handicapped boy was referred after a recent diagnosis of moderate to severe sensorineural deafness. Because of this diagnosis he was discharged from the children's nursing home where he had lived, as nursing staff felt they could not manage this second handicap. His parents tried fruitlessly to achieve hearing aid compliance at home. They doubted the diagnosis as they had been reassured about hearing tests performed when he was young. His return to the family home caused extreme difficulty for the parents. Electrocochleography demonstrated normal cochlear function. There was no middle ear disease. The parents discarded the hearing aids with relief, but the child remains in the family home as there is no public or private facility prepared to offer him placement.

Case 3

This 20-month-old boy had been investigated in Ireland with behavioural and brainstem audiometry. After migration to Australia, he was again tested with behavioural audiometry, and results varied from mild to profound hearing loss. He had been fitted with one hearing aid in Ireland, but compliance was poor. He had begun to attend an early intervention program for hearing impaired children. Assessment revealed a very active, distractable toddler with language delay. He achieved normal scores in all of The Griffiths Test[1] scales except for the hearing and speech scale. Electrocochleography demonstrated normal cochlear function and normal brainstem auditory potentials. There was mucus in the middle ears at the time of electrocochleography. The parents discarded the hearing aid and concentrated on language stimulation. Subsequently grommets were inserted in his ears because of recurrent middle ear fluid.

Discussion

These cases illustrate the problems resulting from incorrect diagnosis of hearing loss and suggest two conclusions. Firstly, for difficult children and those with inconsistent results on behavioural audiometry, definitive non-behavioural testing should be considered. The physical and psychological risks occasioned by a brief anaesthetic administered by experienced paediatric staff are far outweighed by the benefit of rapid, accurate results and by the avoidance of the stress of wrong diagnosis and wasted hours of trying to achieve hearing aid compliance.

Secondly, just as we must "listen to the parents" when a mother or father suggests that their child is deaf[2], we must also "listen to the parents" (particularly in the case of a developmentally abnormal child) if it is suggested that the diagnosis of deafness is wrong.

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CASE REPORTS

Adverse reaction to a Chinese herbal remedy

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Objective: **To report a multisystem illness in a patient after ingestion of Chinese herbal medicines, together with an analysis of the herbal medicine and to alert physicians to the growing clinical importance of adverse reactions to herbal remedies.**

Clinical features: **A 61-year-old Chinese Vietnamese man with a history of atrial fibrillation and left cerebral hemisphere infarction three months previously presented after a three-day illness with acute hepatorenal failure, multiple pulmonary emboli, peripheral arterial thromboembolism and laboratory features of consumptive coagulopathy. For three days before presentation, he drank a daily infusion of herbal medicine.**

Intervention: **Intensive supportive medical care including haemodiafiltration resulted in recovery of renal function, liver function and return of coagulation parameters to normal over a one-month period. Toxicological analysis of an infusion prepared from a sample of the patient's herbal medicine revealed the potentially toxic compounds benzaldehyde, cinnamoyl alcohol and ephedrine.**

Conclusion: **The ingestion of herbal medicine caused or contributed to the patient's illness.**

(Med J Aust 1992; 157: 484-486)

Current medical practice generally assumes little understanding of oriental or other herbal medical practices. A case of multisystem illness after herbal medicine ingestion exemplifies the need for practitioners to consider such influences in the assessment of their patients.

Acceptance of herbal medicines as tonics or medicinal treatments is widespread in our community and often these are taken together with Western medicines.[1] Recent Australian reports of herbal 'medicine toxicities have included cases caused by adulteration of herbal arthritis remedies with Western ingredients, illness from bacterial contamination and adverse reactions to herbal medicines.[2-6]

Hepatic veno-occlusive disease caused by pyrrolizidine alkaloids contained in various herbal teas such as comfrey (*Symphytum officinale*) has been widely reported.[7-9] Other herbs known to cause dose-related toxicity include monkshood (*Aconitum* spp.) which can cause arrhythmias and hypotension, and *Ephedra* spp. which contain ephedrine, used to treat asthma. Recognised toxicities include the ginseng abuse syndrome, with hyperarousal and hypertension, and hypertension from licorice contained in *Glycyrrhiza* spp. Examples of the range of herbal toxicities are shown in the Table, and readers are referred to texts for further information.[10-14]

