Uterine leiomyomata – a feature of acromegaly

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In order to assess the prevalence of leiomyomata in patients diagnosed with acromegaly, files of all women so diagnosed were obtained (n = 25). Eight of these patients had undergone hysterectomy (8/8) or who underwent gynaecological examination (5/8). In conclusion, the very high prevalence of leiomyomata in patients diagnosed with acromegaly warrants the inclusion of growth hormone excess as a cause of leiomyomata. Leiomyomata are a feature of the organomegalic syndrome associated with acromegaly.

Key words: acromegaly/growth hormone/leiomyoma

Introduction

Organomegaly is a prominent feature of acromegaly (Melmed, 1990; Barkan, 1989). The significance of organomegaly for the diagnosis of acromegaly is well known, as is its role in the increased morbidity and mortality from the disease. Organs characteristically described as affected by growth hormone (GH) excess are heart, lungs, liver, brain, colon, kidneys, tongue and thyroid. Increased growth of these organs is due to complex interactions between systemic and local excess of GH and GH-dependent factors, principally insulin-like growth factor 1 (IGF-1) and their receptors and binding proteins. Recent reports have described the presence of GH and IGF-1 receptors in the myometrium and increased IGF-1 in fibroid tissue (Tommala et al., 1989; Rein et al., 1990; Murphy and Gharay, 1990; Chandrasekhar et al., 1992; Guidice et al., 1993; Vollenhoven et al., 1993; Sharara and Neiman, 1995).

It is thus reasonable to predict that female patients with acromegaly will have increased prevalence of uterine leiomyomata and increased endometrial thickness. Surprisingly, we have found no recent data on the prevalence of uterine abnormalities in this group. No major endocrine and gynaecological textbooks have addressed this issue or mentioned leiomyomata as a part of the organomegalic syndrome of acromegaly. We therefore reviewed the gynaecological history of patients with acromegaly and examined available patients with transvaginal ultrasound (TVS). The purpose was to assess the prevalence of uterine abnormalities in patients with longstanding growth hormone excess.

Materials and methods

Files of all women diagnosed as suffering from acromegaly between the years 1967–1992 were obtained. The indication for hysterectomy, if performed, was verified. The remaining patients were called for assessment of the uterus by gynaecological examination and transvaginal ultrasound (TVS).

Ultrasonographic examination was performed with an Aloca SSD 680® (Aloca Co., Tokyo, Japan) with a 5 MHz vaginal transducer. Acromegaly was diagnosed by clinical symptoms and signs and confirmed by the finding of basal GH concentrations above 10 µg/l, which were not suppressible below 2 µg/l after administration of 100 g oral glucose load.

Results

A total of 25 female patients were diagnosed as acromegalic during the 25 year period. Eight patients had undergone hysterectomy due to excessive bleeding secondary to leiomyomata of the uterus. In five patients, a distinct myomatous uterus was noted on TVS and gynaecological examination. No abnormalities were noted in the uterus of three patients. Nine patients were not available for TVS for the following reasons: one death due to breast cancer; one debilitated due to Tay Sachs disease; one lost for follow-up; six declined gynaecological examination. Clinical data are presented in Table I.

Discussion

The exact prevalence of uterine leiomyomata is unknown, but is estimated to be 20–30% of Caucasian women in their reproductive years (Weingold, 1979). In the women diagnosed with acromegaly in our medical centre the prevalence of leiomyomata was 81% (13/16). Oestradiol is an important factor in the growth of uterine leiomyomata and IGF-1 is thought to be a mediator of oestradiol action (Guidice et al., 1993).

Extensive evidence in animal models show that GH can synergize with oestradiol in increasing uterine weight and RNA synthesis (Miura and Koide, 1970; Sharara and Neiman, 1995). The results of several human studies, presented recently, are consistent with the possible causative role of GH in myomatous changes of the uterus. Correlation between IGF-1 secretion and the proliferative state of fibroids was reported by Rein et al. (1990), though not by Vollenhoven et al. (1993).
Increase in IGF-1 receptor concentration in leiomyomata has been reported in several studies (Tommala et al., 1989; Chandrasekhar et al., 1992; Guidice et al., 1993). Recently, Sharara and Neiman (1995) reported the presence of GH receptors in leiomyomata and surrounding tissue, suggesting that GH may have a direct effect on the myometrium in promoting or maintaining tumour growth. These changes in general are influenced by the presence of oestrogen (Murphy and Gharay, 1990). In a recent review, Stewart and Nowak (1996) described the potential of growth factors and their receptors to mediate leiomyoma related complications. This, and evidence from neoplasia of other organs (Cheung and Boyagus, 1997; Colao et al., 1997) suggest that growth factors promote leiomyoma growth rather than initiating growth as the latter is primarily affected by genetic and environmental factors.

Increased prevalence of leiomyomata in our patients diagnosed as acromegalic, together with the data reported on the potential role of GH and its related growth factors on the uterus warrant, in our opinion, the inclusion of GH excess as a cause of leiomyomata. In addition we suggest that leiomyomata is an additional feature of the organomegaly associated with acromegaly. Further comparative data from other clinics is required, in addition to serial follow-up of patients with leiomyoma and acromegaly during and following therapy for acromegaly.

References


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