Idiopathic plasmacytic lymphadenopathy with polyclonal hyperimmunoglobulinemia: A syndrome related to giant lymph node hyperplasia of plasma cell type

Shigeo Mori,* Noboru Mohri,** Toshikazu Uchida,*** Tetsuro Shimamine****

*Department of Pathology, Faculty of Medicine, The University of Tokyo
**Department of Pathology, Faculty of Medicine, The University of Tokyo
***Department of Pathology, Nihon University School of Medicine
****Department of Pathology, Faculty of Medicine, The University of Tokyo

INTRODUCTION

Keller et al. (1972) classified giant lymph node hyperplasia (GLH, also known as Castleman lymphoma) into two subtypes: the hyaline vascular (HV) and plasma cell (PC) types. They described the clinicopathological features of the two subtypes and noted that while both had their own unique characteristics, many cases had characteristics of both types. They considered that the PC type might be an earlier, more active phase and the HV type may be a late phase, or that the two might be different phenotypes of a single disease. Since then, many PC-type GLHs have been reported, although it is questionable whether these reported cases are consistent with the PC-type GLH described by Keller et al.

Apart from GLH, since 1977, we have been interested in the existence of cases of unknown etiology characterized by extremely severe polyclonal hyperglobulinemia and swelling of the superficial systemic lymph nodes, and thus we have been compiling cases. It is unclear whether the etiology of these cases is the same, and whether they can be considered a single syndrome remains to be investigated. However, they share many characteristic clinical and histopathological findings and present a unique picture in terms of the outcome and prognosis, in that they have an indolent course, and no cases have been cured. In addition, when the clinicopathological characteristics of these cases were compared with those of PC-type GLH, almost all of the features were found to be consistent, except that the present cases did not have a localized mass. This article compares the clinical and histopathological data of the present cases [designated hereafter as idiopathic plasmacytic lymphadenopathy with polyclonal hyperimmunoglobulinemia (IPL)] with those of PC-type GLH and considers the distinctiveness of PC-type GLH.

1. Cases

The cases considered to be IPL in this article met the following criteria:

(1) Polyclonal hyperimmunoglobulinemia with serum IgG > 4,500 mg/dl and no M-protein.

(2) Generalized superficial lymphadenopathy, the largest of which should be the size of a fingertip on palpation or ≥ 1.8 cm in maximum diameter when actually measured, as well as a high degree of plasmacytosis shown by histology, with little or no destruction of the architecture.

(3) No known diseases associated with hyperglobulinemia.

Patients with the following diseases were excluded as described above (3):

Various infectious diseases
Collagen diseases, rheumatoid arthritis and its subtypes, Sjogren syndrome, various allergies, including drug allergies, hypersensitivity, so-called adjuvant diseases, myasthenia gravis, and hyperthyroidism
Hepatitis and liver cirrhosis
Hodgkin disease, non-Hodgkin malignant lymphoma, and other malignant tumors
Immunoblastic lymphadenopathy (polyclonal immunoblastosis)

Ten patients met the criteria described above (Table 1). Eight of these cases were from the University of Tokyo and Nihon University, and two (VI and X) were provided by Kanto-Teishin Hospital and Kawasaki Medical School. Cases I, II, III, VII, and X3 have been reported. Cases with markedly increased immunoglobulins and lymph nodes less than the size of a fingertip, as well as cases with IgG < 4,500 mg/dl were excluded from the present study.

2. Clinical findings of IPL and comparison with PC-type GLH

The clinical data for the ten IPL cases are summarized in Table 1. As shown in the table, the patients were mainly young adults at the time of consultation, and there was no remarkable medical or family history. In terms of occupation, cases I and II were a chemist and glassworker, respectively. The others were students, housewives, office workers, cab drivers, etc. The chief complaints were not severe at the time of the visit, and often consisted of a persistent low-grade fever or feeling somewhat tired. Some patients visited the clinic for a thorough examination after being diagnosed with increased blood sedimentation during a physical examination. In other words, almost all patients were discovered by chance and the actual point of onset could not be confirmed.