Adverse reactions to herbal medicines may be a potentially relevant consideration in many clinical situations and specific enquiry about use of non-Western medicine should be part of the everyday clinical assessment. The wide acceptance of herbal remedies and the broadening cultural diversity of our society suggests that such enquiries will become increasingly rewarding. It is recommended that medical practitioners have access to toxicology and herbal medicine references to meet these needs. There is, however, limited scientific information available on this subject, and further case reporting along with the publication of a monograph relevant to our community is to be encouraged.[4]

Clinical record

A 61-year-old Chinese Vietnamese man was admitted to hospital with hepatorenal failure, multiple pulmonary emboli and arterial thrombosis coincident with recent ingestion of Chinese herbal medicine. He had emigrated from Vietnam two years previously, and had

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Potential toxicities of some herbs

System	Herb	Active compound	Toxicity
Cardiovascular	Foxglove (*Digitalis purpurea*) Lily of the Valley (*Convallaria majalis*) Oleander (*Nerium oleander*)	Digitalis and related cardioactive glycosides	Arrhythmia, hypotension
	Hellebore (*Veratrum viride*) Monkshood (*Aconitum* spp.)	Various alkaloids	Arrhythmia, hypotension
Gastrointestinal	Numerous species, e.g., Pokeweed (*Phytolacca* spp.)	Phytolaccatoxin	Nausea, vomiting, diarrhoea
	Mistletoe (*Viscum album*)		Hepatitis
	Heliotrope (*Heliotropium* spp.) Comfrey (*Symphytum* spp.) Coltsfoot (*Tussilago farfara*) Ragwort, groundsel (*Senecio* spp.)	Pyrrolizidine alkaloids	Hepatic veno-occlusive disease
Renal	Mushroom (*Amanita phalloides*) Juniper (*Juniperus communis*) Grindelia (*Grindelia* spp.)		Nephrotoxic
Neurological	Monkshood (*Aconitum* spp.) Hellebore (*Veratrum* spp.) Eucalyptus oil Pennyroyal oil		Convulsions
Other	Aloe		Dermatitis
	Galega (*Galega officinalis*) Ginseng (*Panax* spp.)		Hypoglycaemia
	Periwinkle (*Vinca* spp.)		
	Pennyroyal oil Devil's claw (*Lotus corniculatus*)		Abortifacient
	Horse chestnut (*Aesculus* spp.) Tonka bean (*Dipterix odorata* spp.)	Coumarin glycosides	Anticoagulant

a past history of chronic sinusitis and glycosuria without overt diabetes mellitus. He was an ex-smoker.

Two months before admission he had presented to another hospital with chest pain and a transient cerebral ischaemic event with dysphasia. A cerebral CT scan at that time was consistent with a recent left frontoparietal infarct. He was in atrial fibrillation and an echocardiogram revealed no abnormality. After a period of treatment with heparin, digoxin was given, without reversion of the arrhythmia.

On admission to our centre he had a three day history of cough, dyspnoea, pleuritic right-sided chest pain and haemoptysis. Three weeks before admission he had developed a painful swollen right leg, which resolved spontaneously. Four days before admission he had sought a remedy for pain from a Chinese herbalist, and was prescribed an infusion of herbs which he drank daily for three days. The infusion was prepared each day by boiling a sachet of the herbal mixture with three cups of water in a porcelain vessel until one cup of liquid remained. This was then strained. He had also attended his family physician who treated him with erythromycin and a codeine and aspirin compound analgesic (Codral Forte).

On presentation he was cyanosed with a respiratory rate of 40/minute, pulse atrial fibrillation 155/minute and blood pressure 105/80 mmHg. He was afebrile. Urinalysis after catheterisation revealed protein ++ and blood trace. There were crepitations at the right lung base and absent right pedal pulses with ischaemic changes in the digits.

Initial investigations gave the following values: capillary blood glucose 2.4 mmol/L; serum creatinine 275 μmol/L (normal range, 30–120 μmmol/L); urea 12.3 mmol/L (normal range, 3.4–9.3 mmol/L); potassium 7.2 mmol/L (normal range, 3.5–5.0 mmol/L); bicarbonate 16 mmol/L (normal range, 22–32 mmol/L); and lactate >10 mmol/L (normal range, 0.5–1.0 mmol/L). Full blood examination showed: haemoglobin 158 g/L; white cell count 15×10^9/L with neutrophilia; and platelets 48×10^9/L. There was evidence of consumptive coagulopathy, with a normal activated partial thromboplastin time, an international normalised ratio of 2.1, D-dimer level of 4 to 8 mg/L (normal range, 0.5–1.0 mg/L) and normal fibrinogen titre.

