

# ACROMEGALY AND CEREBROVASCULAR ACCIDENTS

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## SYNOPSIS

Patients with Acromegaly have been observed to have an increased mortality and morbidity from non-pituitary causes, including cardiovascular, respiratory and cerebrovascular diseases. The reasons for some of these observations are not clear. We describe a young female patient who had acromegaly and recurrent cerebrovascular accidents. Our studies revealed multiple arteriovenous abnormalities in her cerebral circulation. This association has not been reported before, and might be related to some of the causes of the increased mortality found in Acromegaly.

*Keywords:* Acromegaly, Arteriovenous malformations, Cerebrovascular accidents, Chinese, Pituitary tumour.

SING MED J. 1988; 29: 476 – 479

## INTRODUCTION

Acromegaly is an uncommon endocrine disease resulting from excess of growth hormone. Wright et al clearly demonstrated in 1970 that there was an increased mortality and morbidity from non-pituitary causes in this disorder(1). They observed a sex difference; in male patients the increase was in cardiovascular and respiratory disease, while in female patients, the increase was in cerebrovascular disease. Others studies have confirmed these observations (2,3), but satisfactory explanations for these interesting associations are still lacking.

The presence of multiple arteriovenous malformations is also an uncommon disorder. This can certainly cause neurological signs and symptoms directly and may be considered as 'cerebrovascular disease.'

We describe a young Chinese lady who initially presented with a cerebrovascular accident. Our studies demonstrated that she had acromegaly, and in addition, had multiple arteriovenous malformations in her cerebral circulation.

## CASE REPORT

A 27 year old Chinese lady presented with a six day history of weakness in her left arm and hand. She reported having several previous transient episodes of slurring of

speech, each lasting three to five minutes, in the preceding month. She also described having recurrent headaches for the previous 10 years, but there had not been any recent change in the severity nor pattern of these headaches. She had no symptoms of excessive sweating and had not noticed any increase in size of her hands and feet.

On examination, she had features typical of acromegaly. Her height was 1.7m(5ft 8in), which is above the 95th centile for Chinese women in Singapore. Power was diminished in her left arm and hand(MRC Grade 3). Examination of her cardiovascular system showed a normal blood pressure of left arm and hand(MRC Grade 3). Examination of her cardiovascular system showed a normal blood pressure of 120/80 mm Hg, without any evidence of cardiomegaly clinically or on electrocardiography. The rest of her physical examination was also normal. Examination of her fundi was normal and there was no defect in her visual fields.

Her basal growth hormone level was elevated: 14ng/ml (Normal range 2-10 ng/ml). After ingestion of a 75 gm glucose load orally, there was no suppression of her growth hormone: the values were 16, 17.5, 25, 24, 25 ng/ml at 0, 30, 60, 90 and 120 minutes respectively. The corresponding blood glucose levels were 65, 180, 147, 132, 84 mg/dl respectively. There was no deficiency in her other pituitary hormones and her serum prolactin was not elevated.

All other biochemical and endocrine investigations were normal. A skull X-ray suggested an enlarged pituitary fossa, A CT scan of the pituitary fossa showed a small pituitary tumour.

In view of her age and her neurological findings, carotid angiography was carried out. Multiple small fusiform aneurysmal dilatations were present in the branches of both middle cerebral arteries. In addition, a single large arteriovenous malformation was present (see figure).

A diagnosis of acromegaly with multiple arteriovenous malformations was made. In view of the presence of the multiple blood vessel abnormalities, the risk of surgery or radiation therapy was considered to be too high. The patient was

