Multiple Myeloma Incidence in Metropolitan Atlanta, Georgia: Racial and Seasonal Variations

By Peter McPhedran, Clark W. Heath, Jr., and Joan Garcia

Between 1963 and 1967, 120 cases of multiple myeloma were diagnosed in residents of metropolitan Atlanta, Ga. These cases represent an incidence of 4.0/100,000 per yr for black people and 2.1 for white people. While the rate for black people is the highest yet identified for any population, it is probably an underestimate because of underreporting for older age groups. More cases were diagnosed in winter than in summer months. Retrospective data regarding symptoms at onset suggest that this seasonal variation may at least in part reflect the winter occurrence of acute respiratory infections, which may bring existing neoplasia to medical attention.

It has been suggested that the incidence of multiple myeloma (MM) is higher for black Americans than for white Americans. In a retrospective survey of MM occurrence in Brooklyn, N.Y., between 1943 and 1952, MacMahon and Clark found that the incidence for black people was more than twice as high as for white people. In contrast, however, data on MM mortality in the United States as a whole, published for each year from 1950 through 1966, show considerably less disparity between rates for nonwhite people (largely blacks) and for white people, and crude mortality for white subjects often exceeded mortality for nonwhite subjects.

The question of racial variations in MM occurrence is potentially important. While an excess among white people might be attributed to more thorough case detection, an excess among black people is less easy to explain and might be traceable perhaps to some specific genetic or environmental influence.

Since the period of MacMahon and Clark's survey, the frequency of MM in the United States has more than doubled, an increase most likely due to wider use of protein electrophoresis and bone marrow aspiration. Such diag-
nnostic advances, together with the potential etiologic significance of excess incidence in black people, make further studies of the epidemiology of MM desirable.

We have recently completed a survey of MM in the metropolitan area of Atlanta, Ga., which, like Brooklyn, N.Y., is a large, racially mixed, urban population. This report describes the findings of that survey with regard both to race and to the unexpected finding of a distinct seasonal variation in MM incidence.

MATERIALS AND METHODS

Information was gathered about all cases of MM (including its two major clinical variants, plasmacytoma and plasma cell leukemia) diagnosed in residents of the five-county metropolitan Atlanta area between January 1, 1963, and December 31, 1967. Incidence rates for MM were calculated on the basis of 1960 population data, corrected for growth to 1965, with the assumption that increases in population since 1960 had occurred in equal proportions in each race and age group. In 1960, the population of the five-county area was 1,017,188, including 785,019 white people and 232,169 nonwhite people. All but 335 of the nonwhite people were black people. The 1965 population was estimated to be approximately 1,180,000, including 911,000 white people and 269,000 nonwhite people.

Names of patients diagnosed as having MM were obtained from hospital records, including hospital tumor registries, and from death certificates. The medical record of each patient was reviewed. Cases diagnosed as MM were included in the survey if the medical record contained adequate supporting laboratory data. Evidence sufficient for inclusion of a case in the survey was: a histologic diagnosis of definite MM on a bone marrow, biopsy, or autopsy report; a histologic diagnosis of probable MM, if supported by a convincing description of the specimen (at least 20% plasma cells, or at least 10% with numerous morphologically abnormal forms); or, in the absence of histologic evidence, a combination of osteolytic bony lesions (with or without pathologic fractures) with monoclonal proteins in serum or urine detected by electrophoresis or by Bence Jones urinalysis. Neither osteolytic lesions nor protein abnormalities alone was considered sufficient for inclusion.

The results of urine electrophoresis and of immunoelectrophoresis of serum and urine were rarely available in the medical records of these patients and therefore were not used as diagnostic criteria.

RESULTS

The diagnosis of MM, acceptable under the foregoing criteria, was made in 120 persons during the 5-yr period. Of the 120 diagnosed, 109 were supported by histologic evidence, and 11 only by combinations of osteolytic lesions and protein abnormalities. Of those included on histologic grounds, 98 were diagnosed by bone marrow (76 called definite, 22 probable with adequate supporting descriptions), eight were diagnosed by biopsy, and three by autopsy. Nearly all of the histologically diagnosed patients also had other clinical abnormalities supporting the diagnosis of MM, such as osteolytic lesions and protein abnormalities. Of the 11 patients accepted in the survey with less than “definite” or “probable” histologic evidence, all had osteolytic lesions—six with monoclonal serum proteins, three with Bence Jones proteins in the urine, and two with both. Five of the six with monoclonal “spikes” as their only protein abnormality had a greater than 2 g increase in the protein of the abnormal fraction.
Table 1. Appendix: Selected Clinical Features* of Patients With Plasma Cell Leukemia

