Medical Memoranda

Massive Generalized Alopecia After Poisoning by *Gloriosa superba*

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A case is reported of massive generalized alopecia and menorrhagia after eating the tubers of *Gloriosa superba*, which contain the alkaloids colchicine and gloriosine.

Case Report

The patient, a married woman aged 21 years, was admitted on 17 September 1964 at about 2 p.m. to the University Medical Unit, General Hospital, Kandy. She had fallen ill after an afternoon meal the day before which consisted of a variety of boiled yams. The plant and the ingested tubers were identified as *Gloriosa superba*. The colchicine content of the tubers is 0.3%. Therefore, as the patient had eaten about 125 g. of tubers, the total amount of colchinine taken was in the region of 350 mg. About two hours after this meal she had started vomiting, and about eight hours later had profuse watery diarrhoea, which continued throughout the night. She had vomited 25 times that night and had 20 watery stools.

The patient had no children. Her past history revealed nothing of note. She attained puberty at 13 and her periods were regular. She had no physical abnormalities. Her hair had never been cut since childhood, as is the custom among Ceylonese girls, and it came down to her knees.

On admission she was unconscious, restless, dehydrated, and collapsed. Her pulse rate was 122/min., of moderate volume and in sinus rhythm ; blood-pressure was 95/70 mm. Hg, and respiratory rate was 18 per minute. Apart from these findings, nothing abnormal was noted. She had no cyanosis or dyspnoea. Her white-cell count was 8,800/c.mm., with a differential count of polymorphs 76%, lymphocytes 21%, eosinophils 3%. Her blood urea was 37 mg./100 ml. ; serum potassium 3.7 mEq/litre ; serum sodium 142 mEq/litre. She did not pass any urine on the day of admission. On the day of admission she was treated with a slow intravenous drip-infusion of 3 pints (1.7 litres) normal saline and 1 pint (0.6 litres) 5% dextrose with added vitamins.

Her condition improved on this regimen. Blood-pressure rose to 100/70 mm. Hg, and the pulse rate fell to 110/min. The following morning she collapsed again, the blood-pressure could not be recorded, and the pulse was imperceptible. Hydrocortisone hemisuccinate, methoxamine, and noradrenaline were then added to the drip.

Two days after admission, the day after her collapse in the ward, her general condition improved, blood-pressure was 90/70 mm. Hg, pulse rate 104/min., of moderate volume, and in sinus rhythm. No other abnormalities were detected clinically. Examination of her urine showed "pus cells—field full," probably because she was catheterized previously. She was given sulphadimidine and the urine report came back to normal in four days. Blood urea was 39 mg./100 ml.

Five days after admission the patient was found to have a subconjunctival haemorrhage in her left eye. Her menstrual period, which was ending the day she ate the tubers, continued for a further 20 days. A platelet count carried out at this stage was 475,000/c.mm. ; white-cell count was 5,000/c.mm., with polymorphs 50%, lymphocytes 49%, eosinophils 1%, and packed cell volume 35%. Haemoglobin was 11.3 g./100 ml., and mean corpuscular haemoglobin concentration 30 mg./100 ml.

Twelve days after admission marked alopecia was noticed, especially affecting the scalp hair (Fig. 1), and within two days most of the hair on her scalp had dropped out, as had her axillary hair and part of the pubic hair. She was seen in the clinic subsequently, and within a week after her discharge from hospital, 23 days after admission, she was completely bald. Two months later her scalp hair had regrown to half an inch (12.7 mm.) (Fig. 2). Pubic hair showed regrowth. Her axillary hair remained very scanty. After five months her scalp hair was 2–3 in. (5.1–7.6 cm.) long.

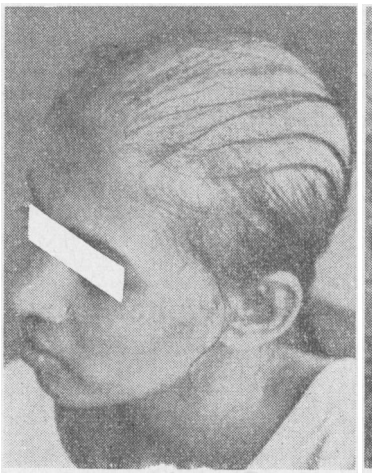

Fig. 1

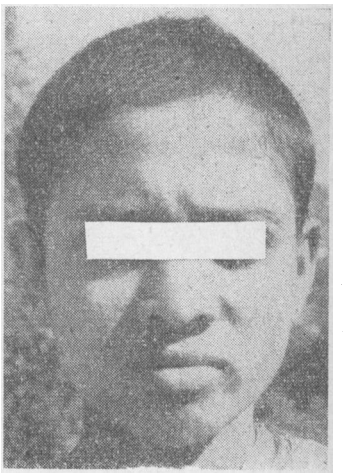

Fig. 2

Fig. 1.—Alopecia 13 days after eating tubers of *Gloriosa superba*. Fig. 2.—Regrowth of scalp hair two months after discharge from hospital.