Physical examinations revealed enlarged superficial lymph nodes in all of the patients. The lymph nodes rarely exceeded the size of a thumbtack, and in terms of location, they were not confined to any part of the body but were systemic. In addition, hepatosplenomegaly was observed in many cases, and as a noteworthy sign, erythema of the skin often appeared in case II.

The laboratory findings showed marked hypergammaglobulinemia and hyperimmunoglobulinemia in all of the patients. In the fractions, IgG was increased to more than three times the standard value in all cases, whereas IgA and IgM increased markedly in most cases but were noticeably lower in two cases. M protein was negative in all cases. Urinary Bence-Jones protein was detected in four cases, consisting of both κ and λ chains. In addition, in most cases, the α2-globulin levels increased slightly and the serum cholesterol levels decreased.

Hematological examination revealed mild-to-moderate anemia in the majority of cases. The anemia was normocytic or normo-hypochromic. The serum iron levels were often low. In many cases, the number of plasma cells in the bone marrow increased.

Other relatively common laboratory abnormalities included increased erythrocyte sedimentation rate, strong positive C-reactive protein (CRP), positive direct Coombs reaction, and negative dinitrochlorobenzene (DNCB) skin reaction. Other abnormal findings among those omitted from the table were a small number of cases with elevated serum fibrinogen levels (cases II and IV), elevated serum copper levels (I and V), slightly increased leucine aminopeptidase (LAP) (V and VIII), and markedly decreased serum transferrin (I and VII). On the other hand, there were a few cases in which the rheumatoid arthritis (RA) reaction and various viral antibody titers were elevated, but these values fluctuated constantly with repeated testing, suggesting a pseudopositive biological reaction.

In most cases, the peripheral white blood cell fraction was normal. The lymphocyte counts were within normal limits. The T and B lymphocyte fractions were examined in cases I, II, VI, and IX and these were within normal limits. Peripheral lymphocyte function tests were performed in cases I and IV under the care of Professor Yata of the Department of Pediatrics, Tokyo Medical and Dental University, who reported that the peripheral T-cell suppressor function was enhanced in both cases.

The courses of many IPL cases remained unchanged or showed a slight exacerbation tendency (specifically, a gradual increase in serum gamma-globulin and serum immunoglobulin) for several years or more. During this period, only minor complaints, such as fatigability and feverishness, appeared, and the globulin levels were suppressed with small doses of steroids but returned to high levels after discontinuation. No patient achieved complete remission. Cases VII and VIII deserve special mentions in terms of their clinical courses and outcomes. As described above, case VII was a glass worker. A physical examination revealed the presence of abnormal chest shadows. He was referred for further testing and was found to have hyperproteinemia and hyperglobulinemia. He died after 16 years of treatment and observation. The patient was autopsied, and a significant plasmacytic interstitial pneumonia was found. In case VIII, their polyclonal immunoglobulin level continued to rise for six years. The corresponding polyclonal IgG-producing plasma cells infiltrated all reticuloendothelial organs of the body, initially reactively and later in an almost tumor-invasive manner, leading to their death. In both cases, the outcome was more progressive and uncontrolled until death, compared with the other cases of controllable hyperglobulinemia with no or slow progression.

Next, the clinical manifestations and IPL data described above were compared with PC-type GLH. The left side of Table 2 lists all the clinical findings for PC-type GLH in the original publication by Keller et al. The right side shows the frequency of these findings in IPL.

