was arranged to correlate this illness with ingestion of the herbal tablets and to exclude chronic active hepatitis. Symptoms of nausea and general malaise returned after 10 days of continuous ingestion of the herbal tablets, and after 14 days' ingestion liver biopsy (fig 1) showed severe changes with heavy infiltration (chiefly of lymphocytes and plasma cells), considerable focal necrosis, and distortion of liver architecture. Hepatitis B surface and core antigens were not detected. There was a polyclonal increase in serum IgG concentration (26.4 g/l); complement concentrations (C3, C4) were normal, as were results of screening for autoimmune antibodies.

Liver function tests and liver histology (fig 2) had returned virtually to normal by June 1979, though her serum gave a positive latex test result, and a sheep-cell agglutination test was positive at a titre of 1/40. In June 1980 the patient was well with no liver dysfunction.

Discussion

Mistletoe is one of the oldest and most widely used herbal remedies. It has been advocated for many conditions including infertility, asthma, and epilepsy and has been used as an aphrodisiac.¹ We can find no record of toxic reactions to kelp, motherwort (*Leonurus cardiaca*), or skullcap (*Scutellaria galericulata*). Wild lettuce is reportedly potentially poisonous, but no toxic compound has been isolated and cases of poisoning are not well

Results of liver function tests

Date	Albumin (g/l)	Bilirubin (mmol/l)	Alkaline phosphatase (U/l)	Lactate dehydrogenase (U/l)	Aspartate transaminase (U/l)
March 1976	34	42	123	395	250 +
September 1976	37	14	55	235	23
July 1978	41	13	72	381	62
October 1978 (challenge test)	41	38	144	419	250 +
June 1979	42	6	61		38
June 1980	41	9	70		36

Conversion: SI to traditional units—Bilirubin: 1 mmol/l $\approx$ 58 mg/100 ml.

Case report

In March 1976 a 49-year-old housewife presented with nausea, general malaise, and a dull ache in the right hypochondrium. Results of liver function tests (table) suggested hepatitis, and liver biopsy showed light inflammatory-cell infiltration of portal tracts with preservation of liver architecture. Hepatitis B surface antigen was not detected, and a cholecystogram was normal. No history of drug ingestion was obtained, and the symptoms settled with bed rest, though liver function tests did not return to normal for six months.

In July 1978 the patient presented again with similar symptoms, and we discovered that both illnesses coincided with several weeks' ingestion of herbal tablets for "nervous tension." These tablets contained motherwort, kelp, wild lettuce, skullcap, and mistletoe.

FIG 1—Needle biopsy specimen of patient's liver in 1978 after challenge with herbal tablets, showing extensive inflammatory-cell infiltrate with piecemeal necrosis.

Queen Alexandra Hospital, Cosham, Portsmouth PO6 3LY

JOHN HARVEY, MB, MRCP, senior registrar

D G COLIN-JONES, MD, FRCP, consultant physician

FIG 2—Needle biopsy specimen of liver six months after stopping herbal challenge. The inflammatory changes shown in fig 1 have resolved.

authenticated.² Mistletoe, however, contains several potential toxins (β -phenylethylamine, tyramine, acetylcholine, and propionylcholine). The herbal tablets used by our patient contained 90 mg mistletoe extract, which is not a large dose—for example, Potters' *Cyclopaedia of Botanical Drugs and Preparations* recommends 2–8 g.

We have found no record of any toxic reactions to mistletoe in man, and it has not been implicated in drug-induced hepatitis,³ though other herbs may cause severe liver injury.^{4 5} Although

mistletoe was the most likely toxin in this case, we thought that trying to obtain definitive proof with a second challenge test using mistletoe extract alone was not justifiable because of the severity of the histological change after the first challenge test.

Mistletoe is widely used in herbal remedies and until May 1978 a bronchodilator preparation (Felsol) containing mistletoe extract was listed in MIMS. Herbal remedies may be purchased without prescription and are much more commonly consumed than many doctors realise. This case shows that active hepatitis may result from their consumption, but there may well be cases in which the hepatitis remains subclinical and so progresses insidiously. Herbal remedies might also be an aetiological factor in the development of so-called cryptogenic cirrhosis.

We thank Dr Gerald Blunden, reader in pharmacy at Portsmouth Polytechnic, for advice on herbal toxins, and Dr John Burston, consultant pathologist, St Mary's Hospital, Portsmouth, for interpreting the liver biopsies.

References

- 1 Brian VA. The medicinal mistletoe. *Nursing Mirror* 1977 December: 25.
- 2 North P. *Poisonous plants and fungi*. 150th ed. London: Blandford Press, 1967.
- 3 Sherlock S. *Diseases of the liver and biliary systems*. 5th ed. Oxford: Blackwell, 1975.
- 4 Mokhobo KP. Herb use and necro-degenerative hepatitis. *S Afr Med J* 1976;50:1096–9.
- 5 Anonymous. Liver injury, drugs, and popular poisons. *Br Med J* 1979;i: 574–5.

(Accepted 11 November 1980)

Congenital rubella affecting an infant whose mother had rubella antibodies before conception

J W PARTRIDGE, T H FLEWETT, J E M WHITEHEAD

Abstract

A woman who had had high titres of rubella antibodies some months before she became pregnant gave birth to an infant in whom congenital rubella was confirmed at 4 months.

Rubella haemagglutination inhibition tests, complement fixation tests, and immunofluorescence tests with anti-human IgG were carried out on sera from the mother. Rubella antibody titres in sera obtained in March 1971, seven and a half months before conception, were equivalent to 400 units, which is usually taken as indicating good immunity. Rubella virus was isolated from the baby's nose and throat in July 1973 but was not isolated from a cervical swab taken from the mother in December 1973; tests of her immunological competence did not show any definite abnormality.

The presence of high levels of rubella haemagglutina-

tion inhibition antibodies does not invariably confer immunity or exclude the possibility of congenital rubella in a subsequent pregnancy.

Introduction

Virologically confirmed rubella reinfections, with disease of a fetus, are rare.^{1–3} We describe a baby severely affected by congenital rubella whose mother had high titres of rubella antibodies some months before she became pregnant. This case may be important with regard to current policies in rubella prophylaxis and the diagnosis of congenital rubella.

Case report

The baby was born in March 1973 and died in October 1976, the first child of healthy, unrelated parents who were both laboratory technicians. The mother had been told that she had contracted rubella when aged 7; she had not been immunised. Because she was considering becoming pregnant she deliberately came into contact with a colleague with suspected rubella in early October 1971. She did not develop any symptoms and arranged to have her rubella haemagglutination inhibition titre estimated at East Birmingham Hospital on 30 October. The titre (400 units) suggested good immunity, but rubella-specific IgM antibodies were not estimated. Blood samples for laboratory reference purposes taken from her in September 1970 and March 1971 were later found to have similar antibody levels. She

Warwick Hospital, Warwick CV34 5BW

J W PARTRIDGE, MRCP, DCH, consultant paediatrician

Regional Virus Laboratory, East Birmingham Hospital, Birmingham B9 5ST

T H FLEWETT, FRCP, FRCPATH, consultant virologist

Public Health Laboratory Service, London NW9 5EQ

J E M WHITEHEAD, MB, FRCPATH, deputy director, formerly Public Health Laboratory, Coventry