Mock Scientific Experiment: Prevention in Progression of MGUS to Multiple Myeloma

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Abstract

Background
MGUS is a condition in which M proteins are created by plasma cells in the bone marrow. MGUS by itself is not a serious condition, but if it progresses, it could lead to other much more serious conditions such as multiple myeloma. In studying characteristics of MGUS that could lead to multiple myeloma, we could be able to stop the progression of MGUS to other diseases.

Methods
After observing general characteristics of MGUS and multiple myeloma, the hypothesis was written to reflect the information that we would be testing out in this experiment. Since this experiment is not fully evaluating the study but rather is presenting an experiment which could be done to test for prevention, no actual data was collected to be used in this experiment. Information can be taken from sample patient data, or, if given the resources, actual patient data may also be used. This experiment looks for the size of the M proteins and the type of M proteins, and how that affects the potential development of multiple myeloma in later stages.

Results
The results would be evaluated in such a way that even if the information collected does not match the hypothesis, the data would still be able to be used to make conclusions. The data would be charted for a proper visual representation of the data that was collected. This would also make it easier to interpret the results. First, looking at the data about the size of the M proteins, we can draw information about that and make an inference about whether or not it actually had an affect on the progression of MGUS to multiple myeloma. Then, the same thing is done for the types of M proteins, and information is drawn about the data collected to make an inference about whether or not it actually had an affect on the progression of MGUS to multiple myeloma.Then, at the end, a statement is made about the accuracy of the hypothesis, and about the new information that was found through the experiment.

Discussion
In the discussion section, the limitations of the experiment are brought up, and we will talk about how the research has proved or disproved the hypothesis. There are also general conclusions made from the data that is collected.

Introduction

MGUS is a disease that has only recently been found, and we are still learning a lot about it. MGUS, which stands for monoclonal gammopathy of undetermined significance, is characterized by the M protein that is found in patients with MGUS. MGUS on its own is not a significantly dangerous disease, but MGUS can lead to the development of much more serious conditions. Most of the time, MGUS is not harmful to people who have it, unless they happen to develop a complication from it. In fact, only about 1% of MGUS cases each year end up developing into multiple myeloma, which is a disease in which myeloma cells multiply quickly[1]. Multiple myeloma is a treatable but incurable disease which could become dangerous if not treated quickly[2]. And even though 1% of MGUS cases may develop into multiple myeloma, a huge number of multiple myeloma cases were said to have begun with MGUS progression.

There are some risks that are associated with progression of MGUS, such as the size of the monoclonal protein, the type of monoclonal protein, and the FLC ratio, or free light-chain ratio[3]. By assessing these factors, we may be able to map out the possible progression of MGUS in a patient. Environmental and genetic factors are usually taken into account when studying the causes of MGUS and multiple myeloma. People who have more exposure to toxic and dangerous substances may have an increased risk of developing MGUS[4]. Genetic factors are taken into account in multiple myeloma, because a family history of people who have had multiple myeloma increases the risk of a person developing it[5].

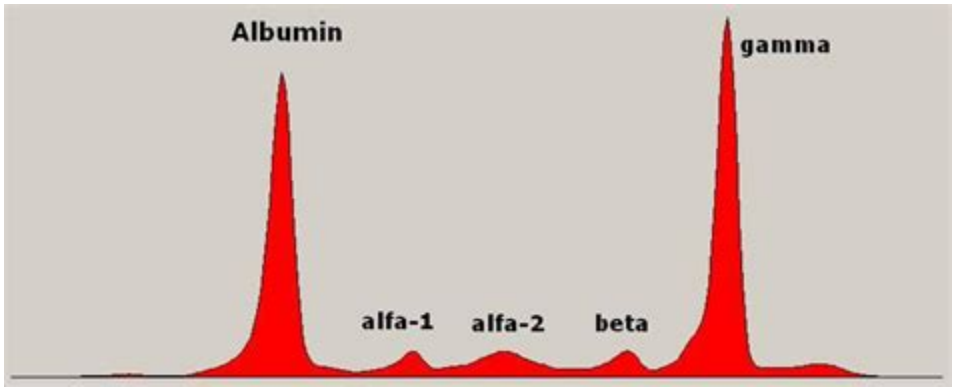
To assess the extent to which the risk factors may actually cause disease progression to multiple myeloma, we would have to analyse the M protein sizes and types, and compare them to see if there are any correlations between a certain size or type and the progression of MGUS to multiple myeloma. We can also look at the FLC ratio in different patients and see how the difference in ratios could affect MGUS progression to multiple myeloma.

