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Respiratory problems in acromegaly

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Abstract

Death from respiratory causes in acromegaly is three times more common than in the general population and is most often the result of upper airways obstruction, although less commonly pulmonary dysfunction and disturbance of the central nervous system may occur. These factors may be found alone or in combination.

Despite several reports of laryngeal involvement, upper airway obstruction in acromegaly is usually regarded as being due to macroglossia and pharyngeal soft tissue hypertrophy. We present four cases of acromegaly in which tracheostomy was required for laryngeal obstruction, with a review of the literature concerning the nature of respiratory problems in acromegaly.

Introduction

Acromegaly is a disease characterized by generalized visceral and skeletal enlargement. Death from respiratory cause is three times more likely in an acromegalic than in a normal subject (Wright *et al.*, 1970). Respiratory problems in acromegalics may be due to involvement of the upper or lower airway or the CNS.

Extra-thoracic airway obstruction in acromegalics has been demonstrated by pulmonary function testing (Evans *et al.*, 1977; Rees *et al.*, 1982) by radiological assessment (Hassan *et al.*, 1976) and by pulmonary function testing together with radiological assessment (Moorewood *et al.*, 1986). Evans *et al.* (1977) give a figure of 30 per cent (six out of 20 patients) for the incidence of upper airways narrowing in acromegalics and go on to suggest that the severity of the obstruction is related to the length of the history of acromegaly. Moorewood *et al.* (1986) found extrathoracic airway narrowing in 23 per cent (six out of 26) of their patients and conclude that all acromegalics should undergo X-ray tomography of the larynx and respiratory function testing prior to any general anaesthetic. The upper airways obstruction may be due to thickening and hypertrophy of the soft tissues of the tongue, pharynx and larynx (Moorewood *et al.*, 1986); in addition there may be vocal cord palsy and tracheal compression from associated thyroid enlargement. These factors may occur alone or in combination and may cause non-acute obstruction with stertorous breathing, snoring, sleep disturbance and daytime somnolence or the full blown sleep apnoea syndrome (SAS). Acute upper airways embarrassment may supervene on this situation or appear de-novo in a previously asymptomatic patient.

Case reports in the literature of laryngeal involvement in acromegaly date back to the end of the nineteenth century (Table I). Abnormalities described include hypertrophy of the laryngeal mucosa and vocal cord fixation. The mucosal hypertrophy may involve any part of the larynx (Chappell, 1896; Bhatia *et al.*, 1966; Burn, 1972; Kitahata, 1971; Ovassapian *et al.*, 1981) and may resolve after treatment of the acromegaly (Cassar *et al.*, 1979).

Restriction of vocal cord movement may be unilateral or bilateral and either partial or total. Grotting and Pemberton (1950), in their review of 453 acromegalic patients, described seven patients with vocal cord fixation as well as mucosal hypertrophy (although one of these was post-thyroidectomy). Jackson (1918), Siegler (1952), Bhatia *et al.* (1966) and Rees *et al.* (1982) have all described limitation in vocal cord movement together with mucosal hypertrophy in acromegalics. Dujovny *et al.* (1976) reported the case of a patient who had required tracheostomy for bilateral vocal cord fixation who was decannulated three months after treatment of his acromegaly, having regained the mobility of his vocal cords.

Vocal cord fixation has been attributed to a number of factors:

1. Cartilaginous overgrowth with stretching of the recurrent laryngeal nerve (Grotting and Pemberton, 1950).
2. Arthritis of the crico-arytenoid joint. (Grotting and Pemberton, 1950).
3. Mucosal hypertrophy within the larynx interferring with arytenoid movement (Grotting and Pemberton, 1950).
4. Goitre with recurrent laryngeal nerve compression and dysfunction (Bhatia *et al.*, 1966). Of the 12 patients with decreased cord mobility found in the literature, three had a goitre and one was post-thyroidectomy. Trauma to the recurrent laryngeal nerves cannot be excluded in those patients who have had previous thyroid surgery.
5. Axonal demyelination with perineural and subepineural proliferation is also described in acromegaly (Frohman, 1985) and may affect the recurrent nerve.
6. Myopathies have been described in acromegaly sufferers (Pickett *et al.*, 1975) and may affect the laryngeal muscles.

