

# Leukemia and Other Malignancies Among GH Users

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## SYNOPSIS

The number of reported cases of leukemia developing in growth hormone (GH) users worldwide has reached 31. Twelve Japanese cases are briefly reviewed; five each of AML and ALL, and one each of CML and malignant histiocytosis. The underlying diseases of these patients consisted of 8 idiopathic disease, 3 tumors and one Fanconi's anemia. Leukemia occurred during GH treatment in 9 cases and after cessation of GH in 3. The longest interval from the cessation of GH therapy was 10 years. GH administration from a younger age tended to be linked to myeloid type. Risk factors and possible mechanisms of leukemogenesis by growth hormone are discussed, and proposals for the future have been made by the Foundation for Growth Science in Japan.

## INTRODUCTION

Administration of growth hormone is unavoidable for the treatment of pituitary dwarfism. Although a risk of leukemia has been predicted based on experiments in rats [1], no previous reports in humans has permitted a feeling of safety concerning its applications in children. In 1986, however, occurrence of acute myeloid leukemia (AML) in a GH user was reported at a conference of pediatric endocrinologists in Japan, and another case of acute lymphocytic leukemia (ALL) was reported at a

pediatric hematology meeting in 1987. The Foundation for Growth Science in Japan collected two other cases of ALL through a survey of GH users. The Leukemia Study Group has been established within the Foundation for epidemiological analysis of leukemia occurrence [2-8]. Five cases of leukemia were reported before 1987 in Japan, and are reviewed here. The observed/expected ratio of leukemia occurrence among growth hormone users became 10 times higher than in the general population. Since other leukemia cases were also found in Europe and the USA, a workshop was held in Bethesda, Maryland in May, 1988. After critical review, 15 cases of leukemia world-wide were judged to be related to the administration of GH and it was decided that the danger of leukemia occurrence could not be ignored, although the risk of leukemia was 1/1000 to 1/7000 [9].

Since then, new cases of hematological malignancies have sporadically occurred in Japan: two in 1988, two in 1989, two in 1990 and one in 1992. Other cases have also occurred in the USA, Canada and Europe. This report presents a brief review of the Japanese cases and comments on possible future developments.

## NUMBER OF GH USERS IN JAPAN AND THE FREQUENCY OF LEUKEMIA

The first occurrence of GH-related leukemia was reported in 1982. There was some debate at the Bethesda workshop concerning whether some kind of agent could have been mixed with the extracted GH, as in the case of Creutzfeldt-Jacob disease. This possibility was ruled out, however, because the types of leukemia varied,

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