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# STUDY ON THE DIAGNOSIS OF MULTIPLE MYELOMA 2547 CASES

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**Analysis of 2547 cases of multiple myeloma (MM) reported in China in 1980s showed that the clinical manifestations are characterized by multipliey. High misdiagnosis rate (69%) and multiple complications. while the monoclonal protein had more than 25 immunological types, IgG myeloma was the commonest (43.1%). Light chain subgroup trended to have a higher incidence of renal demage (76.9%). Plasma cell leukemia evenetually developed in 30 cases. In order to improve diagnosis and avoid misdiagnosis, the key points are 1, to better the recognition of clinical features of MM. 2. Patient should receive urine Bence-Jones protein, immunoglobulins, immunoelectrophresis, bone X-ray and multiple site bone marrow puncture whenever one of such manifestations as unexplained anemia, skeletal pain, proteinuria, elevation of ESR, hyperviscosity syndrome, hypercalcemia, hyperuricemia, elevation of alkaline phosphatase, pathological fractures and diffuse osteoporosis, 3. Immuno-binding electrophoresis and immunofluorence antibody detection should be done for suspected cases with normal immunoglobulin level.**

**Key words: Multiple mueloma, diagnosis, Immunological classification**

Multiple myeloma (MM) is characterized by the neoplastic proliferation of plasma cells. It has so many clinical manifestations that it is hard to make a correct diagnosis. We analysed 2547 cases of MM in order to avoid the misdiagnosis of this disease.

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## METERIALS AND METHODS

Source of cases: We treated 30 patients in our hospital.[1,2] The other 2517 cases are from the report of "Chinese medical Abstract" of 1981-1990.

According to the data from the references, we made a statistical analysis.

86 cases out of 2547 with definite immunological classification and related record of renal function. We applied $X^2$ test to the morbility of renal damage between every subtype as well as the rate of transforming to plasma cell leukemia between every immunological subtypes.

## RESULTS

### General Data

The rate of male to female in the 2547 cases of MM was 2.5: 1. aged 6-83 years old. 87.8% of them was above 40. Among 30 cases from our hospital, 19 adult male patients aged 60-69. 5 of 8 adult female patients aged 50-59. It suggests that the peak of onset age of female was 10 years younger than that of mele. The time of onset of the disease to definite diagnosis varied from a half month to 20 years.

### Initial Symptom

Th initial symptom of MM varies (Table 1), it is easy to lead to a misdiagnosis (Table 2).

*Table 1. Initial symptoms of 1240 cases**

| Initial symptoms | Number | % |
|---|---|---|
| Bone pain | 684 | 55. 2 |
| Anemia | 352 | 28. 4 |
| Fever | 210 | 16. 9 |
| Bleeding | 171 | 13. 8 |
| Gastrointestinal symptoms | 154 | 12. 4 |
| Edema/ Proteinuria | 141 | 11. 4 |
| Neurological symptoms | 129 | 10. 4 |
| Polyuria | 32 | 2. 6 |
| Others | 79 | 6. 4 |

*: There were 1 to 3 initial symptoms in every case.

*Table 2. Analysis of 758 cases of misdiagnosis*

| Disease of misdiagnosis | Number of cases | % |
|---|---|---|
| Nephritis | 116 | 15. 3 |
| Rheumatic arthritis | 58 | 7. 7 |
| Anemia | 55 | 7. 3 |
| Neurological disorder | 51 | 6. 7 |
| Infectious disease | 47 | 6. 2 |
| Hepatitis/cirrhosis | 30 | 4. 0 |
| Bone tumor | 28 | 3.7 |
| Bone tuberculosis | 26 | 3. 4 |
| psoatic strain | 12 | 1. 6 |
| Coronary heart disease | 11 | 1. 5 |
| Others (more than 80 kinds | 89 | 11. 7 |
| Total | 523 | 69. 1 |

## Sign

995 cases were reported with obvious sign. 33.8% of them with hepatomegaly, 17.1% with splenomegaly. Most of them are slightly palpable. 12.1% with node under skin and local bone bulge. 9.9% with bone tenderness. 5.9% with enlargement of superficial lhmphnode. 3.8% with neurological damage. 3 cases with enlargement of their tongue, some pleurisy with effusion.