As detailed in Table I, 12 of the patients with acromegalic involvement in the larynx required tracheostomy, either electively or as an urgent procedure. In addition, there is one case report of a patient requiring elective tracheostomy for gross pharyngeal hypertrophy despite a normal larynx (Southwick and Katz, 1979). Tracheostomy may also be required in those acromegalics who develop SAS of the obstructive or mixed type.

Sleep apnoea syndrome (SAS) is defined as the presence of at least 30 apnoeic episodes of ten or more seconds duration occurring in a 7 hr nocturnal sleep period (Guilleminault and Dement, 1978). This may be of central, peripheral obstructive or mixed obstructive aetiology (Gastaut *et al.*, 1966).

SAS of the obstructive type has been documented in acromegalics in several case reports. The mechanism of this obstruction is unclear; Mezon *et al.* (1980) attributed it to the enlarged tongue bulging back into the pharynx to obstruct the airway, whereas Cadieux *et al.* (1980) described invagination of the posterior and lateral walls of the pharynx with airway obstruction before any posterior movement of the tongue occurs. Both authors used fibre-optic nasendoscopy to assess

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TABLE I

A summary of the laryngeal manifestations of acromegaly in the literature to date.

Author	Age/sex	Presentation	Laryngeal hypertrophy	Vocal cord fixation	Goitre	Tracheostomy	Outcome
Chappell 1896	M—	Stridor	Yes	NK	NK	No	Sudden death
Jackson 1918	M43	Dyspnoea	Yes	Yes	NK	Yes	Sudden death
Grotting and Pemberton 1950	F38	Dyspnoea/ hoarseness	Yes	Yes	Yes	Yes	Permanent tracheostomy
	M40	Stridor	Yes	Yes	No	Yes	Permanent tracheostomy
	M31	Dyspnoea	Yes	Yes	NK	No	Discharged
(7 cases)	M56	Somnolence/ dyspnoea	Yes	Yes	Yes+	Yes	Permanent tracheostomy
	M63	Somnolence/ hoarseness	NK	Yes*	No	No	Discharged
	M51	Dyspnoea	Yes	Yes*	No	No	Discharged
	F36	Dyspnoea	No	Yes*	Yes	No	Discharged
Siegler 1952	M35	Dyspnoea	Yes	Yes*	No	Yes	Permanent tracheostomy
Bhatia 1966	M55	Stridor	Yes	Yes*	Yes	No++	Continued stridor
	M35	Hoarseness	Yes	NK	No	No	No Change
(3 Cases)	F22	Stridor/ hoarseness	Yes	No	NK	No	NK
Kitahata 1971	F50	Hoarseness	Yes	NK	NK	Yes	Decannulated after 4 days
	F62	Both patients asymptomatic;	Yes	NK	NK	Yes	Decannulated after 4 days
	F38	Changes noted at operation	Yes	NK	NK	No	Discharged
Burn 1972	M52	Hoarseness	Yes	NK	NK	Yes	Decannulated after 4 days
Dujovny 1976	M54	Dyspnoea/ stridor	Yes	Yes	No	Yes	Decannulated at 3 months
Romanczuk 1977	M44	Sleep apnoea syndrome	Yes	Yes	NK		Decannulated after arytenoidectomy
Cassar 1979	M49	Stridor/ hoarseness	Yes	NK	NK	Yes	Decannulated after 7 years
(2 cases)	M60	Stridor	Yes	NK	NK	Yes	Decannulated at 6 months
Ovassappian 1981	M54	Changes noted at operation	Yes	NK	NK	No	Intubated awake using fibrescope
Goldhill 1982	M67	Stridor	No	NK	NK	No	Discharged
Rees 1982	M54	Somnolence/ Dyspnoea	Yes	Yes	NK	Yes	Pituitary irradiation

