Congenital malaria in one non-identical twin

Only seven cases of congenital malaria have been reported in Britain.[1] [4] The case described here is believed to be the first to be reported in a binovular twin.

Case history

Shortly after her arrival in England from India in 1974, the mother, a 23-year-old primigravida, was found to have pulmonary tuberculosis, which was treated with streptomycin, rifampicin, and isoniazid. She became pregnant in September 1975, and her treatment was changed to para-aminosalicylic acid and isoniazid. Twin pregnancy was diagnosed radiologically in April 1976. The mother was admitted to hospital later that month in premature labour and delivered live male twins on 26 April 1976. The placenta and membranes were normal and consistent with the twins being binovular.

Twin I was delivered as a vertex presentation using Wrigley's forceps. Apart from transient anaemia his progress was uneventful. Repeated blood films showed no evidence of malaria.

Twin II was found to have a transverse lie. External version was unsuccessful. The membranes ruptured spontaneously and a hand prolapsed. He was subsequently delivered by internal version and breech extraction under general anaesthesia. He weighed 2·3 kg and was estimated to be of 35 weeks' gestation. A mild degree of Erb's palsy on the left soon resolved. He became jaundiced in the neonatal period, the serum bilirubin level reaching 229 μmol/l (13·4 mg/100 ml) on the fifth day, then rapidly subsiding. He continued to thrive until 42 days, when he became febrile with a rectal temperature of 38·2° C. There was no obvious cause for this and he was feeding well, though he was noticed to be pale. The pulse rate was 160/min and there was a soft systolic ejection murmur at the apex. The liver and spleen were enlarged.

A blood count was performed, the haemoglobin level being 6 g/dl; the total white cell count 5×10^9/l, with 8% neutrophils, 86% lymphocytes, and 6% monocytes. *Plasmodium vivax* was seen in the film. Blood films were subsequently examined at the Malaria Reference Laboratory at the London School of Hygiene and Tropical Medicine, confirming the diagnosis. The results of a chest *x*-ray film, lumbar puncture, and cultures of blood and urine were all normal. Treatment was begun with chloroquine base, 75 mg orally, repeated after six hours, and then 37·5 mg orally daily for four days. Response to treatment was excellent, the liver and spleen rapidly becoming impalpable. No parasites were seen in the blood films after the fourth day and subsequent follow-up has shown continued improvement in the anaemia and no recurrence of the malaria.

Serological studies on blood from the mother and both twins gave results consistent with the findings described. The results are summarised in the table. The titres for the mother and twin II are consistent with recent *P vivax* malaria, the fall in titre for twin II suggesting successful treatment. The antibodies in twin I were thought to be of transplacental origin and might be expected to persist for several months. Blood films from the mother were not examined.

Malarial antibody titres in the mother and twins

		Antibody titre to:	
		P falciparum	*P fieldi* (for *P vivax*)
Mother	(21 June)	64	>64
Twin I	(21 June)	16	64
	(3 August)	16	16-64
Twin II	(21 June)	16	256
	(3 August)	0	16-64

Comment

In discussions on the mode of transmission of the malarial parasite to the fetus some authors have mentioned the possibility of transmission in the absence of placental damage. Others have suggested that placental trauma may be important. Wilcocks and Manson-Bahr[5] state that congenital infection may occur without obvious placental damage, but suggest that microscopic areas of damage may be present. In the case reported it may be relevant that only the second twin appears to have been infected and that he was delivered after manipulations which could possibly have damaged the placenta, while the unaffected first twin was delivered without difficulty.

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Erythema elevatum diutinum and IgA myeloma: an interesting association

Erythema elevatum diutinum (EED) is a rare skin disease, thought to be an allergic cutaneous vasculitis of the necrotising leucocytoclastic type.[1] It consists of symmetrical red or purple nodules or plaques, mainly on the extensor surfaces of joints, which heal after many years leaving hyperpigmentation but no scarring. We report a case of IgA myeloma in a patient who was previously known to have both EED and IgA paraproteinaemia.

