NEWS IN ACROMEGALY

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Abstract

Recent updates on the epidemiology, diagnosis, complications and therapy in acromegaly have been published in the 1st 2017 issue of Pituitary journal. A review of 12 epidemiological studies published since 2004 shows that the prevalence of acromegaly ranges 2.8 - 13.7 cases per 100,000 people and the annual incidence rates range 0.2 - 1.1 cases/100,000 people. The median age at diagnosis ranges between 40.5 and 47 years. At the time of diagnosis, over 2/3 of the patients have macroadenomas.

Acromegalic osteopathy is characterized by increase in bone turnover, alterations in bone microarchitecture and high risk of vertebral fractures, which occur in about 1/3 of acromegaly patients. Fractures may occur even in the presence of normal bone mineral density (BMD), in close relationship with male gender, hypogonadism, and active acromegaly. Following treatment for acromegaly in 48 patients, the mean trabecular bone score decreased by 3.0 (± 7.0) %, whereas BMD at the lumbar spine increased by 3.2 (± 4.9) % (both $P < 0.01$). Alterations in trabecular bone architecture may explain the persistent fracture risk despite the increase in BMD after disease control.

Stereotactic radiotherapy in acromegaly after surgery and/or during medical therapy provide tumor control in 93–100% of patients at 5–10 years and endocrinological remission in 40–60% of patients at 5 years, with a hypopituitarism rate of 10–50% at 5 years. Hypofractionated radiosurgery is an optimal option for tumors located near the optic structures, due to its lower toxicity for the optic nerves compared to single-dose radiosurgery. A dose-response model for visual pathway tolerance to SRS has been recently published.

Key words: acromegaly, epidemiology, fracture risk, stereotactic radiotherapy, radiosurgery.

INTRODUCTION

Recent updates on the epidemiology, diagnosis, complications and therapy in acromegaly have been published in the 1st 2017 issue of Pituitary journal.

Epidemiology

A review of 12 studies published since 2004, most including European populations, shows that the total prevalence of acromegaly ranges between 2.8 and 13.7 cases per 100,000 people and the annual incidence rates range between 0.2 and 1.1 cases/100,000 people (1). Compared with the previously published prevalence between 3.8 and 6.9/100,000 and incidence rates between 0.28 and 0.4/100,000 in studies between 1980 and 2001, the higher rates of the contemporary studies may be attributed to the source of data, advances in the diagnostic tools, earlier diagnosis or they may reflect a true increase in the prevalence (1).

The median age at diagnosis ranges between 40.5 and 47 years, with a median diagnostic delay of 4.5–5 years. At the time of diagnosis, over 2/3 of the patients have macroadenomas, thus posing challenges for the neurosurgical interventions (1).

Acromegalic osteopathy, a usually under-evaluated complication of acromegaly in clinical practice, is characterized by increase in bone turnover, deterioration in bone microarchitecture and high risk of vertebral fractures (2). Vertebral fractures, as diagnosed by a radiological and morphometric approach, occur in about 1/3 of acromegaly patients (2). Fractures may occur even in the presence of normal bone mineral density (2). In a meta-analysis including 1935 patients, the high frequency of vertebral fractures (odds ratio, 8.26; 95% CI, 2.91–23.39; $P < .0001$) was in close relationship with male gender, hypogonadism, and active acromegaly (3). A recent study in Norway assessed the longitudinal change in trabecular bone score (TBS, which is related to bone microarchitecture) and bone mineral density (BMD) following treatment for acromegaly in 48 patients (4). In treated patients, the mean TBS decreased by 3.0 (± 7.0) %, whereas the BMD at the lumbar spine (LS) increased by 3.2 (± 4.9) % (both $P < 0.01$). The changes in BMD LS and TBS were not correlated and were more pronounced in men. Alterations in trabecular bone architecture may

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explain the persistent fracture risk despite the increase in BMD after disease control (4).

Radiotherapy (RT) in acromegaly remains an effective treatment option for patients with residual tumor mass following surgery, if medical therapy is unavailable, unsuccessful, or not tolerated, as recommended by the 2014 Endocrine Society guidelines (5). Stereotactic RT methods have been developed with the aim to provide more precise targeting of the tumor with better control of the radiation dose received by the adjacent brain structures. A recent review of 35 studies using stereotactic radiosurgery (SRS) in 1868 acromegalic patients shows a weighted mean biochemical control rate of the disease of 44.3% at a median follow-up of 59 months (6). The tumor control rate (i.e. stable or decreased tumor size) was 93–100% at 5–10 years (6). Another review of 10 studies (including 700 patients) where a Kaplan Meyer estimate of disease control was available and the criteria for normalization were GH < 1 ng/mL and normal age-corrected IGF-1, shows a biochemical control of 52% at 5 years, while median time to normalization ranged from 12 to 144 months (median weighted 41.5 months) (7). Comparable efficacy was reported with gamma knife, cyberknife, modified linear accelerator systems and proton therapy (most of the studies using single-session of radiotherapy), similar with the efficacy of fractionated stereotactic radiotherapy (FSRT), in which the total radiation dose is divided into over 20 daily fractions (6;7). The rate of new hypopituitarism after stereotactic radiotherapy varies from 10% to 50% at 5 years and increases with the duration of follow-up. The risk for other radiation-induced complications is usually low (0–4% for new visual deficits, 0–5% for cranial nerves damage or brain radionecrosis and 0–1% for secondary brain tumors). The risk for radionecrosis and second brain tumors may be slightly lower after SRS and FSRT than after conventional radiotherapy (CRT); the risk of stroke also seems lower after SRS than after FSRT and CRT, but longer follow-up studies are needed in order to evaluate the potential brain-sparing effects of the stereotactic techniques compared to CRT (6). A meta-analysis comparing the outcomes of SRS and fractionated RT (including FSRT and CRT) in acromegaly analyzed 30 eligible studies including 2464 patients, with a FU between 12–240 months (5). SRS was associated with a nonsignificant trend of higher IGF-I-based remission rate (52 vs. 37%, $P = 0.14$) or GH-based remission (49 vs. 36%) at the latest FU period. SRS had a lower incidence of hypopituitarism than RT with borderline statistical significance (32% vs. 51%, $p = .05$), the difference being largely due to hypogonadism. Current data suggest that SRS may be potentially more effective

than conventional RT regarding biochemical remission and may have lower rate of induced hypopituitarism, but long term FU is limited and the large heterogeneity of the studies makes the comparison difficult (6, 8).

Hypofractionated SRS (in 2–5 fractions) has been used with good results and few visual side-effects in patients with perioptic tumors (within 2–3 mm from the optic nerves or chiasm) for which single session SRS is not suitable, due to the high risk of optic neuropathy (9). A dose-response model for visual pathway tolerance to SRS has been recently published (10). Based on a retrospective evaluation of 262 patients with perioptic tumors, the model suggests a less than 1% incidence of radiation induced-optic neuropathy, when the maximum point dose (i.e. the radiation dose on a small zone of 1–2 mm) of the optic apparatus pathway is 12 Gy delivered in 1 fraction, 19.5 Gy in 3 fractions and 25 Gy in 5 fractions (10).

Conflict of interest

The author declares that she has no conflict of interest concerning this article.

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