As shown in Table 2, many of the clinical findings for PC-type GLH were also observed in IPL. Both conditions shared the following 15 abnormalities: male predominance, fever and fatigability, splenomegaly, superficial lymph node swelling, accelerated blood sedimentation, anemia, thrombocytosis, bone marrow plasmacytosis, hypergammaglobu-
Table 1. Clinical data of the ten cases of IPL

| Case No. | Age (years) | Sex | Observation time (years) | Outcome | Chief complaints at the first visit | Hepatomegaly | Splenomegaly | Lymph node swelling | Erythrocyte sedimentation rate (mm/h) | Red blood cell count (x10^12/mm³) | White blood cell count (x10^9/mm³) | Lymphocyte count (x10^9/mm³) | Platelet count (x10^12/mm³) | Bone marrow plasma cell (%)
|----------|-------------|-----|--------------------------|---------|-----------------------------------|--------------|--------------|-------------------|-------------------------------------|----------------------------------|-------------------------------|-------------------------------|----------------------|-------------------|
| I        | 32          | M   | 6                        | Stable  | Fatigability                       | ++           | ++           | +++               | 172                                | 327                             | 3500                          | 770                           | 30                   | 4.4               |
| II       | 22          | M   | 4                        | Stable  | Nothing in particular (health check)| +            | +            | +                 | 150                                | 401                             | 7000                          | 2520                          | 30                   | 3.2               |
| III      | 34          | M   | 11                       | Stable  | Fatigability, mild fever           | ++           | ++           | +++               | 168                                | 191                             | 3600                          | 900                           | 13                   | 13.0              |
| IV       | 28          | F   | 4                        | Slightly progressive           | Fever       | ++           | ++               | 125                                | 298                             | 7300                          | 1970                          | 41                   | 9.0               |
| V        | 20          | M   | 5                        | Stable  | Fatigue, fever                     | -            | -            | ++               | 158                                | 350                             | 7000                          | 1400                          | 30                   | 7.0               |
| VI       | 57          | M   | 6                        | Stable  | Lymph node swelling                | +++          | -            | ++               | 152                                | 430                             | 7000                          | 2000                          | 35                   | 1.0               |
| VII      | 26          | M   | 16                       | Death   | Abnormal chest X-ray               | ++           | +            | ++               | 120                                | 330                             | 3300                          | 890                           | 13                   | 6.6               |
| VIII     | 28          | F   | 6                        | Death   | Fever, hepatosplenomegaly          | ++           | +++          | +++               | 140                                | 260                             | 5500                          | 275                           | 20                   | 3.6               |
| IX       | 35          | M   | 2                        | Stable  | Health check                       | -            | -            | +++               | 103                                | 510                             | 6000                          | 150                           | 25                   | 0.8               |
| X        | 31          | F   | 6                        | Stable  | Fever, lymph node swelling         | +            | -            | ++               | 347                                | 5300                             | 1590                          | 30                             | 3.3                 |                   |

| Serum protein | Serum iron | CRP | Direct Coombs test | Tuberculin test | DNCB skin test | Antinuclear antibody | Agglutination test for rheumatoid factor detection | Antiviral antibody | Antitoxoplasma antibody |
|---------------|------------|-----|-------------------|-----------------|----------------|----------------------|---------------------------------------------------|------------------|------------------------|
| Total protein | 11.5       | 0.80| 5.6              | 7800            | 1100           | 350                  | 100                                               | 32               | 6+                    |                      |
| α2G           | 5.6        |     | 7800             | 1100            | 350            | 100                  | 32                                               | 6+               | 6+                    |                      |
| γ-G           | 5.7        |     | 6800             | 950             | 271            | 125                  | 80                                               | 6+               | 6+                    |                      |
| IgG           | 12.0       | 6.00| ↑↑↑              | ↑               | ↑↑            | ↑↑                   | 96                                               | 6+               | 6+                    |                      |
| IgA           | 12.0       | 1.20| 6.0              | 271             | 125            | 80                   | 102                                              | 6+               | 6+                    |                      |
| IgM           | 12.0       | 2.12| 5.4              | 4500            | 350            | 400                  | 140                                              | 6+               | 6+                    |                      |
| Total cholesterol | 3.4        | 1.80| 5.9              | 6900            | 433            | 533                  | 126                                              | 6+               | 6+                    |                      |
| CRP           | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| Direct Coombs test | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| Tuberculin test | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| DNCB skin test | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| Antinuclear antibody | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| Agglutination test for rheumatoid factor detection | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| Antiviral antibody | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |
| Antitoxoplasma antibody | 13.4       | 0.74| 5.7              | 6800            | 950            | 271                  | 125                                              | 80               | 6+                    |                      |