Case report

A 53-year-old woman was admitted to hospital complaining of severe weakness and pain in the chest, right shoulder, and right hip. About nine years previously she had developed a symmetric, non-pruritic erythema consisting of papules, nodules, and reddish plaques affecting mainly the extensor surfaces of the hands and legs. After various unsuccessful treatments over a period of four years she was admitted to the dermatology department of another hospital. Multiple skin biopsies showed changes characteristic of EED—endothelial swelling of the capillaries and perivascular hyaline degeneration, intense inflammatory infiltration consisting mainly of neutrophils, some of which showed apparent leucocytoclasis; extravasation of red cells; and intensive fibroblastic and histiocytic proliferation with fibrosis of the corium and subcutis. Serum immunoelectrophoresis showed an IgA paraproteinaemia. The bone marrow smears were compatible with an autoimmune disease but showed no evidence of myeloma. She was treated initially but unsuccessfully with azathioprine and then with sulphapyridine with satisfactory results. This was continued for some months.

On admission to our department the patient was pale. She had areas of skin atrophy and pigmentation on her buttocks, thighs, extensor surfaces of arms, and especially on the posterior and interior surfaces of her legs. The right clavicle was fractured and some ribs were painful on pressure. Investigations showed haemoglobin 9·4 g/dl; WBC 7×10^9/l (7000/mm^3), differential count normal; ESR 63 mm in first hour; blood urea nitrogen 22·1 mmol/l (62 mg/100 ml); serum albumin 43 g/l; serum globulins 29 g/l; serum calcium 4·0 mmol/l (16 mg/100 ml). There was a trace of proteinuria. Serum protein electrophoresis showed albumin 57·9%, α_1-globulin 4·6%, α_2-globulin 7·4%, β-globulin 4·6%, γ-globulin 7·9%. An M-component between β- and γ-globulins measured 17·6%. Immunoelectrophoresis with mono- and polyvalent immune sera showed IgA paraproteinaemia with a decrease of IgM and IgG. No Bence Jones proteinuria was found. Result of Sia water dilution test was negative. Bone marrow smears showed extensive infiltration by abnormal plasma cells. Radiographs showed osteolytic lesions in ribs, left humerus and clavicle, skull, and pelvis and a fractured right clavicle. The patient clearly had an IgA myeloma but no evidence of active skin disease was found. She was given melphalan and corticosteroids and radiotherapy for the painful bone deposits. After 10 weeks she was discharged feeling much better. A year later she relapsed and was readmitted.

Comment

Paraproteinaemia is associated with various autoimmune skin diseases (especially pyoderma gangrenosum)[2] [3] and hypersensitivity reactions.[2]

A case of paraproteinaemia associated with leucocytoclastic vasculitis and pyoderma gangrenosum has also been described.[3] In that case the authors suggested that because of the histological findings the pyoderma gangrenosum could be regarded as a type of leucocytoclastic vasculitis. We may therefore reasonably assume in our case that the EED was associated from the beginning with paraproteinaemia. It is further consistent that the paraproteinaemia was of the IgA type. Most cases of pyoderma gangrenosum with paraproteinaemia are of the IgA type. EED associated with frank or possible myeloma was described some years ago,[4 5] the myeloma being diagnosed four to six years after the EED. The evolution of "benign paraproteinaemia" to malignant gammopathy, if it occurs, could take some years. This was the sequence of events in our case since the myeloma was diagnosed nine years after the appearance of the erythema and five years after the discovery of the paraproteinaemia.

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Fatal chlormethiazole poisoning in chronic alcoholics

Chlormethiazole edisylate (Heminevrin) is a sedative, hypnotic, and anticonvulsant drug widely used in the treatment of depression. It is stated to be of low toxicity, but its action is enhanced by alcohol.[1] I describe four fatal cases of self-poisoning in chronic alcoholics, all of whom were being treated for depression with chlormethiazole edisylate in tablet form.

