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Monoclonal Gammopathy in General Practice

Associated Clinical Conditions

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The clinical diagnoses in all 88 cases of monoclonal gammopathy, detected by general practitioners in Northern Jutland during a 3-year period, were investigated: 15 % had malignant monoclonal gammopathy, 5 % had non-haematologic cancers, and in 80 % a benign disorder was found. These results indicate that the finding of a monoclonal gammopathy in general practice deserves attention, but it is rarely accompanied by a grave prognosis. Malignant monoclonal gammopathy should be suspected, but search for another type of cancer is not indicated. ***Key words: monoclonal gammopathy, malignant monoclonal gammopathy, monoclonal gammopathy of undetermined significance, clinical diagnosis, general practice.***

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Monoclonal gammopathy (MG) is characterized by proliferation of a single clone of cells with the capacity of synthesizing and secreting homogeneous/identical immunoglobulins or some of these. This production of a homogeneous immunoglobulin is detected as a narrow band, a M-component, at electrophoretic investigation of proteins in serum (and/or urine).

A classification of disorders found with MG, modified from Kyle (1), dividing the MGs into malignant monoclonal gammopathy (MMG) and monoclonal gammopathy of undetermined significance (MGUS), was used (Table I). Multiple myeloma, primary amyloidosis, Waldenströms macroglobulinaemia and heavy-chain diseases are generally considered as plasma cell dyscrasias, although the latter two are perhaps more correctly identified as lymphocyte diseases (2). Some types of leukaemias and lymphomas may be classified as MMG, while others do not reflect a gammopathy (2, 3). Regarding non-haematologic malignancies, it has been stated that the occurrence of MG in these diseases is coincidental (4). The production of a monoclonal immunoglobulin may be caused by infections and autoimmune disorders (antigenic stimulation), while the occurrence of MG in other conditions in the group of MGUS is probably coincidental.

Knowledge of the clinical significance of MG has usually been gathered from screening of blood donors (5–8), populations in smaller communities (9–12), or investigations of many cases collected by

Table I. *Classification of monoclonal gammopathies (modified from Kyle)*

Malignant monoclonal gammopathy (MMG)
A) Multiple myeloma
B) Waldenström's macroglobulinaemia
C) Primary amyloidosis
D) Heavy-chain diseases
E) Lymphomas and leukaemias
Monoclonal gammopathy of undetermined significance (MGUS)
A) Non-haematologic cancers
B) Associated with severe acute infections
C) Associated with chronic infections
D) Associated with auto-immune diseases
E) Associated with miscellaneous disorders
F) Associated with no recognized disease

Table II. *Distribution of MG concerning diagnosis and age in 88 persons from general practice*

Clinical diagnosis	Age (in years) <50 (*N*=4682)	50–59 (*N*=1513)	60–69 (*N*=2296)	70–79 (*N*=2004)	≥80 (*N*=531)	Total (*N*=11026)
MMG						
Multiple myeloma			2	3	1	6
Waldenström's macroglobulinaemia	1		1	1	1	4
Lymphoma/leukaemia		1		1	1	3
MGUS						
Non-haematologic cancer				1	3	4
Severe acute infection	2		2	2		6
Chronic infection	1	2	2	5	1	11
Autoimmune diseases			2	2		4
Miscellaneous disorders	3	3	5	4	3	18
No recognized disease	5	7	7	8	5	32
Total	12	13	21	27	15	88

one laboratory (13–15), while it rarely has its origins in general practice (16).

We therefore decided to investigate the clinical conditions behind the finding of a MG in serum protein electrophoresis (SPE) requested by general practitioners.

MATERIAL AND METHODS

All SPE requested by general practitioners in Northern Jutland, a county in Denmark with 482000 inhabitants, are performed in one of two departments of Clinical Chemistry (Hjørring and Aalborg). At Hjørring, SPE is done using the Microzone Electrophoresis System, whereas agarose gel electrophoresis (17) is used at Aalborg. All sera with suspected MG are further examined at Aalborg by immunofixation (18), and immunoglobulins are quantified using specific antibodies.

Table III. *Distribution of MG in groups of MMG and MGUS according to age*

	Age (in years) <70 (*N*=8491)	≥70 (*N*=2535)	Total (*N*=11026)
Persons	46	42	88
MMG	5	8	13
MGUS	41	34	75
MMG/Total	0.11	0.19	0.15

All cases of previously unknown MG identified from May 1, 1979 to April 30, 1982, were studied retrospectively. The diagnosis of associated disorders was obtained from the general practitioner and, in the case of hospitalization, from the patient's record. A diagnosis conforming with the classification in Table I was made within 3 months after the detection of MG. The observation period was 18–54 months. During this period no patient changed from MGUS to MMG.

RESULTS

In the 3 years of investigation, close to 10000 SPE were requested from general practice. Eighty-eight cases of MG were found, i.e. in less than 1% of the SPE performed a M-component was demonstrated. The distribution of MG on clinical conditions and age groups is given in Table II (no person had primary amyloidosis or heavy-chain disease) and, as the results were similar, men and women are grouped together. MG was most often found in patients between 60 and 80 years of age. Thirteen persons (15%) had MMG, and 75 (85%) MGUS. Although 28 were classified as "no recognized disease", they actually had symptoms that made their general practitioner ask for SPE. Only one out of 13 persons below the age of 50 years with a MG had a malignant disease (Waldenströms macroglobulinaemia).

In Table III the number of MMG and MGUS

cases in persons younger than vs. 70 years or older are shown. It appears that MMG is more common in the elder group, but even in this group only 19% had MMG.

DISCUSSION

The results from an investigation of this type depend on many factors. The age composition of the population in question and the attitude of some physicians not to make diagnoses in the elderly are crucial, as the incidence of MG rises with age. For instance Axelsson et al. (9) found in a community study that 1% older than 25 years, 3% older than 70 and 6% aged between 80 and 90 years had MG. Moreover the use in general practice of a certain laboratory analysis, *in casu* SPE, might change with time and must necessarily differ among physicians from different backgrounds. The incidence of MMG is also important, because symptoms combined with these diseases are so alarming and progressive, that the detection rate equals the incidence.

These reservations should be kept in mind if our results are to be transferred to other populations. On the other hand, we have no reason to believe that general practitioners in Northern Jutland should react differently from colleagues elsewhere, with respect to SPE.

It is interesting that fewer than 0.2% (13 out of 10000) of the persons, in whom a SPE was requested, had MMG. A similar incidence has been found in a study of hospitalized patients (19) and in a study comprising both ambulatory and hospitalized persons (20).

In a study from his own general practice, Bird (16) found 5 (28%) with MMG among 18 persons (11 men, 7 women) with MG, during a period of 7 years.

Studies on hospitalized patients report that 50% or even more of detected MGs are caused by MMG (13, 19, 21). In an investigation (20) comprising 50000 ambulatory as well as hospitalized patients, in whom a SPE was requested, 574 cases of MG were found, and 28% of these were due to MMG. In contrast, investigation of blood donors or all adult persons in smaller communities describes prevalence rates of MG around 1% and a much lower frequency of MMG (8, 9, 11). These findings can be explained by the difference in study population, with the more severe symptoms being seen in hospitalized patients.

Our results indicate that the finding of a MG in general practice deserves attention, but is not generally accompanied by a grave prognosis.

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