Comment

Gloriosa superba L. (Sinhalese: Niyangala) was known to ancient medical writers in Sanskrit as "Gharbha ihatin"—that which causes abortion. This plant grows wild in all parts of Ceylon. The tubers of *Gloriosa superba* closely resemble the yams of the sweet potato (*Ipomoea batatas*), which form a part of the average Ceylonese villager's diet. These tubers have been analysed and found to contain the alkaloids gloriosine and colchicine, and other substances—organic acids like salicylic acid and resins (*Wealth of India*, 1956).

Colchicine was used to obtain polyploids from *Datura stramonium* by treating its seeds with the alkaloid. Fresh extracts of tubers of *Gloriosa superba* when applied to maize seed before sowing caused tetraploid sectors in developing roots (Kumar, 1953). When colchicine was being extracted from *Gloriosa superba* the isolation of a new alkaloid, provisionally named gloriosine, was reported (Subbaratnam, 1951 ; 1952 ; 1954). Further experimental work showed that both colchicine and gloriosine have an anti-mitotic effect, and that gloriosine was found to be more effective than colchicine in polyploid formation (Amoroso, 1953).

Colchicine has been used in the treatment of gout for many years. It has also been used as a cytotoxic drug in the treatment of inoperable carcinoma (Brown and Seed, 1945). Therefore, in view of its fairly wide use in therapy, experiments have been conducted—mainly on mice, rats, and sheep—with the aim of discovering its action and toxicity. Colchicine is rapidly excreted in bile and directly into the intestine for only a brief period after administration, and after 16 hours 50% of it has been recovered (Brues, 1942).

Alopecia caused by treatment with colchicine has been known and reported on many occasions (Rook, 1965a and b). In the cases reported the alopecia has been confined to the scalp. This

occurs seven to 14 days after poisoning. In this patient it occurred after 11 days and involved practically all the body hair. So far as I am aware this is the first time that such generalized massive involvement has been reported, and it is probably due to the synergistic effect of poisoning by colchicine and the more powerful related alkaloid gloriosine. Plant toxins like mimosine, a water-soluble amino-acid toxin, have been known to cause alopecia in animals, and nuts of *Lecythis* have caused alopecia in man (Rook, 1965a). Mimosine has not been isolated from *Gloriosa superba* tubers ; the main compounds isolated have been the alkaloids colchicine and gloriosine.

Unfortunately the patient had cut the ends of the hairs to form a wig, and I was unable to distinguish the characteristic effects of poisoning and at what stage of growth the hair was in. In the usual cases of colchicine poisoning one finds characteristic anagen alopecia with zones of constriction on the shaft (depending on the duration and degree of poisoning), and the shaft ending in a point. Inhibition of growth of the hair root and diminution of the diameter of the hair bulb and/or the keratogenous zone also occur (Crounse and Van Scott, 1960).

I am grateful to Dr. T. Varagunam for allowing me to study this patient, and to my wife, Dr. M. Y. Gooneratne, Ph.D., for her invaluable help.

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REFERENCES

Amoroso, E. C. (1935). *Nature (Lond.)*, **135**, 266.
Brown, W. O., and Seed, L. (1945). *Amer. J. clin. Path.*, **15**, 189.
Brues, Austin M. (1942). *J. clin. Invest*, **21**, 646.
Crounse, R. G., and Van Scott, E. J. (1960). *J. invest. Derm.*, **35**, 83.
Kumar, L. S. S. (1953). *Nature (Lond.)*, **171**, 791.
Rook, A. (1965a). *Brit. J. Derm.*, 77, 114.
—— (1965b). *Brit. med. J.*, **1**, 609.
Subbaratnam, A. V. (1951). *Chem. Abstr.*, **45**, 2152.
—— (1952). *J. scient. ind. Res.*, **11B**, 446.
—— (1954). Ibid., **13B**, 67.
Wealth of India (1956). Vol. IV, p. 239–240, Council of Scientific and Industrial Research, New Delhi.