## Main Complications

Main complications of 1058 patients: 38.7% with infection of various parts of the body, mainly respiratory and urinary systems. 38.3% with renal failure. 5.4% with neurologic damage. 0.5% with amyloidosis. There were 15 kinds of complications in all. 3 cases complicated with different carcinoma, carcinoma of the stomach, bladder carcinoma, nasal pharynx and gum carcinomas.

## X-ray

1095 cases with X-ray report. 70.2% with osteolytic lesions. 27.5% with pathologic fractures. 12.8% with soteoporosis. They were mainly located at skull, pelvis, costae, vertebrae, sternum 1.7% with osteosclerosis. 6.4% wtih no bone involvement.

## Examination of Bone Marrow, Blood And Urine

Examination of bone marrow and abnormal protein of blood and urine: 95.5% (698/731) with abnormal plasma cell of bone marrow. 10%— 84% was abnormal plasma cell. 88.3% (453/513) Serum M-protein, 44.3%(521/1176) with Bence Jones protein. 66.3%(688/1037) with Proteinuria. The maxima of was 24 hr urine protein is 13.7g.

## Immunology

1341 cases with immunological classification. (Results as Table 3). 30 of them transformed to plasma cell leukemia.

*Table 3. Immunologic classification of 1341 cases*

| Type | Number of cases | % |
|---|---|---|
| IgG | 519 | 38.70 |
| gG κ | 47 | 3.50 |
| IgG λ | 6 | 0.40 |
| IgG-BJP | 6 | 0.40 |
| Total | 578 | 43.10 |
| IgA | 250 | 18.60 |
| IgA κ | 5 | 0.40 |
| IgA λ | 9 | 0.70 |
| IgA-BJP | 2 | 0.10 |
| Semimolecular IgA | 2 | 0.10 |
| IgA double component | 1 | 0.07 |
| Total | 269 | 20.10 |
| Light chain κ | 74 | 5.50 |
| Light chain λ | 47 | 3.50 |
| Light chain D | 1 | 0.07 |
| Light chain disease | 142 | 10.60 |
| Total | 264 | 19.70 |

| | | |
|---|---|---|
| IgD | 89 | 6.60 |
| IgD κ | 5 | 0.40 |
| IgD λ | 15 | 1.10 |
| Total | 109 | 8.10 |
| IgM | 9 | 0.70 |
| IgM κ | 1 | 0.07 |
| Total | 10 | 0.80 |
| IgE | 0 | 0 |
| Cold BJP | 3 | 0.20 |
| Osteosclerotic myeloma | 1 | 0.07 |
| Smoldering myeloma | 4 | 0.30 |
| Solitary type transferred to light chain disease | 1 | 0.07 |
| Biclonal type* | 36 | 2.70 |
| Nonsecretory type | 40 | 3.00 |
| Unclassified | 26 | 1.90 |
| Total | 1341 | 100.00 |

*: Including light chain κ λ 21 cases, IgG κ-IgA κ 6 cases, $IgG_3$ κ λ, κ light chain γ heavy chain, λ light chain γ heavy chain, $IgG_2$ κ- $IgG_3$ λ, IgG-IgA λ, IgG-IgMκ, $IgG_2$-IgM, Mono-M transformed to bi-M protein 1 case and Bi-M protein 1 case.

### Laboratory Tests

Other laboratory findings: Hb<110g/L in 76% of the patients. In periferal blood, 11.9% of them with abnormal plasma cells, 2.4% with nucleated red blood cell, 1.5% with immature granulocyte. The peripheral blood smear showed rouleaux formation of the red cells in 6.6% cases. BUN>7. 1 mmol/L in 37.7%. Blood crea>177 μ mol/L in 38.3%. Serum level of uric acid>380 μ mol/L in 49.5%. Alkamic phosphatase>12 K-AU in 46.8%. Blood calcium level>2. 75 mmol/L in 24.9%. blood viscosity>3.0 in 24.2%. ESR increased in 79.4%.