Electrocardiogram showed rapid atrial fibrillation and right bundle branch block, chest x-ray revealed normal heart size with an opacity at the right base. Ultrasound examination of the liver and kidneys revealed no abnormality, and cultures of blood and urine grew no pathogens. Therapy was begun with ceftriaxone and erythromycin administered intravenously, acidosis was corrected and vitamin K supplements administered along with platelet transfusion and fresh frozen plasma. On the second day he remained in oliguric renal failure and was transferred to Monash Medical Centre Prince Henry's campus for veno-venous haemodiafiltration.

The aspartate aminotransferase level peaked on Day 2 at 13 849 U/L (normal range, 15–45 U/L), and steadily fell to normal by Day 8. Other liver enzyme levels peaked on Days 4 to 5 with a twofold increase in alkaline phosphatase and a twelvefold increase in γ-glutamyl transpeptidase levels. The bilirubin level peaked at 254 μmol/L (normal range, 3–20 μmol/L).The serum albumin level was normal on presentation at 40 g/L. A liver–spleen nucleotide scan on Day 2 revealed normal liver and spleen tracer pattern with, however, some colloid shift to the bone. A computed tomography scan of the abdomen performed on the same day with and without contrast demonstrated normal hepatic imaging along with normal-sized kidneys (which, however, failed to excrete the contrast medium).

All investigations relating to viral illness gave negative results, apart from that for hepatitis B core IgG antibody, which was positive. Serum ferritin, caeruloplasmin and α_1-antitrypsin levels were normal. A urinary drug screen on admission was negative for paracetamol and salicylate.

The chest x-ray changes at the right lung base persisted, and a ventilation–perfusion lung scan on Day 6 was consistent with multiple pulmonary emboli. A lung scan on Day 13 showed some resolution of the previous perfusion defects along with other new emboli.

Anticoagulation therapy was delayed because of the initial coagulopathy and progressive thrombocytopenia. Platelet counts reached a nadir of 17×10^9/L on Day 9, and then rapidly rose to normal levels. Platelet surface IgG levels were not increased and platelet aggregation studies with heparin gave negative results. Anticoagulation therapy was initiated with warfarin alone. There was no clinical evidence of further pulmonary emboli, and the chest x-ray changes slowly resolved.

Urinary sediment was repeatedly normal, and renal function recovered to normal after one month.

X-rays revealed venous calcification in the right leg consistent with the history of a deep venous thrombosis before admission. Carotid duplex studies revealed bilateral 40%–60% stenoses of the internal carotid arteries. Investigation for an underlying hypercoagulation disorder was unrevealing; repeated peripheral blood film examinations revealed no microangiopathic red cell changes, lupus anticoagulant was not detected and the anticardiolipin antibody titre was not elevated. The sucrose water lysis test was negative.

The clinical picture was inconsistent with vasculitis. Autoantibodies, including antinuclear factor and antineutrophil cytoplasmic antibodies, were not present. Cryoglobulins and cryofibrinogens were not detected. A test for syphilis serology gave a negative result.

The patient remained in atrial fibrillation despite digoxin therapy. Thyroid function tests gave normal results. A two-dimensional echocardiogram on Day 5

1. Ingredients of the herbal mixture implicated in the reported case

Salvia miltiorrhiza root
Pinellia spp. tuber
Panax pseudoginseng root
Safflower
Trichosanthes spp. (Mongolian Snakegourd) peel
Ephedra spp.
Corydalis spp. root
Paeonia lactiflora root
Typha spp. pollen
Curcoma aromatica root
Trifoliate orange peel
Ganoderma japonicum
Pigeon droppings

revealed no abnormality, and an echocardiogram with Doppler ultrasound performed later revealed normal left ventricular dimensions with low normal contraction, mild left atrial enlargement and mild mitral regurgitation. There was no evidence of interatrial shunting or cardiac thrombus.

A sachet of the herbal mixture was retained by the patient, and with the assistance of the prescribing Chinese herbalist, it was possible to identify the ingredient herbs (see Box 1). This sample was also used to prepare an infusion, using the method described, for spectrographic analysis. Analysis showed evidence of several compounds of a toxic nature among those reported: benzaldehyde; cinnamoyl alcohol; ephedrine; methylephedrine; coumarin artefacts; and glaucine. Ephedrine was the most abundant compound detected. Aconitine was not detected.