<table>
<thead>
<tr>
<th>ARS</th>
<th>Symptoms</th>
<th>Hct. (%)</th>
<th>Pts. (x 1000/cu mm)</th>
<th>WBC (ml)</th>
<th>Plasma Cells (%)</th>
<th>Proteins</th>
<th>X-Rays</th>
<th>Other</th>
<th>Dates</th>
<th>Diagnoses</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>40NF</td>
<td>Back pain, cough</td>
<td>33</td>
<td>N.S.</td>
<td>11.9</td>
<td>18</td>
<td>N.S.</td>
<td>Lytic lesion in L4, collapse L1 and L4</td>
<td>—</td>
<td>MM 10/63</td>
<td>Leuk 10/63</td>
<td>Death 10/63</td>
</tr>
<tr>
<td>49WM</td>
<td>Shoulder pain, fever, epistaxis, anorexia, diarrhea (Hb 6.7)</td>
<td>23.1</td>
<td>7.7</td>
<td>16</td>
<td>Normal</td>
<td>Osteoporosis</td>
<td>Bruises liver 3 lb</td>
<td>1/65</td>
<td>MM 1/65</td>
<td>Leuk 1/65</td>
<td></td>
</tr>
<tr>
<td>51NM</td>
<td>Back pain</td>
<td>19</td>
<td>38.0</td>
<td>45.8</td>
<td>58</td>
<td>ρSpike</td>
<td>Lytic lesions</td>
<td>Cachexia, liver 6 cm, spleen 2 cm, Calcium 15.5</td>
<td>9/67</td>
<td>MM 9/67</td>
<td>Leuk 4/68</td>
</tr>
<tr>
<td>56WM</td>
<td>Back pain</td>
<td>18†</td>
<td>Decr.†</td>
<td>5.7</td>
<td>40</td>
<td>γSpike</td>
<td>Lytic lesions</td>
<td>Calcium 12.3</td>
<td>MM 11/66</td>
<td>Leuk 2/68</td>
<td>Death 2/68</td>
</tr>
</tbody>
</table>

*Blood counts are those obtained when leukemia was diagnosed. Other observations were made when MM was diagnosed. †After treatment of MM.
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Among the 120 cases of MM accepted in the survey, there were one case of solitary plasmacytoma and five cases of plasma cell leukemia. The plasmacytoma affected the mastoid portion of the temporal bone. The five patients with plasma cell leukemia were clinically similar to other patients with MM in the survey. Four had definite diagnoses of MM by marrow aspiration, and one was diagnosed at autopsy. Three had osteolytic lesions, two had pathologic fractures, two had myeloma protein spikes, and one had gross hyperglobulinemia attributed to myeloma. White counts were 5700, 7700, 11,900, 12,800, and 45,800 with 40, 16, 18, 22, and 58% plasma cells, respectively, when plasma cell leukemia was diagnosed. These and other details of these cases are shown in Table 1.

Of the 120 cases accepted in the survey, 60 were male and 60 female. Seventy-nine were white patients and 41 nonwhite. All of the nonwhite patients were black except one, an oriental male. Age at time of diagnosis ranged from 31 to 96 yr; the largest number of cases occurred in the sixth, seventh, and eighth decades of life.

Incidence by Race

The over-all annual incidence of MM in Atlanta was 4.1 cases/100,000 nonwhite people (4.0 for black people) and 2.1/100,000 white people. (In the current study the large majority of "nonwhites" among the cases and in the population were black people. The designation of this group as nonwhite is retained here for comparability with other studies and because rate calculations are based on published census data that combine black people with other nonwhite groups.) These rates are shown in Table 2, together with previous data comparing MM incidence in different racial groups.8 In each set of data, rates are higher for nonwhite people than for white people. However, this disparity emerges from the 1960 U.S. Vital Statistics only after age adjustment. The published crude statistics showed slightly higher rates for white people of both sexes.9 Whereas the Atlanta morbidity and U.S. mortality data are adjusted to the distribution of the total U.S. population in 1960, neither of the other two sets of data is recorded in sufficient detail to allow such an adjustment.

Age-specific incidence rates for nonwhite and white people in Atlanta are

| Table 2. Incidence of Multiple Myeloma by Race in the U.S. With Four Sets of Data Compared |
|---------------------------------|------------------|------------------|------------------|------------------|
| Area                            | Population       | Time Period      | Incidence*       | Ratio            |
|                                 | (x 10^4)         |                  | Nonwhite         | White            |
| Metropolitan Atlanta            | 1.2              | 1963–67          | 4.1              | 2.1              | 2.0:1            |
| Brooklyn¹                        | 2.7              | 1943–52          | 2.5              | 1.0              | 2.5:1            |
| 10 U.S. cities⁶                 | 14.6             | 1947             | Male 1.9         | 1.0              | 1.9:1            |
|                                 |                  |                  | Female 0.8       | 0.8              | 1.0:1            |
| U.S.⁷,⁸                         | 179.3            | 1960             | 2.1              | 1.6              | 1.3:1            |

*Rate/100,000 population per year. Data for metropolitan Atlanta and for U.S. are standardized by 10-yr age groups using total U.S. population in 1960. Rates given for Brooklyn were standardized using white population of Brooklyn. Rates given for ten U.S. cities were crude.
shown in Table 3 and Fig. 1. In both racial groups, cases occurred from the fourth decade on, and rates increased with age. Rates for nonwhite individuals exceeded rates for white individuals in most age groups but were equal in the oldest group.