### Renal Damage

Incidence of immunologic classified renla damage in 82 cases: 29.3% (12/41) of them were IgG type, 38.1% (8/21) IgA type, 42.9% (3/7) IgD type, 76.9% (10/13) light chain type. The differences between every type was significant ($P$<0.005). The light chain type was most significant.

### Plasma Cell Leukemia

30 cases transformed to plasma cell leukemia. 17 of them had obvious origin. 6 of them were IgG type, 5 were IgA type, 4 were light chain type, 2 were IgD type.

## DISCUSSION

### The Incidence of MM

MM is not rare in hematologic disorders. The author collected 2547 domestic cases published in 1980's. The number has increased to 4.9 times of what was published by Yao in 1950 — 1970's which was 522 cases in all.[3] The causes is unkown.

### Causes of Misdiagnosis

The statistical results of 2547 cases indicated that the clinical manifestations of MM is complex. The rate of misdiagnosis reaches 69.1%. The rate ranged from 54 — 100% published in literatures. Analysis of the causes: 1)The MM patients selected different departments when he went to hospital for the first time as the initial symptom and hysical finding varies; 2) MM has various complications while the aged patients tend to be acompanied by a lot of other diseases; 3) Over emphasis on the age of onset is over 40 years; and 4) At the beginning of MM it is usually of no typical manifestation. One patients in this group was diagnosed 20 years later after the onset.

By analysis of the cases, we have the following lessons to learn: 1) Pay more attention to the variety of its clinical manifiestation; 2)These patients who have one of the following symptoms: unexplained animia, bone pain, proteinuria, increase of erythrocyte sedimentation rate, hyperviscosity syndrome, hypercalcimia, hyperuricemia, hyperalkaline phosphatase, pathologic bone fracture and diffuse osteoporosis, should examine Bence Jones protein in uria, immunoglobulin analysis, immunoelectropheresis, examination of bone marrow at different sites and bone X-ray examination; 3) To the suspected cases whose immunoglobulin is not elevated, the immuno-binding electrophoresis and immunoflurescent antibody should be examined.

### Immunological Classification

By comparison, this group of patients had the following differences from that reported by Oken[4] in

1980: The incidence of IgG type was lower that Oken's group (56.8%), IgD type, nonsecreting type and biclonal type were higher than Oken's (0.67%, 0.33%, 0.67%). As same as the incidence reported abroad,[5] IgM type was very low in this group. The incidence of IgA type and light chain type was almost as the same as reprted by Oken. The majority of this group was monoclonal type. Only 2.7% was biclonal. One case λ llight chain type was transfered to κ λ light chain disease. Hobbs[6] had reported the same. The other case was transformed to MM from solitary plasmacytoma. The literature reported the incidence of this kind of transformation can be as high as 58,[7] 2.2% of our 30 cases transformed to plasma cell leukemia. This rate was almost as the same as 1/50 which was the literature had reported.[8] It seems to suggest that solitary plasmacytoma, MM and plasma cell leukemia have common pathogenesis base. In this group of patients, the incidence of IgA type, IgD type and light chain type of MM complicated with plasma cell leukemia was high. By statistics, there was no significant difference among the three. Because the sample was too small, we need further observation.

**Renal Damage**

Renal damage is the main complication and the early manifestation of MM. It can be 1-6 months early than the occurrence of other symptoms.[9] Raymond[10] reported that precede to its clinical manifestations, renal biopsy has found there is deposition of light chain in the renal glomerulus and tubules complicated with pathologic changed. So that the renal biopsy is helpful for early diagnosis. In this group of cases, the light chain type of renal involvement was 76.9% It was higher than the other types. $P<0.05$.

**ALP**

Generally, ALP is considered to be normal in MM. In our study, the level was elevated in 46.8% of cases. Usually, the elevation of ALP is considered one of the characteristics of osteoneoplasm, hyperparathyroidism or Paget's disease. The cases of our group were not accompanied by these diseases. The elevation of ALP may be due to one of the following reactions: Proliferation of osteoclast cells following the osteolytic lesion; The concentration of ALP in bone and renal cortex is high because MM mainly affect bone and kidney. Elevation of ALP is one of the clues to diagnose of the disease.

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