Idiopathic plasmacytic lymphadenopathy
cases, small lymphocytes were present among the plasma of cells possessing various heavy and light chains. In many the peroxidase anti-peroxidase (PAP) method, with a mixture found to be polyclonal through immunohistochemistry using filled with mature plasma cells. These plasma cells were through the interfollicular areas and medulla, which was shown to be polyclonal IgG architecture, which is considered a form of neoplastic infiltration. However, these plasma cells still possessed polyclonal IgG autolysis, there appeared to be mild destruction of the archi-}

| Table 2. Comparison between the clinical data of PC-GLH and IPL |
|---------------------------------------------------------------|
| Features observed in PC-type Castleman disease     | Frequency in IPL |
| Male predominance                                          | yes              |
| Fever, fatigability                                        | 6/10             |
| Splenomegaly                                               | 6/10             |
| Superficial lymph node swelling                            | 10/10            |
| Increased erythrocyte sedimentation rate                   | 10/10            |
| Anemia                                                     | 9/10             |
| Leukocytosis                                               | 0/10             |
| Thrombocytosis                                             | 1/10             |
| Plasmacytosis in bone marrow                               | 8/10             |
| Hypergammaglobulinemia                                     | 10/10            |
| Hyperalpha2globulinemia                                    | 5/7              |
| Hyperfibrinogenemia                                        | 2/3              |
| Elevated alkaline phosphatase                              | 6/9              |
| Abnormal BSP retention                                     | 0/0              |
| Low serum iron                                             | 5/6              |
| Low serum transferrin level                                | 3/3              |
| High serum copper                                          | 2/4              |
| High serum ceruloplasmin level                             | 0/0              |
| increased leucine aminopeptidase level                     | 2/4              |
| Localized mass formation in one area of the body           | 0/10             |
| Relieved with mass removal                                 | not done         |

linemia, hyper-a2-globulinemia, hyperserum fibrinogen, elevated serum alkaline phosphatase, low serum iron, low serum transferrin, elevated serum copper, and elevated LAP. On the other hand, elevated white blood cell and platelet counts, which were usually seen in PC-type GLH, were rarely seen in IPL. In addition, in all cases of PC-type GLH, there was a localized mass in one area of the body, and removal of the mass often relieved the clinical symptoms. However, in IPL, although there was generalized lymphadenopathy, a localized mass in one region of the body was not found, despite careful workup.

3. Histology of IPL lesions and comparison with the histology of PC-type GLH

Twenty-eight lymph nodes biopsied from ten IPL cases and the excised spleen from case VIII were re-examined for histology.

The histological images of the lymph nodes were very similar, except for the late-stage lymph node of case VIII, which showed an extreme form of reactive plasmacytosis, with varying degrees of change depending on whether the patient was on steroid therapy. These lymph nodes were enlarged, mostly between 1.5 and 2.5 cm at the maximum diameter, without destruction of the underlying structure. The most conspicuous feature was the marked expansion through the interfollicular areas and medulla, which was filled with mature plasma cells. These plasma cells were found to be polyclonal through immunohistochemistry using the peroxidase anti-peroxidase (PAP) method, with a mixture of cells possessing various heavy and light chains. In many cases, small lymphocytes were present among the plasma cells, and a few large blasts were observed in some cases. The area of plasmacytosis extended from just below the capsule to the deep medulla. Therefore, in many cases, it was not easy to distinguish between the cortex and medulla (Figures 1, 2), resulting in follicles appearing as islands in the sea. However, in patients undergoing treatment, the area of plasmacytosis could be identified as the medulla (Figure 3).