Observation

The amount of M protein is typically measured in g/L or g/dL (grams per liter or grams per deciliter). According to a table compiling the monoclonal protein content in MGUS and multiple myeloma, multiple myeloma typically has more than 3.5 g/dL while MGUS has less than 3.5 g/dL[6]. This study was done more in focus of multiple myeloma and effects of MGUS on kidney health. Different types of proteins can also affect the development of multiple myeloma. Some different protein types include proteins with the heavy chains IgG, IgA, IgD, IgM and IgE[7]. Multiple myeloma is most commonly associated with the proteins IgA and IgG, so those could be proteins tested in correlation to multiple myeloma. All of the proteins could cause multiple myeloma, but IgG and IgA seem to be most common.

	MGUS	Smoldering myeloma	Indolent myeloma	Multiple myeloma
Bone marrow plasmacytosis	<10%	10–30%	>30%	>30%
Monoclonal protein	IgG < 3.5 g/dl; IgA < 2 g/dl	IgG > 3.5 g/dl; IgA > 2 g/dl	IgG = 3.5–7 g/dl; IgA = 2–5 g/dl	IgG > 3.5 g/dl; IgA > 2 g/dl
Laboratory studies	Normal hemoglobin, serum calcium, and creatinine	Normal hemoglobin, serum calcium, and creatinine	Normal hemoglobin, serum calcium, and creatinine	Anemia, hypercalcemia, and increased creatinine common; Reduced normal immunoglobulins; Bence-Jones protein in urine
Lytic bone lesions	Absent	Absent	≤3 lytic lesions; no compression fractures	Present
Symptoms	None	None	None	Present

Image[8]



Image[9]

The right most part of the graph, labeled gamma, shows the monoclonal gammopathy. In this instance, the graph is showing multiple myeloma.

