

The German Acromegaly Register – Surgical outcome in 400 patients

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Summary

At the time of abstract submission, the German Acromegaly Register included retrospective data of 503 patients, 400 of whom had received primary surgical treatment. Operative results improved over successive time periods, but remained unsatisfactory overall. Secondary operation and SSA analog treatment further reduced the GH concentration considerably, while irradiation (due to the short time period evaluated) and DA had little effect. The data are preliminary and are subject to the influence of biases, since they are based on only 400 out of an expected number of 4.000 to 5.000 patients. Nevertheless, they demonstrate the value of this epidemiological study and are expected to be useful for future improvement of diagnostic procedures and therapeutic choices.

Introduction

Transsphenoidal adenomectomy by an experienced neurosurgeon is the first choice for the treatment of acromegaly. However, results remain unsatisfactory, often due to delayed diagnosis which results in large tumors. Moreover, publications from experienced centres may not represent the overall situation. Although epidemiological studies have been published from different countries covering various aspects of diagnosis and treatment, the number of patients has been relatively low (1, 2). There is not enough information on the causes of delay in diagnosis, of differences between treatment centres and on the quality of treatment outside of experienced centres.

The German Acromegaly Register performs a 10-year epidemiological study and aims to include all acromegalic patients in Germany. At the present time, patients are entered retrospectively, the first cases having been diagnosed in the 1950th. All new patients will be entered as they become diagnosed. Retrospectively and prospectively included patients will be followed with a backup of their data during a 10 year period. The Register aims to extract relevant data on diagnostic procedures, primary and secondary therapeutic strategies and their results, as well as co-morbidity and mortality. The Register will be able to compare experienced with not-experienced centres. It will extract suggestions for improvement. Approximately 4-5000 patients are expected to be finally included. The German Register works in close collaboration with the UK Acromegaly Database and uses the British software, slightly adapted for use in Germany.

Materials and Methods

Two trained nurses visit all centres in Germany and enter the available data into specially developed data sheets, thus ensuring uniform datasets from all different kinds of documentation. These data are then transferred into the database which is located in Berlin. Variations of patient numbers

are due to non-availability of some data in patient documents at various time points. The following abbreviations are used throughout: GH, growth hormone; IGF-I, insulin-like growth-factor I; Tx, treatment; DA, dopamin agonist; SSA, somatostatin analogue; oGTT, oral glucose-tolerance-test; pre-OP, value at time of diagnosis. Data of nine patients who received Pegvisomant were not analyzed because of their small number, esp. in subgroups.

Results

502 patients from 18 centres were entered as of December 2003. Results from 400 operated patients are reported, Table 1 indicates values from three different time periods in which primary treatment was undertaken. Basal, 1 and 3 yrs post-surgery GH and IGF-I data are given. Data at 3 yrs include secondary/tertiary treatment with repeat surgery, medical treatment with either a dopamine agonist or a somatostatin analogue or irradiation. The median pre-operative GH concentration decreased progressively from the first to the last time period, possibly due to improved diagnostic awareness and/or awareness of evolving treatment modalities. In parallel, operative results became remarkably better during consecutive time periods. However, the cure rate as defined by a GH <1.0 µg/L in an oGTT at 1 yr did not surpass 54%. Cure rate defined as both GH<1.0 µg/L plus normal IGF-I concentration (3) was only 38 % at the last time period. The higher cure rates at 3 yrs are due to the effect of secondary treatment

A detailed analysis of the choices of secondary treatment and their results is presented in table 2. Although subgroup numbers of patients are now small, it is apparent, that (1) secondary operation as well as SSA treatment are of considerable benefit, (2) radiation treatment shows only a tendency towards improvement, as expected after a short period of time and (3) DA have little – if any – effect on GH.

Table 3 indicates the distribution of patients who were cared for in (1) university outpatient centres, (2) other hospitals and (3) family doctors, in general specialists in endocrinology. It is clear that the majority of the patients was registered from university outpatient departments (neurosurgical centres were not included, since they mostly return patients to the referring physician following surgery). Whether this represents the overall picture in Germany, remains to be seen. It may at least partly be due to choice of evaluated centres during this early stage of the Register.