The sinus was identified in all cases when observed carefully, although the size of the sinus varied from case to case and from specimen to specimen, even within an individual. The sinus was narrowed by plasma cells and was difficult to identify in many cases. In cases III and VII, many small nests of large histiocyte-like cells appeared in the sinuses, which appeared to be epithelioid.

The number of follicles increased considerably, except in the late stage of case VIII (Figures 1-4). They were distributed just below the capsule to the deep medulla. The germinal centers were in the form of reactive hyperplasia. The cells in the germinal centers were mainly centroblasts, centrocytes, and macrophages, which are normal germinal center components. The germinal centers were well-demarcated from the mantle zone. In nine of ten cases, blood vessels entered the germinal centers from outside the follicles (Figures 7 and 8). In seven of nine cases, the vessel wall was slightly thickened. However, there were no highly-branched, dendritic, or sclerotic vessels, clearly distinguishing them from the vascular changes in the germinal center of HV-type GLH.

The layer of small lymphocytes constituting the mantle zone was not very thick (Figures 4-8). In many cases, small lymphocytes in the mantle zone were arranged in concentric circles and often formed a single file pattern. Areas of plasmacytosis were observed immediately adjacent to the mantle zones (Figures 6 and 10).

Blood vessels also proliferated in the areas where plasma cells proliferated (Figure 5). Many of these vessels had a post-capillary-venule-like morphology.

In all cases, so-called tertiary follicles (translator’s note: nodular aggregates of T cells in the cortex) were found mainly under the capsule, but they were not well developed.

In contrast, the histopathology of case VIII was unique. The lymph node biopsied two years before death showed a histology almost consistent with that described above, with no destruction of the architecture, and the infiltrating plasma cells were mature and completely polyclonal, as shown by immunohistochemistry using the PAP method. The simultaneously excised spleen was massive (2,135 g) and showed a high degree of mature plasma cell proliferation in the medulla and paracortical regions. Two years later, autopsy revealed marked infiltration of mature plasma cells into various organs, including the lymph nodes and bone marrow. Although the lymph nodes were difficult to observe due to autolysis, there appeared to be mild destruction of the architecture, which is considered a form of neoplastic infiltration. However, these plasma cells still possessed polyclonal IgG antibodies.

A comparison of the histology of IPL lymph nodes
Idiopathic plasmacytic lymphadenopathy

Figure
(Translator’s note: The Japanese text in the blank space above Figure 1, including the Japanese calendar year of Showa 55, means “1980 Volume 20 Supplement”. The original Japanese article has been cited in several papers as having been published in 1980 or 1981, causing some confusion, but 1980 is the correct year.)

1: Lymph node in IPL, enlarged to 2.4 cm at the maximum diameter. The interfollicular area is highly hyperplastic. The follicles are also hyperplastic and distributed in an insular pattern throughout the lymph node. The sinusoids are compressed and difficult to see. (Case IV)

2: Same as Figure 1. (Case X, maximum diameter 2.2 cm)

3: Lesser degree of change, with marked hyperplasia of the follicle and interfollicular area, but the sinuses are clearly visible. (Case I, ×8)

4: Well-developed germinal centers, thin mantle zone, and enlarged parafollicular area. (Case IV, ×50)

5: There is a marked increase in the number of blood vessels in the parafollicular area. (Case II, silver impregnation stain, ×60)

6: There is a marked increase in plasma cells in the parafollicular area, which is in contact with the mantle zone. (Case I, ×120)

7: Vascular penetration into the germinal center; in IPL, the vessels in the germinal centers show only this level of development at best. (Case VIII, ×60)

8: Barely Hassall-like structure in the germinal center, which is significantly less developed than those in HV-type GLH. (Case IX, ×180)

9: Proliferating plasma cells are of a mature type. A small number of small lymphocytes are admixed. (Case VII, ×600)

10: PAP immunostaining, a: anti-kappa, b: anti-lambda, kappa-, and lambda-chain-bearing cells mixed in the same field of view.
described here with that of PC-type GLH in the original publication by Keller et al. is shown in Table 3.

