The Cheshire Cat syndrome

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One of the pleasures and privileges of working with Sir John McMichael at the Royal Postgraduate Medical School was the encouragement given to speculation, public or private—as with his predecessor, Sir Francis Fraser, with his favourite phrase ‘I'm just thinking aloud....’ While unbridled imagination unsupported by facts met with instant retribution, fair licence was always given to the possible. The ‘forme fruste’ may often be a measure of our imagination rather than of our perspicacity, but the ‘forme sine’, or the ‘Cheshire Cat syndrome’ as I prefer to call it, is simply innate commonsense untrammelled by the rigorous laws of proof. As a tribute to Sir John, I record here three cases of polyarteritis nodosa sine polyarteritis nodosa (I would add that he probably would have shot them down without mercy, but in each of these three cases, there is a small measure of ultimate justification, fulfilling perhaps Carroll’s criteria* rather than Koch’s).

Case 1

B.W.P. (39175), a boy of 6, in December 1965 developed prolonged intermittent fever and 2 months later was admitted to another hospital with abdominal pain, lymphadenopathy and a morbilliform rash, later scaling. Skin oedema and hair fall followed. He was started on prednisone but by May 1956 generalized oedema was present: he had lost weight and had difficulty in walking.

He was admitted to the M.R.C. Rheumatism Unit at Taplow on 6 July 1956 on ACTH gel injections with a tentative diagnosis of dermatomyositis. He was severely ill with fever to 105°F, wasted and dehydrated with vomiting and proteinuria. The limbs showed no contractures but there was a pigmented reticular rash on the legs (Fig. 2). This was thought to be more in favour of a vascular disease such as polyarteritis than of dermatomyositis. There was a polymorph leucocytosis. There was proteinuria, 20 mg/100 ml.

I.V. fluids and hydrocortisone corrected his dehydration and electrolyte depletion but he remained desperately ill and febrile, occasionally reaching a temperature recorded as 106.4°F.

Towards the end of August a urinary infection developed and a blood culture grew coagulase positive *Staph. aureus* for which he was given chloramphenicol followed by other antibiotics and an increase in steroid dosage. Abscesses developed in the right buttock and left forearm.

*’... after watching it a minute or two, she made it out to be a grin, and she said to herself “It’s the Cheshire Cat: now I shall have somebody to talk to.”

‘How are you getting on?’ said the Cat, as soon as there was mouth enough for it to speak with.

‘Alice waited till the eyes appeared, and then nodded. “It’s no use speaking to it,” she thought, “till its ears have come, or at least one of them.” In another minute the whole head appeared, and then Alice put down her flamingo, and began an account of the game...’
haps secondary akinetic mutism. Williams loss of abdominal later convulsions, incontinence in the face developed twitching slightly but towards the end of the month to the right side of face and right leg, drowsiness and amaurosis, later convulsions, incontinence and neck stiffness, loss of abdominal reflexes and right extensor plantar response suggesting cerebral abscess perhaps secondary to vasculitis: this progressed to akinetic mutism.

In September he was seen by Dr Denis Williams who diagnosed a large lesion at the top of the mid-brain affecting particularly the left side and extending into the cerebrum. He died in the same decerebrate and unconscious state on 28 September 1956.

At necropsy (Dr L. E. Glynn) there were widespread areas of necrosis and abscess formation in the white matter of both cerebral hemispheres and in the neighbourhood of the red nucleus (Fig. 3). There was no evidence of polyarteritis nodosa (Dr Blackwood, National Hospital, Queen's Square). The only other lesion of note was in the pancreas which showed a small area of fibrosis and, on re-examination, one vessel with acute fibrinoid arteritis (Fig. 4). No arteritis was found in other organs.

Case 2
A.I., female, 19 when first admitted to M.R.C. Rheumatism Unit at Taplow, gave a 2-month history of pain, weakness and paresthesiae in both legs and later both arms, with loss of weight and dyspnoea, which had necessitated admission to another hospital as suspected poliomyelitis. Eosinophilia was found and a diagnosis of polyarteritis made, although muscle biopsy was negative. She was started on steroid therapy. She had had asthma for 3 years.

Examination showed a raised JVP, a loud pansystolic murmur confirmed on phonocardiography, ankle oedema and respiratory dyspnoea: liver and spleen enlarged 3 fingers’ breadth, absent triceps and Achilles reflexes with loss of sensation in both hands and both feet. There were bilateral pleural effusions and proteinuria. Blood urea 64 mg/100 ml. Eosinophilia 20%.

