



HYPERTENSION ILLUSTRATED

Secondary hypertension and clinical genetics: usual presentation with unusual diagnosis

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A 51-year-old woman with neurofibromatosis type 1 (NF1) was found to have raised blood pressure at a routine follow-up in the Genetic clinic. In view of the recognised association between NF1 and pheochromocytoma, she was referred to the Blood Pressure Unit in November 1997 for further investigations. Physical examination confirmed the presence of multiple neurofibromas (Figure 1), and of diffused pigmented spots ('café au lait') (Figure 2), both mainly present on the trunk, arms and legs. No history of palpitations, chest pain or sweating. Blood pressure at presentation, whilst off pharmacological treatment, was 164/108 mm Hg sitting and 163/106 mm Hg standing, with a pulse rate of 74 and 84 b/min, respectively. Fundoscopy did not reveal haemorrhages or papilloedema. Initial investi-

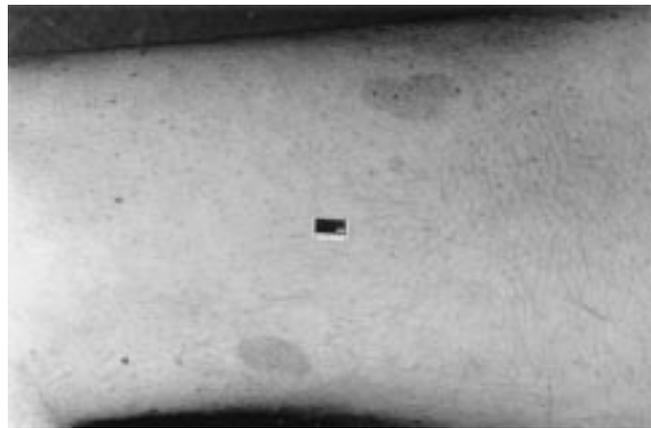


Figure 2 'Café au lait' spots. They are usually the first manifestation of NF1 and may be present at birth. They vary in number and diameter. They usually have smooth contours, but some (particularly the larger ones) have irregular outlines. Their colour intensity varies with background pigmentation.

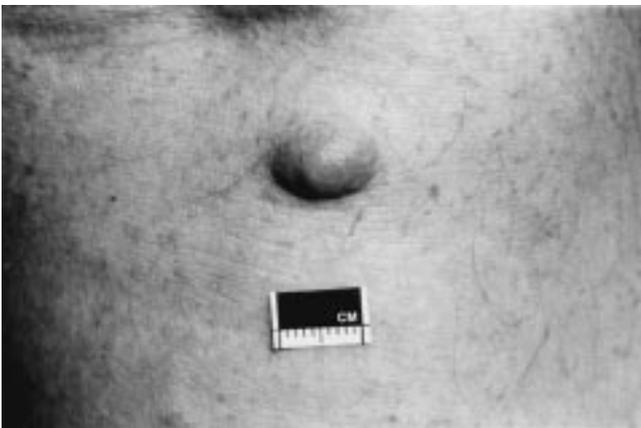


Figure 1 Dermal neurofibroma. They lie within the dermis and epidermis, move passively with the skin and are present in most adults with NF1.

gations showed she had normal electrolytes (serum sodium 139 mmol/l and potassium 4.5 mmol/l) and renal function (serum creatinine 79 μ mol/l), blood glucose 5.3 mmol/l and corrected serum calcium 2.46 mmol/l. However, she had increased urinary excretion (on two consecutive collections) of VMA (188 and 181 μ mol/24h; *nv* \leq 36), noradrenaline (1715 and 1442 nmol/24h; *nv* <500) and adrenaline (1407 and 1223 nmol/24h; *nv* <100). She was started on phenoxybenzamine 10 mg *per nocte* and the blood pressure fell to 140/85 mm Hg. She then underwent an I-123 MIBG scan of the abdomen. Both the 6 and 24-h images (Figure 3), demonstrated two large areas of increased uptake, each in the region of an adrenal gland. Both of these regions had a central photopenic area, consistent with cystic degeneration. Ultrasonography demonstrated bilateral well-defined echogenic large adrenal masses, which had a complex partially cystic and partially