NK = Not known.
* Denotes partial or assymmetrical vocal cord fixation, all others being bilateral and complete.
+ Past history of surgery for goitre.
++ Tracheostomy refused by patient.

their patients during sleep. Romanczuk *et al.* (1977) described an acromegalic with obstructive SAS due to vocal cord fixation as well as pharyngeal and laryngeal mucosal hypertrophy, whose symptoms remitted after arytenoidectomy and vocal cord lateralization. Perks *et al.* (1980) found five out of 11 acromegalic patients studied had complaints of daytime somnolence and/or excessive snoring. Of these five, three had true SAS; one each of the obstructive, mixed and pure central type. Hart *et al.* (1985) found SAS in four of 21 acromegalic patients studied, three of which were obstructive and one of mixed type. They concluded that SAS is associated with active acromegaly and tends to remit after treatment; any persistance of SAS after treatment being ascribed to other factors such as obesity.

The presence of central factors in SAS associated with acromegaly have not been satisfactorily explained. Hart *et al.* (1985) postulated that elevated growth hormone levels may have a depressive effect on respiratory drive. Other possibilities include cerebral irradiation and the mass effect of the pituitary tumour (Romanczuk *et al.*, 1977). Daytime somnolence and snoring were reported in a retrospective study as occurring in seven of a series of 372 acromegalics (Barnes *et al.*, 1979). Symptoms remitted spontaneously in three of these patients after treatment with pituitary implantation of Y^{90} and Au^{198} isotopes. Up to 25 per cent of acromegalics have a goitre which raises the possibility of stretching of the recurrent laryngeal nerves (Bhatia, 1966) and tracheal compression (Mukhtar *et al.*, 1971). However in a series of 20 acromegalics assessed radiographically (Moorewood *et al.*, 1986), no significant decrease in tracheal diameter was found as compared to normal subjects. Only one of these patients had a goitre and only the tranverse diameter was assessed. In addition, surgery for goitre places the recurrent laryngeal nerve at risk.

Acromegalics have been shown to have increased lung volumes as compared to normal subjects (Brody *et al.*, 1970; Toppell *et al.*, 1973; Evans *et al.*, 1977; Harrison *et al.*, 1978), which has been attributed to increased alveolar volume (Brody *et al.*, 1970). If this was the case then one might expect a decreased surface: volume ratio as is found in emphysema, which might contribute to the number of respiratory deaths in this condition. However, the significance of these findings has been called into question as the degree of kyphosis was not assessed in these patients. The presence of significant thoracic kyphosis will produce falsely low expected lung volumes as the patient's

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total body length will be underestimated (Evans *et al.*, 1977). They concluded that upper airways obstruction is more likely to account for respiratory death in acromegalics than pulmonary abnormalities.

Case reports

Case 1

A 63-year-old acromegalic was treated with external beam radiotherapy to the pituitary fossa in 1978. He remained well for ten years when he developed a sensation of a lump in the throat followed by increasing shortness of breath with inspiratory stridor which rapidly progressed to complete obstruction. Attempts at oro-tracheal intubation were unsuccessful and an emergency tracheostomy was carried out. Direct laryngoscopy revealed a large acromegalic tongue, hypertrophy of the pharyngeal soft tissues and gross oedema of the supraglottic and glottic larynx. There was no foreign body or goitre and the tracheal lumen was normal. Ten days later fibre-optic laryngoscopy showed that the oedema of the larynx had settled to leave mild hypertrophy of the laryngeal soft tissues. There was a satisfactory airway and both vocal cords were mobile. The patient was successfully decannulated and discharged from hospital. He remained well without further respiratory problems until his death in 1988. No post-mortem was held.

Case 2

A 68-year-old man developed stridor following prostatectomy in 1981. Indirect laryngoscopy revealed bilateral vocal cord paralysis with a narrow glottic chink. The patient was however able to cope without tracheostomy and was discharged after investigations had confirmed active acromegaly. Prior to definitive treatment, he developed increasing shortness of breath and underwent tracheostomy in November 1981. One month later his pituitary tumour was removed surgically. He remains under review and while he has recovered some mobility of the left vocal cord, the right cord remains immobile. The rest of the larynx is normal in appearance.

