Acromegaly and Neoplasia

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Acromegaly was first described by Marie in 1886 /1/, although earlier reports exist. Minkowski in 1887 /2/ suggested a pituitary source of the disorder, which was later confirmed by Cushing in 1909 /3/, who postulated excessive secretion of a growth-promoting hormone by the pituitary gland.

Acromegaly is a well established syndrome caused by excessive secretion of GH, in more than 99% of cases due to a pituitary adenoma. The acromegalic features result from overproduction of GH, as well as a related increase of GH-dependent tissue growth factors such as insulin-like growth factor-I (IGF-1).

Clinical manifestations of acromegaly are due to local effects of the pituitary mass and the systemic effects of increased growth hormone secretion. Symptoms consist of the typical coarsening of facial features, soft-tissue swelling, nerve compression, visceral enlargement, cardiac hypertrophy and metabolic changes such as diabetes mellitus and hyperlipidemia /4/.

In 1980, Alexander *et al.* /5/ published an epidemiological study of acromegaly based on a 2-year survey in the Newcastle region in England. An incidence of 4.2 per million inhabitants was found, identical to the incidence we observed in Gothenburg, Sweden /6/. Our study comprised 166 patients seen over a 30 year period (1955-84) at our Endocrine Unit, which is the referral centre for the western region of Sweden. The prevalence in the Newcastle study was 38 and in Gothenburg 69 per million inhabitants. This difference could be explained by the longer period of collection of the cases or by better prognosis in our series.

INCREASED MORTALITY IN ACROMEGALY

For many years physicians have been interested in the long-term prognosis of patients with acromegaly, and decreased life-expectancy was early observed. In the patient series of Evans *et al.* /7/ and Wright *et al.* /8/ 50% and 26% of the patients, respectively, had died before the age of 50, and 89% and 64% had died before the age of 60. In our recent study from Gothenburg, the corresponding figures were 16% and 29%, respectively.

The causes of death in these patients have been extensively studied. In the 1920s, Cushing and Davidoff /9/ alluded to diabetic coma as an important cause of death in patients with acromegaly. Later series found cardiovascular disease to be the most important cause of death, whereas the incidence of carcinomas did not appear increased. Wright *et al.* investigated the morbidity and mortality in 194 patients. Patients were selected from five different hospitals in England in order to avoid biased specialist referral. The patients were diagnosed between 1937 and 1967. The number of deaths was almost twice the expected number. Cardiovascular, respiratory and cerebrovascular disorders accounted for 24%, 18% and 14.5%, respectively. There was a significantly increased mortality in cardiovascular disorders among males, in cerebrovascular disorders among females and in respiratory disorders in both males and females. Although malignancies accounted for 18% of all deaths, this was not significantly different from that expected from the control population.

Alexander *et al.* /5/ found in their survey of 164 acromegalic patients from the Newcastle region a more than 3-fold increased overall mortality rate. Deaths in male patients were significantly higher than expected due to cardiovascular and cerebrovascular disorders, malignancy and respiratory diseases. Deaths in female patients were significantly higher than expected due to cerebrovascular disorders only.

Notwithstanding the less serious course of the disease suggested by the figures above, showing fewer patients dying before the age of 50 and 60