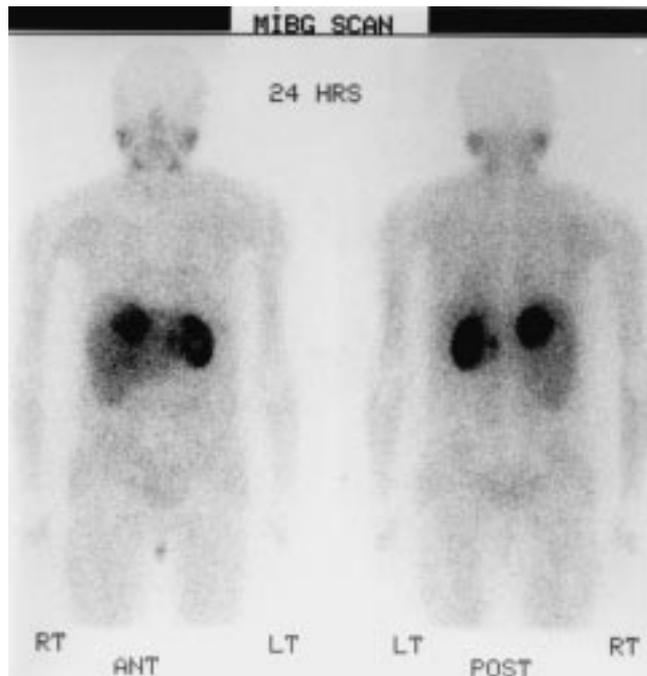


Figure 3 Quite markedly abnormal MIBG scan. There is dramatically increased uptake into both adrenal glands which appear significantly enlarged. There is a large photopenic area in the region of the left adrenal gland and a smaller one in the right implying possible cystic degeneration.

solid internal structure. The left gland measured $7.4 \times 7.4 \times 6.0$ cm and the right $5.2 \times 4.3 \times 5.8$ cm. There was no evidence of invasion into the liver, spleen, kidneys or IVC. CT scan confirmed these findings. The patient underwent bilateral adrenalectomy. Two large pheochromocytomas were removed (84 g on the right and 226 g on the left). Microscopy confirmed the clinical diagnosis. Six weeks after surgery blood pressure was 158/89 mm Hg whilst on replacement therapy with hydrocortisone and fludrocortisone and no antihypertensive medication. Urinary and plasma catecholamines were within the normal range.

Neurofibromatosis 1 (NF1), also known as von Recklinghausen's disease, is one of the commonest autosomal dominant disorders in man with an estimated birth incidence of one in 2500 to 3300.¹ The major features are 'café au lait' spots and peripheral neurofibromas. However, the morbidity and mortality caused by NF1 are largely dependent on the numerous complications that can involve any of the body systems (eg, nervous, skeletal, genitourinary,

endocrine, cardiovascular, respiratory, gastrointestinal, haematopoietic, skin).¹ The most important medical complication to occur in NF1 is hypertension (about 6% of patients with NF1).² It can be essential hypertension or secondary to renal artery stenosis, coarctation of the aorta or pheochromocytoma. Pheochromocytomas occur in about one in 1000 hypertensive patients in the general population (though this may be an underestimate). They are a known cause of hypertension amongst patients with NF1 (1–2%), and NF1 is more common amongst patients with pheochromocytomas (5–25%). However, bilateral pheochromocytomas are extremely rare. The majority of the pheochromocytomas in NF1 develop within the adrenal medulla, about 10% being extra-adrenal.

In our patient, biochemical markers showed that the pheochromocytomas were producing both adrenaline and noradrenaline, which is commonly observed in NF1.³ Furthermore, the MIBG scan—which is particularly sensitive at detecting pheochromocytomas (sensitivity is 90% and false positives are 1–5%)—provided clear-cut diagnostic images and allowed us to localise the masses, to exclude the presence of extra-adrenal uptake and to view degenerative changes within the masses, later confirmed with ultrasound and computerised tomography.

In conclusion, patients with NF1, even with no symptoms, should be screened for pheochromocytoma.

Acknowledgements

We thank Dr AK Saggarr-Malik, Mrs ND Markandu, and the nurses in the Blood Pressure Unit for their help, Mr RS Taylor and his team for performing the bilateral adrenalectomy and Dr V Thomas for the histopathology report. FPC and GAM are members of the St George's Cardiovascular Research Group.

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