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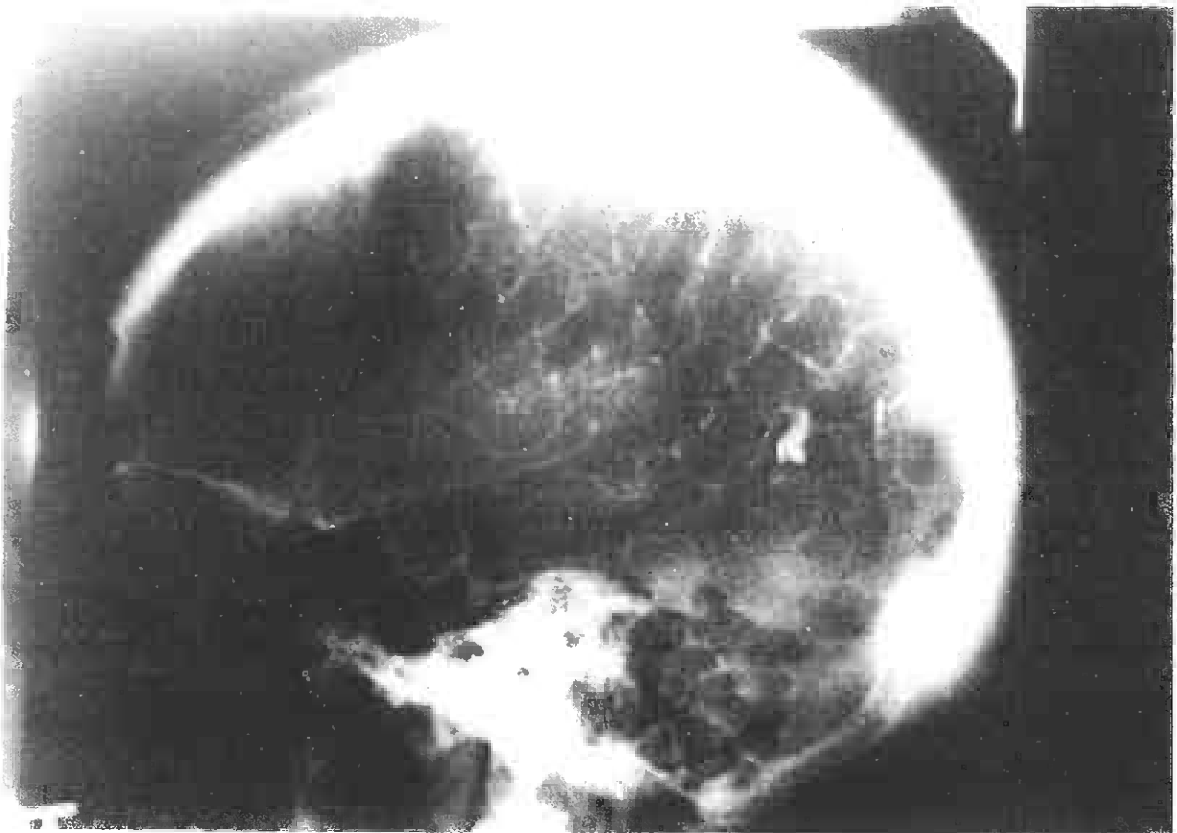
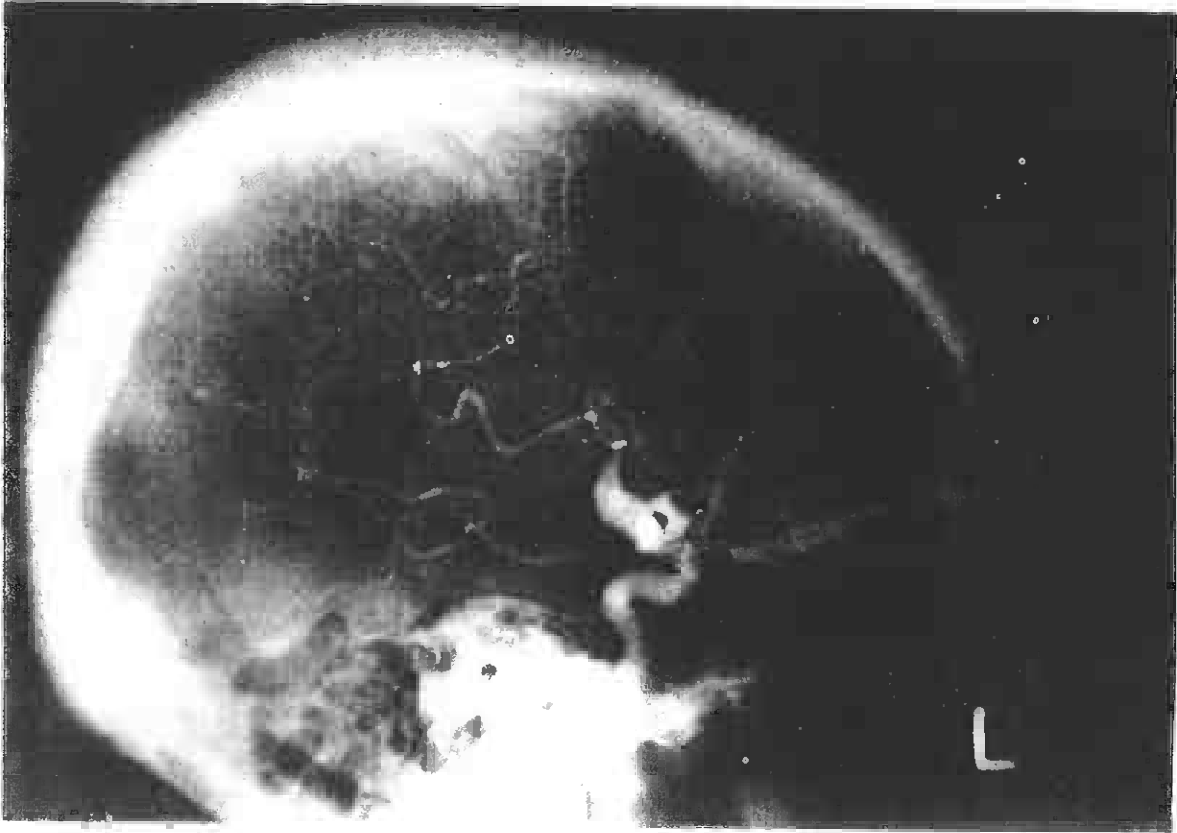
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Figure 1 Carotid angiogram showing multiple small fusiform arteriovenous malformations and a single large arteriovenous dilatation.