117 patients received pre-surgical SSA treatment. This represents a bias, due to the inclusion of some specialized centres in the early stage of data acquisition in the Register. However, in these patients pre-surgical medical treatment reduced GH in most patients, but less so than the following surgery. The median GH concentration at diagnosis in this patient group was 39.6 and at the end of SSA treatment 13.7 µg/L.

Conclusions

The German Acromegaly Register samples data from potentially all acromegalic patients in Germany. It is expected to be useful for improvement of diagnostic strategies and therapeutic results. The close cooperation between the UK and the German Acromegaly Registers will provide an opportunity to compare results in countries with very different

health care systems. It is hoped that the cooperation will soon be extended to other European countries. At the time of this writing the German Registers contains data from 1003 patients and will add 500 more patients – including follow-up data – each year.

References

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Captions

Table 1

Operative results in different time periods. GH ($\mu\text{g/L}$), IGF-I (normal according to age and sex). In brackets: Total number of patients for median GH concentrations in the respective groups. Values at diagnosis, at one year and three years after the operation are indicated. Furthermore, the percentage of patients is given, which attained the criteria, indicated in the respective sections of the table. In brackets: Number of patients/total number).

Table 2

Analysis of secondary treatment one year after primary operation. GH concentrations (median values; $\mu\text{g/L}$) at diagnosis, before start of secondary treatment and at time point 1 year after surgery. In brackets: Total number of patients in group. IGF-I values are normal according to age and sex for the number of patients indicated. In brackets: Total number of patients in group.

Table 3

Distribution of patients according to treatment centres and choice of secondary treatment. In brackets: Percent of total.

Table 1

Time period of surgery		<Dec. 83	1984-92	93-present
GH (median)	Pre-OP	30.4 (10)	23.0 (45)	13.7 (226)
	1 yr	13.0 (10)	3.7 (33)	2.4 (189)
	3 yrs	8.0 (8)	2.4 (26)	2.2 (51)
% GH <1.0/oGTT	1 yr	43 (3/7)	50 (10/20)	54 (49/91)
	3 yrs	40 (2/5)	67 (10/15)	63 (19/30)
% IGF-I normal and GH <1.0/oGTT	1 yr	no data	20 (4/20)	38 (35/91)
	3 yrs	no data	40 (6/15)	60 (18/30)
% random GH <2.5	1 yr	0 (0/0)	25 (5/20)	63 (53/94)
	3 yrs	0 (0/3)	44 (7/16)	67 (39/58)

Table 2

		Secondary treatment					
		2 nd OP	Rad.	DA	SSA	No 2 nd Tx	No F-up
GH	baseline	34 (9)	9.1 (15)	30.1 (24)	15.8 (19)	12.8 (136)	15.8 (31)
	after 1 st OP	13.4 (6)	5.6 (12)	3.1 (10)	5.3 (8)	-----	2.6 (33)
	after/during 2 nd Tx	5.5 (12)	4.1 (14)	3.3 (15)	1.7 (12)	1.7 (126)	-----
IGF-I normal							
	Baseline	1 (7)	0 (11)	1 (17)	1 (17)	9 (105)	1 (34)
	after 1 st OP	0 (5)	3 (12)	1 (4)	2 (8)	-----	24 (34)
	after/during 2 nd Tx	4 (8)	6 (14)	5 (13)	3 (10)	73 (98)	-----

Table 3

	2 nd OP	Rad.	DA	SSA	No 2 nd Tx	No F-Up
University Total=251	16 (6.4)	15 (6.0)	21 (8.4)	16 (6.4)	156 (62.2)	27 (10.8)
Other Hospital Total=52	4 (7.7)	1 (1.9)	4 (7.7)	3 (5.8)	36 (69.2)	4 (7.7)
Family doctor Total=97	3 (3.1)	10 (10.3)	6 (6.2)	9 (9.3)	61 (62.9)	8 (8.3)