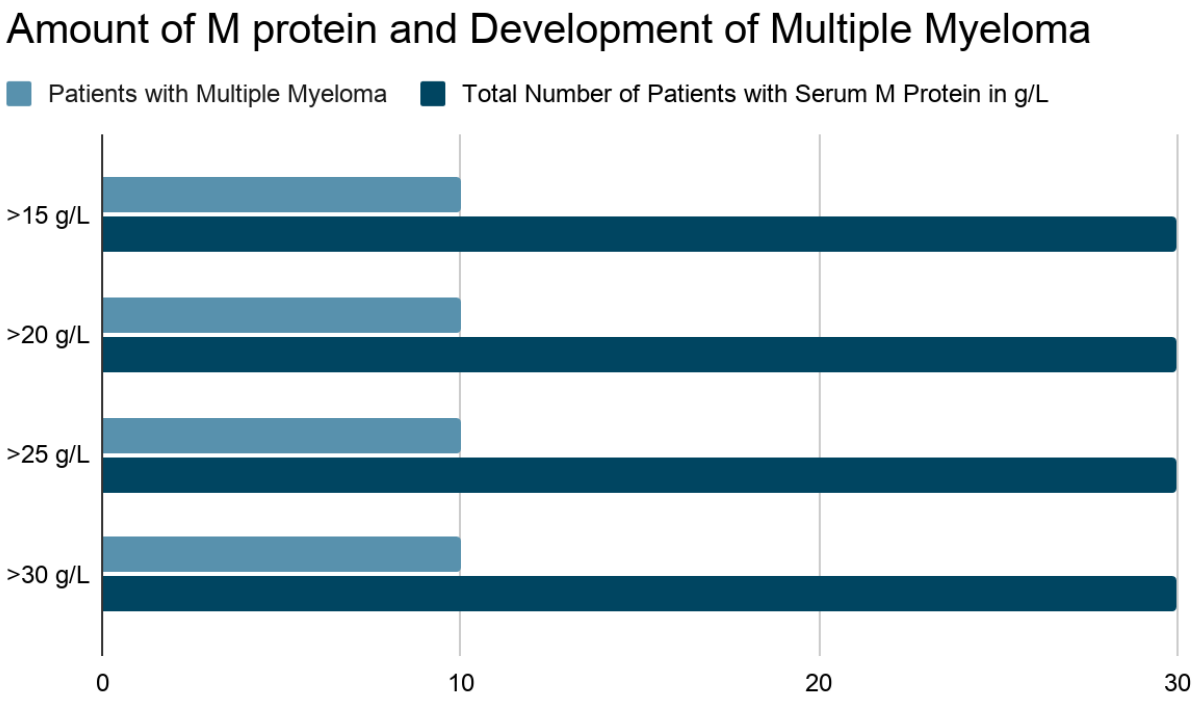
Hypothesis

If there is >20 g/L of serum monoclonal protein and the presence of IgA or IgG type proteins, then there will be an increased risk of MGUS progression to multiple myeloma.

Results
Upon completion of this trial:

It was found that of the patients who had >15 g/L of serum monoclonal protein, __ out of __ patients developed multiple myeloma. Of the patients who had >20 g/L of serum monoclonal protein, __ out of __ patients developed multiple myeloma. Then, out of the patients who had >30 g/L of serum monoclonal protein, __ out of __ patients had multiple myeloma. These results indicate that the content and size of M protein found had an impact on the development of multiple myeloma, because having a larger size of M proteins (did/did not) cause development of multiple myeloma.

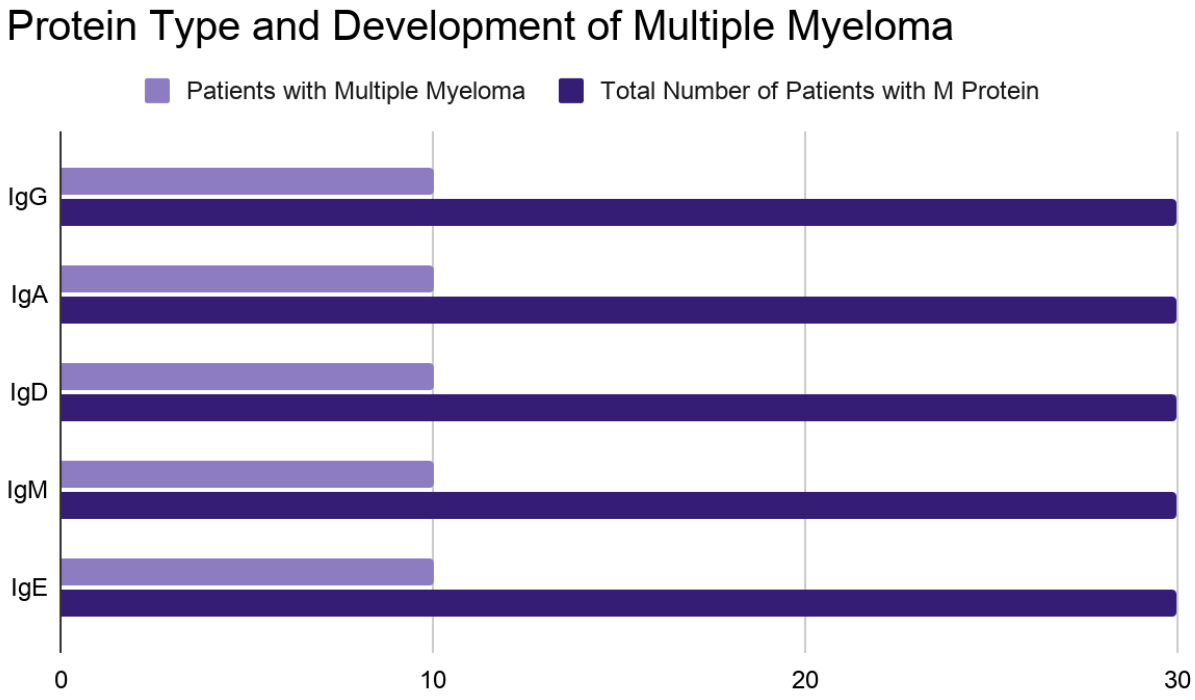
(The following chart would be filled in with accurate information as a result of the findings, but as this is merely a set-up, the data shown is not accurate).