Acute Gout Apparently Precipitated by Frusemide

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It is well documented that among the newer oral diuretics the thiazide drugs and chlorthalidone may precipitate gout in susceptible persons. According to the available literature on frusemide it is agreed that oral therapy might precipitate this disorder because of the rise in plasma urate it produces (Schaefer, 1964 ; Schirmeister and Willmann, 1964 ; Wölfer *et al.*, 1964). Bartorelli and Gargano (1963) also noted that in 10 hypertensive patients the plasma uric acid rose while they were being given 100 mg. of frusemide daily. No case of gout occurring *de novo* in a patient treated with frusemide has yet been reported. The case now presented is one of acute gouty arthritis arising in a patient under treatment with this diuretic.

CASE HISTORY

A man aged 52 was admitted on 24 August 1965, having had attacks of pulmonary oedema over some 11 successive nights ; these culminated in severe and unremitting dyspnoea the night before admission. He further complained of frequent palpitations, and of dyspnoea and tightness in the chest during previous respiratory-tract infections. He had had Sydenham's chorea in 1925, mitral stenosis was diagnosed in 1942, and was relieved by valvotomy in 1956. He denied any previous attacks of gouty arthritis or any family history of such illness. He had been treated successfully for the past two years with phenobarbitone 60 mg. b.d. for "black-outs."

On examination he was found to have atrial fibrillation, an accentuated apical first sound with a variable apical mid-diastolic murmur. He also had fluctuating pulmonary oedema, which precipitated two attacks of nocturnal dyspnoea while he was in hospital. These were successfully relieved by intravenous frusemide. His liver was slightly enlarged and tender. There were no signs of arthritis or loss of joint mobility at this time.

The results of investigations were as follows: Hb 106% (14.8 g./100 ml.), W.B.C. 6,500/c.mm., E.S.R. 7 mm. in first hour, P.C.V. 52% ; plasma urea 44 mg./100 ml., Cl^- 104 mEq/l., K^+ 5.3 mEq/l., Na 144 mEq/l., CO_2 combining power 29 mEq/l. Liver-function tests were normal. Radiology showed pulmonary oedema, which cleared on follow-up films, and moderate enlargement of the transverse diameter of the heart.

The patient was treated with digoxin 0.25 mg. three times a day five days out of seven, oral frusemide 80 mg. daily with intravenous supplements if he was disturbed by nocturnal pulmonary oedema, and potassium additives in the form of Ciba-K^+. He continued to take phenobarbitone 60 mg. thrice daily.

On 8 September 1965 he complained of a painful left metatarsophalangeal joint, which on examination was swollen, red, inflamed, and acutely tender to touch and movement. The level of plasma uric acid during this attack was 10 mg./100 ml. General examination revealed no other arthritic disturbance and no septic foci. In two days the swelling, pain, and discoloration subsided spontaneously. Frusemide was discontinued and mersalyl prescribed in its place. Subsequently the plasma uric acid was 8.2 mg./100 ml. Repeat investigation showed Hb 112% (15.5 g./100 ml.), P.C.V. 57%, plasma urea 65 mg./100 ml., Cl^- 94 mEq/l., CO_2 combining power 29 mEq/l., K^+ 5.0 mEq/l., Na^+ 135 mEq/l.

After a few days without any diuretic creatinine and uric acid clearances were performed over two 24-hour periods. Plasma uric acid was 5.7 mg./100 ml., and plasma creatinine 1.3 mg./100 ml. The results of other tests are set out in the Table.

Results of Tests Carried Out Over Two 24-hour Periods

	24-hr. Period	
	Sept. 14/15	Sept. 15/16
Urine volume (ml.)	1,460	940
Urinary uric acid (mg./100 ml.) ..	31	22
" " " (mg./24 hr.) ..	450	207
Uric acid clearance (ml./min.) ..	5·5	2·5
Urinary creatinine (mg./100 ml.) ..	86	58
" " (g./24 hr.) ..	1·3	
" " (mg./24 hr.) ..		545
Creatinine clearance (ml./min.) ..	67	29

A second mitral valvotomy was then performed on 7 October 1965. After operation and blood transfusion the patient's haemoglobin reached 130% (18.2 g./100 ml.), and a second attack of gouty arthritis occurred. A radiograph of the patient's feet at this time showed some vascular calcification with juxta-articular erosion of the first left metatarsal. He was given colchicine for the acute attack and was started on probenecid in standard dosage.

The high haemoglobin and packed cell volume in the absence of clinical dehydration indicated polycythaemia. The patient might therefore have had a predisposition to gout, and it is interesting that his first clinical attack of gout occurred while on this new diuretic, which, in common with the thiazides, shares the sulphamoylbenzene grouping.

PILOT SCHEME

The interest in this case prompted us to run a small pilot scheme with frusemide, using only the biochemical facilities to be found in a good teaching hospital. Random, isolated plasma