Case 3

A 66-year-old female was diagnosed as acromegalic in 1980 and was treated with external beam radiotherapy and bromocriptine. In 1981, she required a thyroidectomy for a large multi-nodular goitre, immediately after which the patient became stridulous and required reintubation. Direct laryngoscopy showed gross hypertrophy of the soft tissues of the oropharynx, together with thickening and decreased mobility of both vocal cords. A tracheostomy was performed. Six days later the pharyngeal and laryngeal soft tissue swelling had subsided and both vocal cords were noted to be mobile; the patient was successfully decannulated and discharged. In 1984, the patient was readmitted with a recurrence of her airway problems and direct laryngoscopy revealed grossly swollen vocal cords with a narrow glottic chink, the rest of the larynx and pharynx being normal. A second tracheostomy was therefore performed which remained *in situ* until her death in 1986. No post mortem was held.

Case 4

A 61-year-old man had been diagnosed as being acromegalic in 1958. He underwent direct laryngoscopy and bronchoscopy in 1978 as part of the investigation of a large retro-sternal goitre. The larynx was noted to show 'gross hypertrophy and oedema'; the goitre was not compressing the trachea. The anaesthetist was able to intubate the patient, and an elective tracheostomy was performed at the time of subtotal thyroidectomy. The oedema of the larynx settled over the next few weeks to leave the typical hypertrophic changes of the acromegalic larynx. However, there was a good airway and decannulation was successful.

Discussion

Four patients are presented who all required tracheostomy because of laryngeal involvement attributed to their acromegaly. There have been only 12 other such cases described in the literature. All four patients showed the typical mucosal thickening of the acromegalic larynx. In case one there was normal mobility of the vocal cords, cases 2 and 3 had bilateral vocal cord fixation in addition to the mucosal changes. The fixed cords were both seen to regain mobility to a greater or lesser extent with the passage of time. In case 2 this was after definitive tretment of the acromegaly, in keeping with the finding of occasional reversal of repiratory problems after treatment as reported by Dujovny *et al.* (1976), Cassar *et al.* (1979) Hart *et al.* (1985) and Barnes *et al.* (1979).

One patient had a multi-nodular goitre (case 3) and there is the possibility of a neuropraxic injury to the recurrent laryngeal nerves at the time of surgery causing her immediate post-operative respiratory obstruction. However, in addition to this, there were acromegalic soft tissue changes present, which in the presence of mobile vocal cords (as noted six days post-operatively) constituted the reason for her second tracheostomy. In case 2, there was no goitre and no previous thyroid surgery, so the bilateral cord palsy was attributed to one of the other factors mentioned above. In the patient with a restrosternal goitre (case 4), there is no record of cord mobility although the typical laryngeal appearances of acromegaly were noted.

These four patients were known to have their disease for 10, 5, one and 30 years respectively (although active acromegaly may be present for a number of years prior to diagnosis). In such a small group it is not possible to make any comments about the suggestion of Evans *et al.* that the severity of the obstruction is related to the length of history of the disease.

Conclusions

Acromegalics are three times more likely to die of respiratory disease than normal subjects and this is more likely to be due to extra thoracic airway obstruction than to pulmonary dysfunction. Extra thoracic obstruction is present in up to 30 per cent of acromegalics may be at the pharyngeal, laryngeal or tracheal level or any combination of these.

We seek to reemphasize the need for pre-operative assessment of all acromegalics, preferably by indirect or fibreoptic larynscopy, together with pulmonary function testing, and to remind the clinician that upper airway obstruction in these patients is not due solely to macroglossia and hypertrophy of the pharyngeal wall mucosa. We would also suggest that futher work be undertaken to assess the frequency, site and severity of upper respiratory obstruction in acromegaly and that a long term study be undertaken to assess the effect of treatment on these problems.

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