Discussion

This patient's illness was seemingly chronic atrial fibrillation complicated by an initial embolic cerebral infarct. He later developed deep venous thrombosis complicated by multiple pulmonary emboli, consumptive coagulopathy and arterial thrombosis or thromboembolism. The development of acute hepatitis and acute oliguric renal failure, which both abated with supportive therapy only, may have been due to acute ischaemia of these organs occurring before presentation. (In particular, the pattern of the abnormalities seen on liver function tests, with marked elevation of lactic dehydrogenase, was suggestive of ischaemic hepatitis.[15]) However, there was no history consistent with severe hypotension before presentation.

Extensive investigation revealed no cause for the patient's consumptive coagulopathy, acute hepatic failure and acute renal failure, and an adverse reaction to herbal medicine remains the "best fit" diagnosis. Difficulties arise, however, in proving a pathogenic role of herbal medicine in this illness. Analysis of the herbal infusion revealed potentially toxic compounds, but interpretation is limited by the possibility of labile compounds and the reproducibility of the preparation method used by the patient. Benzaldehyde, cinnamoyl alcohol and ephedrine are rated as compounds of moderate toxicity. When administered orally, a probable lethal dose in humans is in the range of 0.5 to 5 g/kg.[16]

The possibility that this patient's illness may have been an idiosyncratic reaction to herbal medicine, or promoted by coexisting illness (such as thrombosis), limits recommendations about the general safety of this particular herbal remedy. However, the occurrence of severe hepatic and renal toxicity in this setting highlights the potential for herbal medicine toxicity and should stimulate further investigation of this and similar herbal remedies.

Regulations pertaining to the use of herbal medicines are contained in the *Therapeutic Goods Act 1990* in which therapeutic goods are either "Listed" or "Registered". Listed goods, which generally include most vitamins, herbs and minerals, are evaluated for their quality and safety but not for their efficacy whereas registered goods are subject to wider evaluation, including efficacy. Registered herbs are shown in Box 2. Medicines containing herbs that are either listed or registered are exempt from these regulations when they are produced or dispensed or extemporaneously compounded for a particular person for therapeutic purposes. In these circumstances, herbalists are not required to label or record the supply of their medicines, and herbalists among others are exempted from the licensing of their premises where the place of preparation of the goods is closed to the public and the supply of the goods follows a consultation. The Poison Schedules list herbs which may not be used, such as Monkshood (*Aconitum spp.*) which is a Schedule One proscribed drug.

2. Restricted herbs, Therapeutic Goods Act 1990, Schedule 4

Name (common name)
Abrus precatorius (jequirity)
Acorus calamus (sweet flag, blue flag)
Argyreia nervosa (morning glory)
Aristolochia spp. (snakeroot, birthwort)
Amanita muscaria
Anadenanthera peregrina
Banisteriopsis caapi (banisteria)
Brachyglottis spp.
Cannabis spp.
Catha edulis (khat)
Conocybe siligineoides
Conocybe spp.
Crotolaria spp.
Cynoglossum officinale (hound's tongue)
Echium vulgare (viper's bugloss)
Erthroxylum coca (coca)
Gymnopiius spp.
Haemadictyon spp.
Heliotropium spp. (heliotrope)
Ipomoea burmanni
Ipomoea hederacea
Ipomoea tricolor
Ipomoea violacea
Lithospermum spp.
Lophophora spp.
Opuntia cylindrica (San Pedro cactus)
Papaver bracteatum
Papaver somniferum (opium poppy)
Peganum harmala (wild rue)
Petasites spp. (butterbur)
Phytolacca decandra (americana) (pokeweed)
Piptadenia macrocarpa
Piptadenia peregrina (cohoba)
Psylocybe spp.
Pteridium aquilinum (bracken fern)
Rivea corymbosa
Sassafras albidum (sassafras)
Senecio spp. (liferoot)
Solanum dulcamara (bittersweet)
Sophora secundiflora (mescai bean)
Stropharia cubensis
Strychnos gautheriana
Strychnos ignatii (ignatious bean)
Symphytum spp. (comfrey)
Tussilago farfara (coltsfoot)

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