She improved on steroid, digitalis and diuretics. The flexion contractures were straightened: sensation and power returned although reflexes stayed absent. Symptomless urinary infection (with normal pyelogram) was treated and she was discharged much improved after 7 months with a diagnosis of polyarteritis nodosa despite negative biopsy. Followed in outpatients, she was admitted four times in the next 2 years, first because of increased peripheral neuritis, then because of left loin pain and colic and marked left hydronephrosis due to periureteric fibrosis (relied by operation), again with heart failure and enlargement and finally with a recurrence of left loin pain. During this period she had continued with asthma, cardiac failure, eosinophilia, peripheral neuropathy and urinary infection despite which, with treatment, she led a near normal life and got married. Further biopsy specimens of muscle and periureteric tissue showed no arteritis. She died suddenly in status

**FIG. 2.** Case 1. Left forearm showing livedo reticularis.

**FIG. 3.** Case 1. Cerebrum in cross-section showing softening and abscess formation.
asthmaticus, 2 months after a further ureteroplasty. Necropsy (Dr Gerald Loewi) showed the lungs to be distended with marked alveolar dilatation and rupture. Bronchioles were plugged with mucus and surrounded by eosinophils. The pericardial space was obliterated by old fine adhesions. Valves and myocardium were normal.

The left kidney (109 g) showed hydronephrosis due to periureteric fibrous tissue with pyelonephritis. The right kidney was normal (146 g). Sections showed one healed lesion of polyarteritis in the heart and several in the kidneys, right and left (Fig. 5). None was seen in other organs or in multiple sections from many muscles.

Case 3

H.F., a man of 52 years, was admitted to the M.R.C. Rheumatism Unit at Taplow in September 1965 with a 4-week history starting with acute pain in the left shoulder and right ankle for 3 days, later in the right knee, and continuing with a migratory polyarthritis lasting 3–4 hr in each joint, not responding to salicylates. Four days before admission the right eye became inflamed.

Examination showed episcleritis, polyarthritis affecting wrists, metacarpal and proximal interphalangeal joints, ankles, one knee and tarsal joints, a small intracutaneous nodule on one elbow and a macular rash on the right ankle.

ESR 50 mm/hr; WBC 13,300/mm³; eosinophils 23%; ANF +; LE cells neg.; DAT and Latex neg.; ASO 200; Addis count abnormal with 90 mg/100 ml proteinuria.

Biopsy of the nodule showed an ischaemic lesion but no vasculitis was seen. Blood urea, normal on entry, started to rise and he developed purpura. Treatment with prednisone 60 mg/day reduced to 30 mg effected enough improvement for him to take his own discharge. Seen monthly as an outpatient, he remained clinically well but on 20 January 1966 blood urea was 100 mg/100 ml; ESR 32 mm/hr; BP 145/95; proteinuria 3 g/day.

He was admitted to St Peter's Hospital, Chertsey, under the care of Dr Goadby in August 1966 with haemoptysis and right knee effusion; X-ray showed streaky opacities extending out from the lung hila and pulmonary oedema; BP 150/80 with multiple ventricular extrasystoles. He died 3 weeks later with a 'shock-like' illness.
Necropsy (Dr Ross) showed oedema of legs and purpura. The cerebrum showed oedema, the lungs were oedematous and the heart enlarged (560 g). Kidneys were contracted (85 g each). Histologically no arteritis or healed arteritis was found either by the pathologist or on review at Taplow, but the kidneys showed gross ischaemic changes with the development of granulomatous lesions surrounding the sites of glomeruli, characteristic of the Davson type of polyarteritis (Fig. 6) (Wainwright & Davson, 1950).

Discussion

Dubious but at least ultimate justification is poor present consolation, but I have always felt sorry for those unhappy patients—or rather cases—left in the limbo of the lost, ignored in textbooks, unrecorded in the journals, mouldering in the basement record store, just because they did not have five criteria, just four or perhaps even just three; there are many of these—everyone has them, although we contrive to forget them easily because they have no pigeonhole, but they suffer, they are diseased and sometimes they die. This is a vicious circle; since these unfortunates never achieve the full purple of a recognized nosological entity, medical students, brought up on the classical cases of the teaching hospitals, the textbooks and the Membership examination, never see them and so the circle is perpetuated. To use a different metaphor, the student of geography knows the mountain ranges the river valleys and even the plains, but most people live in places which are really neither mountain, valley or plain but somewhere in between. Diagnostic entities are all very well but every conscientious physician knows that he cannot fit all his patients into these categories without Procrustean measures. The most frequently encountered trouble is lack of data: the patient emigrated to Canada and no follow-up was possible, or was observed before some crucial test was invented, but even in patients with the maximum of follow-up including post-mortem examination, there is occasionally a regrettable lack of evidence conclusive enough for pigeon-holing. These are the patients whose histories fail to get recorded, who dog our memories for a brief period; their only fault was that they failed to achieve the level of textbook diagnosis or of epidemiologic criteria. They therefore failed to influence textbook description. It seems probable that there are more of them than even the most obsessive of us are aware. Is it not possible that there are more formes frustes of a disease than formes pleines? Medical literature is the description of those patients who conform to the mean—give or take a few standard deviations—and leaves out in the cold neglected and undocumented those numerous characters who have not had the fortune to develop all five of the recommended criteria. I sing therefore of the patient with a demi-semi syndrome. Of rheumatism and the man, I sing. These are the underprivileged, the cats known only by their grin. Lewis Carroll was perhaps less than logical not to deploy other Cheshire Cats known only by their grin and never substantiated. This is our everyday dilemma.

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References


Fig. 6. Kidney showing periglomerular lesions. 
a, H & E, ×12.5; b, H & E, ×150.

Fig. 7. Tail piece (sine tail).