treated with bromocriptine 7.5 mg daily in divided doses and her symptoms improved. Growth hormone levels were monitored and decreased to a satisfactory fasting level of 0.4 ng/ml after three months of treatment. There were no significant side effects and the patient was kept on the same maintenance dose.

On follow-up, the patient had four episodes of recurrent mild right hemiparesis in the next three years. There was good recovery of function each time and she was able to continue working as a telephone operator. She then had a dense right hemiplegia which required a hospital stay of more than one month. Recovery was slow and she was unable to work for over a year. She remained well for the next 2 years and then presented with signs of massive cerebral haemorrhage. She did not recover consciousness and died in hospital. A request for a post-mortem examination was refused by her parents.

## DISCUSSION

This patient demonstrated some of the features of excessive growth hormone occurring prior to the complete fusion of the epiphyses of the long bones. Thus she was very tall in addition to having the usual features of acromegaly. She had very few symptoms, and this is not unusual (4,5).

Her initial presentation was with an intracranial vascular bleed resulting in a permanent neurological deficit. This mode of presentation in a patient with acromegaly is an extremely rare one (4,5), especially in our local Singapore experience (4,6-8). Carotid angiography demonstrated multiple cerebrovascular abnormalities. The association of these two rare conditions has not been reported previously.

The problem of management of this patient's acromegaly obviously became more complex as a result of the multiple arteriovenous abnormalities. If these had been absent, any of the conventional forms of definitive treatment would have been suitable: local radiotherapy with implantation of Yttrium rods(9), transphenoidal hypophysectomy(10), or external irradiation(11). The last two forms of treatment have been us-

ed successfully in Singapore with previous acromegalic patients(4,8). However, in this patient, any definitive treatment was contraindicated because of the risk of inducing further intracranial bleeding. Bromocriptine was therefore given in an attempt to suppress the growth hormone levels.

A recent report cast doubts on the efficacy of bromocriptine in acromegaly(12). However, our patient was fortunate and responded very well, in keeping with other reports(13). The long term effects of continuous administration of bromocriptine are not known and thus careful monitoring is still recommended.

The association of two such rare disorders in our patient is an interesting one. The cause for the increase in mortality from cerebrovascular disease in female patients with acromegaly is not known. Recent reports have shown some other interesting associations in acromegaly; there is an increase in skin tags (acrochordons)(14), and of colonic polyps (15). These reports have led to retrospective studies which showed that there might be an increase in neoplasms in acromegaly (16,17). The authors suggested that the presence of persistent elevated levels of growth hormone, somatomedin-C, and other as yet unidentified growth factors in acromegaly (18,19) may cause increases in mitotic activity in a wide variety of different cells such as to predispose to the development of neoplasia(16,17).