As shown in the table, there was no distinction between the two conditions at the histological level. In PC-type GLH, the mass had a lymph node structure with a high degree of plasmacytosis between the follicles, occasional residual sinuses, normal or slightly hyperplastic germinal centers, and occasional vascularization of the germinal centers, all of which are consistent with the histology of the lymph nodes in IPL. In contrast, the maximum diameter of the masses ranged from 3 to 11 cm in PC-type GLH, and the individual components of the fused masses ranged from 2.5 to 7 cm. This is considerably larger than the lymph nodes in untreated IPL cases, which range from 2.0 to 3.3 cm.

DISCUSSION

The essential pathogenesis of the cases reported in this paper is clinically polyclonal hyperimmunoglobulinemia of unknown etiology, with the exception of a particularly severe form of reactive polyclonal plasmacytosis in the lymph nodes. Most of the clinical manifestations of IPL described in this paper are considered to be ancillary to essential conditions. Systematic searches for such a group of cases have rarely been reported, with only a few sporadic case reports.

It is dangerous to assume that all ten cases of IPL described here are a single entity. In addition, the criteria in this article for IPL are highly artificial, and it is undisputed that there are many cases with similar clinicopathological features but to milder degrees. Nevertheless, we are interested in this group of cases and collected them for two reasons. First, patients with this condition share common clinical symptoms, courses, and outcomes, and we hope that this will provide guidance in formulating a treatment plan and estimating the prognosis when we encounter such patients in the future. The other reason is that we believe that some of these cases may have a common etiology, specifically failure of the B-cell proliferation mechanism, and we are seeking clues to the pathogenesis, including this possibility. We hope to accumulate more such cases in the future and deepen the clinical, histological, and cellular immunological data.

Next, we will discuss the relationship between GLH and IPL, which is a key theme of the present study. Keller et al. were the first to define PC-type GLH. They considered GLH a distinct entity and subclassified it into HV- and PC-types. This classification was based on clinicopathological characteristics and not on etiology or pathogenesis. Therefore, when discussing PC-type GLH, it is necessary to assume that only those cases that fit their clinicopathological definition should be referred to as such. The basic clinical and histopathological features of PC-type GLH, as described by Keller et al., are that there is a localized mass formation in one area of the body where the mass is a lymph node (or tissue with a lymph node structure) with markedly increased polyclonal plasma cells in the interfollicular area, and that the various clinical abnormalities, including hypergammaglobulinemia, disappear with removal of the mass.

The clinicopathological features of IPL were compared with those of PC-type GLH. While there are fundamental differences in the size of the enlarged lymph nodes and whether they are localized, and relatively minor differences in the presence or absence of leukocytosis and thrombocytosis, the other abnormalities are almost completely consistent. In other words, if the criteria for localized masses were removed from the Keller et al. criteria for PC-type GLH, and systemic PC-type GLH was allowed to exist, at least the majority of IPLs would fall into this category. However, as mentioned above, we assumed that GLH should not exceed the definition of Keller et al. without limitations, and therefore, the two diseases should be distinguished. The multifaceted similarities between the two diseases pose a question when considering the etiology and pathogenesis of GLH. This similarity raises the possibility that common factors may be involved in the pathogenesis of both diseases (GLH and IPL). It is possible that the same factors that act locally in GLH or processes similar to those occurring locally in GLH may be involved on a systemic scale in at least some IPL cases. However, it would be fruitless to discuss this hypothesis further unless the pathogenesis mechanism of PC-type GLH is further elucidated.