Age-specific mortality rates in the United States as a whole are shown by race in Fig. 2. The age distribution of cases and differences between racial groups were similar to patterns observed in Atlanta. No age-specific comparisons could be made with the Brooklyn study or with the survey of ten U.S. cities. In the Brooklyn study, only data pertaining to white people was given in age-specific form. In the survey of ten U.S. cities, none of the myeloma data was age specific.

Seasonal Variation

The Atlanta data showed a marked seasonal variation in frequency of MM diagnosis (Fig. 3). Over the 5-yr period, the average cumulative number of cases diagnosed in each calendar month was ten. Monthly numbers of cases from October through March all exceeded this average, while all those from
Fig. 2. Multiple myeloma in U.S., 1960. Mortality by age and race.

April through September were ten or lower. In all, 77 cases were diagnosed in October through March, whereas only 43 were diagnosed in April through September. Correlation of these data with average Atlanta monthly temperatures\(^{10}\) (Fig. 3) demonstrates the trend toward diagnosis of MM in the cooler months, although the “fit” is not exact: April with five cases averages two degrees cooler than October with 14 cases.

Analysis of seasonal variation by race showed no differences. Cases in both racial groups were diagnosed predominantly in October through March. Analysis by sex, however, showed that males accounted for nearly all of the seasonal variation: 46 cases in males were diagnosed in October through March and 14 in April through September, while 31 cases in females were diagnosed in October through March and 29 in April through September.

There was enough clinical information for 87 of the 120 patients to estimate a month of symptom onset. No marked variation was found in month or season of onset. Recorded onsets were generally vague, and dates could only be tentatively estimated. The data, however, suggest that the observed seasonal variation is more a reflection of time of diagnosis than of symptom onset.

**DISCUSSION**

**Incidence by Race**

Variations in disease incidence according to race suggest that specific genetic or environmental etiologic factors are at work, if variations in case detection
can be excluded. In the United States, most neoplastic diseases are diagnosed more frequently in white people than in black people, a difference that is usually attributed to incomplete case detection in black people because they have less access to medical care. Since MM, however, is diagnosed more frequently in black people than in white people, the racial difference cannot reasonably be attributed to discrepancies in case detection.

The two-to-one, black-to-white ratio of MM incidence in Atlanta is similar to ratios for residents of Brooklyn and for males in the survey of ten U.S. cities. In addition, the incidence for Atlanta black people, 4.0/100,000, is higher than previously documented in any complete population (all age groups, both sexes). One prior report, dealing largely with black subjects, suggested an even higher MM incidence; McFarlane, studying the occurrence of MM in Jamaica (1962–1964), estimated a rate of 5.0/100,000. However, the size of the population studied was uncertain, and the author did not state his criteria for the diagnosis of MM beyond the requirement of a monoclonal globulin peak in serum or urine.

In all likelihood, the two-to-one, black-to-white ratio observed in Atlanta is an underestimate. The age-specific data (Fig. 1) show that MM incidence for black people is higher than for white people in all but the oldest age group. In studies of leukemia incidence, findings suggest that there is consistent selective underdiagnosis in the older age groups of economically deprived populations. Since MM is diagnosed by much the same means as leukemia and by much the same group of physicians, it also is likely to be underdiagnosed in elderly black people who are generally poor. For this reason and since MM is primarily a disease of older persons, the true incidence of MM in Atlanta is probably considerably higher for black people than we found it.

Why MM is more common in black individuals than in white individuals is not known. English data cited by MacMahon indicate that the reason is not economic. In England, lymphomas of all types are commonest in the highest occupational class, and, within the lymphoma group, MM shows the strongest relationship to class. If we can relate these English data to the United States, we can probably assume that poverty, itself, is not the cause of the high rate of MM in black Americans. Instead, the MM excess in black people may result from an environmental factor unrelated to economics or from some genetic characteristic. The question might be settled by a study of class correlated with MM incidence in a racially mixed U.S. population. Unfortunately, such an analysis could not be made with the data we collected.

**Seasonal Variation**

The meaning of the winter peak of MM diagnosis in metropolitan Atlanta is not clear. Similar seasonal variations have at times been noted for other neoplastic diseases: Hodgkin’s disease, leukemia, and cancer of the rectum, cervix, brain, and skin. The authors of these reports suggest that seasonal variations in frequency of respiratory infections may lead to apparent cold weather peaks in neoplasm incidence by bringing patients with established neoplasia to medical attention. This suggestion may be particularly applicable
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to MM, since patients with MM commonly have reduced antibody globulins and seem exceptionally susceptible to respiratory infections.

To see whether respiratory infections might be related to the cold weather excess in MM incidence in Atlanta, symptoms preceding diagnosis, as recorded in medical records, were reviewed for all 120 Atlanta-area patients. Thirteen had symptoms of respiratory infection during the month prior to diagnosis: the month of diagnosis for 11 of these patients was in the period October through March and for two, April through September. While this excess by no means accounts for the winter excess in the entire series, it does lend weight to the idea that respiratory infection may precipitate the diagnosis of malignancies and MM in particular.

REFERENCES


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