It was found that __ out of __ patients with MGUS who had IgA proteins developed multiple myeloma. __ out of __ patients with MGUS who had IgG proteins developed multiple myeloma. From all of the patients, people with MGUS who had protein type Ig_ were the most likely to develop multiple myeloma because __ out of __ patients with this protein type developed MM. From all of the patients, those with MGUS who had protein type Ig_ were the least likely to develop multiple myeloma because only __ out of __ patients with this protein type developed

MM. As a result, these results indicate that having protein types IgA and IgG (did/did not) cause development of multiple myeloma.

(The following chart would be filled in with accurate information as a result of the findings, but as this is merely a set-up, the data shown is not accurate).



Due to these findings, my hypothesis as stated above that “If there is >20 g/L of serum monoclonal protein and the presence of IgA or IgG type proteins, then there will be an increased risk of MGUS progression to multiple myeloma,” (was/was not) correct because the size of the M protein (did/did not) matter in the overall outcome of the number of people who had multiple myeloma, and the type of M protein (did/did not) matter in the overall outcome of the number of people who had multiple myeloma. Whether or not my hypothesis was correct, I found out that the size of M proteins that was closely related to the highest number of people with multiple myeloma was __.Similarly, I found out that the type of M protein that was closely related to the highest number of people with multiple myeloma was __.

Discussion

In finding out which factors contributed most to the likelihood of developing multiple myeloma, we can be able to possibly prevent the progression of it. Through this experiment, we looked at specific factors in MGUS patients that could lead to myeloma, such as the size and type of monoclonal proteins. However, despite this experiment which has a purpose of combating the progression of MGUS, there are some limitations that also need to be addressed and considered.

One such limitation is that the time of diagnosis of MGUS is important in calculating whether or not there may be a risk of MGUS progressing to another disease[3]. For instance, if someone is diagnosed with MGUS in his/her 40s, there is a higher risk of developing complications from MGUS because the diagnosis was found so early. On the other hand, if someone is diagnosed with MGUS in his/her 70s, there is not as high of a risk of developing complications. Earlier diagnosis of MGUS could indicate that the M proteins are increasing more than they would in another patient, which could also be why a diagnosis earlier on could lead to developing complications.

Another limitation that was looked over in this experiment was biclonal proteins and SMM, or smouldering multiple myeloma[10]. SMM is essentially a stage of disease progression in between MGUS and multiple myeloma, and the factors of progression for SMM are quite different than that of MM[10]. Biclonal proteins typically tend to have a dominant protein over the other, either the multiple myeloma clone, or the MGUS clone[10]. FLC ratios, or free-light chain ratios, were also excluded because they relate to SMM in finding the risk that could be present for progressing to SMM, but it most likely would not have made any new developments in the current multiple myeloma research of this experiment.