It is tempting therefore, in the light of our acromegalic patient, to suggest that excessive growth in vascular endothelium might occur as well. This could cause a weakening of any pre-existing congenital vascular malformations and thus predispose to cerebrovascular disease. There have not been any reports of reviews of cerebral arteriograms in acromegalics. Arteriography is no longer insisted upon by neurosurgeons as a preliminary to pituitary surgery, particularly if a transphenoidal route is used. Thus the association described in our patient will not be able to be studied at present, and any explanations of the increase in cerebrovascular mortality in female acromegalics must remain a speculative one.

## REFERENCES

1. Wright AD, Hill DM, Lowy C, Fraser TR. Mortality in Acromegaly. *Quarterly Journal of Medicine* 1970; 39: 1-16.
2. McGuffin WL, Sherman BM, Roth J, Gorden P, Kahn CR, Roberts WC, Frommer PL. Acromegaly and Cardiovascular disorders, a prospective study. *Annals of Internal Medicine* 1974; 81: 11-18.
3. Alexander L, Appleton D, Hall R, Ross WM, Wilkinson R. Epidemiology of acromegaly in the Newcastle region. *Clinical Endocrinology* 1980; 12: 71-9.
4. Gwee HM, Chua D, Cheah JS, Lim P. Gigantism and Acromegaly in Singapore. *Singapore Medical Journal* 1981; 22: 266-70.
5. Lawrence JH, Tobias CA, Linfoot JA, Born JL, Lyman JT, Chong CY, Manougian E, Wei WC. Successful treatment of Acromegaly: Metabolic and Clinical studies in 145 patients. *Journal of Clinical Endocrinology* 1970; 31: 180-7.
6. Cheah JS. A Singapore giant (gigantism with acromegaly); untreated with long survival. *Medical Journal of Australia* 1970; 2: 1240-52.
7. Teo SK, Cheah JS. Hypersecretion of Growth hormone in an acromegalic of 25 years duration. *Medical Journal of Malaysia* 1973; 27: 220-2.
8. Cheah JS. Gigantism and Acromegaly. *Annals of the Academy of Medicine, Singapore* 1979; 8: 212-6.

9. Greenwood FC, Stewart HJ, Forrest APM, Wood RG. Plasma Growth Hormone in untreated Acromegaly and after radioachie implants into the pituitary. *Lancet* 1965; 2: 555-8.
10. Schuster LD, Bantle JP, Oppenheimer JH, Seljeskog EL. Acromegaly: reassessment of the long-term therapeutic effectiveness of transsphenoidal pituitary surgery. *Annals of Internal Medicine* 1981; 95: 172-4.
11. Eastman RC, Gorden P, Roth J. Conventional supervoltage irradiation is an effective treatment for Acromegaly. *Journal of Clinical Endocrinology and Metabolism* 1979; 48: 931-40.
12. Lindholm J, Rushede J, Vestergaard S, Hummer L, Faber O, Hagen C. No Effect of Bromocriptine in Acromegaly; a controlled trial. *New England Journal of Medicine* 1981; 304: 1450-4.
13. Wass JAH, Williams J, Charlesworth M, Kingsley DPE, Halliday AM, Donaich I, Rees LH, McDonald WI, Besser GM. Bromocriptine in the management of large pituitary tumours. *British Medical Journal* 1982; 284: 1908-10.
14. Leavitt J, Klein I, Kendricks F, Gavaler J, VanThiel DH. Skin tags: a cutaneous marker for colonic polyps. *Annals of Internal Medicine* 1983; 98: 928-30.
15. Klein I, Parveen G, Gavaler JS, Vanthiel DH. Colonic Polyps in patients with acromegaly. *Annals of Internal Medicine* 1982; 97: 27-30.
16. Ituarte EM, Petrini J, Hershman JM. Acromegaly and colonic cancer. *Annals of Internal Medicine* 1984; 101: 627-8.
17. Klein I. Acromegaly and Cancer. *Annals of Internal Medicine* 1984; 101: 706-7.
18. Clemmons DR, Van Wyk JJ, Ridgeway EC, Kliman B, Kjellberg RN, Underwood LE. Evaluation of acromegaly by radioimmunoassay of somatomedin C. *New England Journal of Medicine* 1979; 301: 1138-42.
19. Ashcraft MW, Hartzband PI, Van Herle AJ, Bersch N, Golde DW. A unique Growth Factor in Patients with Acromegaloidism. *Journal of Clinical Endocrinology and Metabolism* 1983; 57: 272-6.