Case reports

Case 1—The patient was a single man aged 45 who was a known chronic alcoholic. He was depressed and had made two previous suicide attempts. He had been implicated in a minor traffic accident and charged with driving while under the influence of drugs. Analysis of a blood sample showed it to contain 51 μmol/l chlormethiazole (2·6 mg/100 ml). No alcohol was detected. Four days later he was found dead in his flat. Postmortem examination showed adherent pinkish-white powder in the upper third of the oesophagus and 10 whole white tablets in the stomach. The lungs were oedematous. No appreciable natural disease was found.

Case 2—The patient, a 60-year-old single man, was a known chronic alcoholic who had had psychiatric treatment for depression. He was found dead in a wood with a bottle nearby that contained chlormethiazole tablets. Postmortem examination showed adherent white powder in the lower third of the oesophagus and 20 whole white tablets with a sickly sweet smell in the stomach. Recent thrombus had occluded the right coronary artery and a large area of fibrosis was present in the interventricular septum.

Case 3—The patient was a man of 47 years. He had been an alcoholic for 20 years with fits of depression and attempts at suicide. He was found dead at home with a nearby bottle of chlormethiazole tablets. Necropsy findings showed 65 whole white tablets and much white granular material with a sickly sweet smell in the stomach. There was no appreciable natural disease.

Case 4—This patient, a known alcoholic, was a single man aged 52 years. Shortly before his death he had become depressed and had been admitted to a psychiatric unit. The day after his discharge he was found dead on a river embankment. White sludge and 18 whole white tablets with a sickly sweet smell were found in the stomach at necropsy. There was adherent white powder in the lower oesophagus, and severe coronary atherosclerosis.

A toxicological analysis was performed in each of the four cases (see table).

Chlormethiazole concentrations in blood and urine (μmol/l), and liver (mg/100 g) from five alcoholic patients who died after self-poisoning with chlormethiazole edisylate tablets

Patient No	Blood		Urine		Liver	
	Chlormethiazole	Alcohol	Chlormethiazole	Alcohol	Chlormethiazole	Alcohol
1	78		127		6·2	
2	117		156		19·0	
3	35	48·6	19	48·8	6·2	NE
4	19	19·1	55	28·9	10·0	NE

NE = not estimated.
Conversion: SI to traditional units—Chlormethiazole 1 μmol/l ≈ 0·051 mg/100 ml; alcohol (ethanol) 1 mmol/l ≈ 4·6 mg/100 ml.

Comment

The plasma concentration of chlormethiazole for a given dose varies with the pharmaceutical preparation. For example—ingestion of two 500-mg tablets of chlormethiazole edisylate produces a maximum concentration of about 19 μmol/l (1·0 mg/100 ml) plasma after 70 minutes.[2] This concentration induces a hypnotic effect.

In a series of nine cases of death from chlormethiazole poisoning, Jakobsson and Möller reported the lowest recorded fatal plasma concentration of the drug—49 μmol/l (2·5 mg/100 ml) (range 49-156 μmol/l (2·5-8·0 mg/100 ml)).[3] Nevertheless, the patient described in case 1 was driving a car, albeit unsuccessfully, with a plasma concentration of 51 μmol/l (2·6 mg/100 ml) chlormethiazole. Clearly there must be individual variation in reaction to the drug or the development of tolerance. Fatal concentrations of the drug when taken with alcohol are very much lower. In cases 3 and 4 death occurred at, or close to, normal therapeutic concentrations. Similar concentrations were found in a series in which the mean plasma concentration of chlormethiazole was 41 μmol/l (2·1 mg/100 ml) (range 10-92 μmol/l (0·5-4·7 mg/100 ml)).[3]

These findings question the statement that the drug is of low toxicity. There is clearly a real danger of accidental death occurring, not only in alcoholics but also in others who ingest alcohol while taking the drug. The hazards of drinking alcohol while receiving treatment with chlormethiazole should be stressed. In the depressed alcoholic it would seem wiser to avoid the drug altogether.

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