Methods

First, the factors that would be evaluated as part of the hypothesis were selected. Those were: size of M protein and type of M protein, and their effect on the overall development of multiple myeloma in patients with MGUS. The data was not given, but it would have been found either using sample patient data, or from actually collecting information from patients for the purposes of this research.

The data to be collected was separated into categories. There would be the first category, which was the total number of people with MGUS who had M protein sizes in one of the four sections: >15 g/L, >20 g/L, >25 g/L, or 30> g/L. Then, of all of those patients, the number of patients in each of the four sections who had multiple myeloma were recorded. Next, the next category would be the total number of people with MGUS who had M protein types in one of the five sections: IgG, IgA, IgD, IgM, and IgE. Then, of all of those patients, the number of patients in each of the five sections who had multiple myeloma were recorded.

This process was done to ensure that the factors would be assessed as fairly as possible. I also expanded the categories out of what was only on the hypothesis because I wanted to have a

greater range of data so I could compare the rest of the data in the case that the hypothesis was wrong. I also added some sentences in the Results section to discuss the other results that pertained to research from the charts, besides only analyzing the data from the hypothesis.

MGUS

MGUS stands for monoclonal gammopathy of unknown significance. It is characterized by the presence of the "M," or monoclonal protein.

How does it form?

MGUS is usually present when there are higher levels of protein found in bone marrow. Plasma cells that create proteins for blood begin to create an unusual and abnormal protein, the monoclonal or M protein. When there is an increase in protein levels, including M proteins, MGUS is usually kept in mind in trying to determine the cause of the protein increase.

What causes it to form in the first place?

While there is not a known cause of MGUS, it was found that certain genetic conditions or environmental factors may contribute to an increased risk of having MGUS. For example, certain chemicals have been linked to an increased risk of having MGUS and even for developing complications from MGUS. One such chemical is Agent Orange, which is a herbicide used largely during the Vietnam War. This chemical contains a heavily dangerous form of dioxin, which is carcinogenic because it can cause DNA alterations such as cancer and other cell mutations.

Is there a certain demographic of people who are affected by MGUS?

MGUS is most commonly seen in males and elderly people who are above the age of 65. It is also more commonly seen in African Americans, as shown in a study which tested for M proteins in people of different races. This racial disparity shows that some groups of people, especially those who are diagnosed with MGUS earlier on, may be more prone to developing progressive complications of MGUS later in their lives. MGUS is still found in people who are younger, but it's just that it's more common to find it in people who are older and male.

Are there different types of MGUS?

The three types of MGUS are:

1. **Non-IgM MGUS -** This includes IgA, IgD and IgG MGUS, and it is the most common form of MGUS.
2. **IgM MGUS -** This is less common, making up roughly 15% of MGUS diagnosis.

Light-Chain MGUS - LC MGUS or Light-Chain MGUS does not contain an immunoglobulin heavy chain component.

What are the complications of MGUS?

Although for most people MGUS doesn't actually develop into a more serious disease later on, MGUS can sometimes develop into conditions. Non-IgM MGUS can develop into multiple myeloma or malignant neoplasms. IgM MGUS can develop into lymphoma, a condition called AL amyloidosis or a rarer type of cancer called Waldenstrom macroglobulinemia. Light-Chain MGUS could progress to multiple myeloma or AL amyloidosis.

What is the connection between MGUS and multiple myeloma?

Only about 1% of cases of MGUS actually progress to multiple myeloma. However, many multiple myeloma diagnoses have a connection to MGUS in earlier stages. The difference between MGUS and multiple myeloma is that MGUS involves the M protein, and protein levels in bone marrow are overall lower and not dangerous. In multiple myeloma, myeloma cells begin to abnormally proliferate, causing cell and tissue growth in the form of tumors.

Attached above is a brochure detailing more information about MGUS the information is mostly simplified, but it serves the purpose of helping people understand more about MGUS, so that the scientific experiment overall makes more sense to people who may not be familiar with it.

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