Lastly, one of the authors (Uchida) reported a thought-provoking case with hyperimmunoglobulinemia and peculiar histology of the lymph nodes, in which the patient died after a lapse of approximately one year. The histology of the lymph nodes in this case, taken at a relatively early stage, showed markedly increased vascularity in the germinal centers, as well as onion-skin fibrosis and hyalinosis of the adventitia of the vessels, giving rise to a Hassall body-like structure. The interfollicular area showed small vessel proliferation and fibrosis, and moderate proliferation of polyclonal mature and immature plasma cells was observed. In the late stage, polyclonal plasma cells (mainly immature) markedly increased in number and took a form that could be described as neoplastic proliferation with mild structural destruction, while the germinal centers were markedly atrophic. The histology of the early resected lymph nodes showed a combination of histological features of both HV-
and PC-type GLH, although immature cells were present in the interfollicular area. It is interesting that such morphological changes can occur in systemic lymph nodes. In addition, the histology of the lymph nodes at the end of the disease was interesting because it was thought that the plasma cells remained polyclonal and grew in a tumor-like manner, suggesting similarity to case VIII in the present report. Furthermore, this case was not included in the present report because the serum IgG level was 3,500 mg/dl, but it can be assumed that such cases are very similar to the group of ten typical cases of IPL in the present report.

CONCLUDING REMARKS

We described the clinical and pathological characteristics of ten patients with severe polyclonal hyperimmunoglobulinemia and extremely high levels of polyclonal plasma cytosis in systemic lymph nodes of unknown etiology (IPL) and compared these characteristics with those of plasma cell-type giant lymph node hyperplasia (PC-type GLH).

We showed that IPL has the majority of the abnormal clinical findings and histological features of PC-type GLH and that the two diseases are clinicopathologically similar. In contrast to PC-type GLH, where the mass is localized and clinical symptoms disappear when the mass is removed, IPL lacks such a localized mass, which is a distinct difference between the two diseases.

We argued that PC-type GLH and IPL should not be regarded as the same disease entity at this time and pointed out that they may share some common pathogenesis mechanisms.

ACKNOWLEDGMENTS

We would like to express our deepest gratitude to Prof. Mizu Kojima for his comments on this article; Dr. Tadahiro Onishi of Kanto-Teishin Hospital, Dr. Kazuhide Yamamoto, Dr. Jishu Ito, and Dr. Hiromichi Sato of Kawasaki Medical School for providing samples and clinical records; Associate Prof. Ryuichi Kamiyama of Tokyo Medical and Dental University, Lecturer Keijiro Kitamura, Associate Prof. Atsuo Mikata of Keio University, Dr. Koji Namba of Kure Kyosai Hospital, and Prof. Masahiro Kikuchi of Fukuoka University for providing ideas and information; and Prof. Junichi Yata of Tokyo Medical and Dental University for providing immunological data.

REFERENCES

1. Keller AR, Hochholzer L, Castleman B. Hyaline-vascular and plasma-cell types of giant lymph node hyperplasia of the mediastinum and other locations. Cancer. 1972; 29: 670-683.
2. Mori S, Mohri N. [Clinical pathological analysis of systemic nodal plasmacytosis with severe polyclonal hyperimmunoglobulinemia]. Proceedings of the Japanese Society of Pathology. 1978; 67: 252-253.
3. The third department of Internal Medicine, The University of Tokyo. [A case of generalized lymph node swelling and hepatosplenomegaly with hyperproteinemia, and marked plasma cell proliferation on biopsy]. Diagnosis and Treatment. 1974; 62: 990-1006.
4. Akanuma Y, Mikami R, Nakamura M, et al. [A case of plasma cytotic interstitial pneumonia of unknown origin associated with hyperproteinemia]. The Medical Frontline. 1964; 19: 2459-2466.
5. Yamamoto K, Ishikawa S, Sakoda H, et al. [A case of lymphadenopathy with plasma cell infiltration and marked polyclonal hyperglobulinemia]. Journal of the Japan Society of the Reticuloendothelial System. 1980; 20(suppl): 113-127.
6. Delsol G, Familiades J, Voigt JJ, et al. [Dysimmunologic and pseudolymphomatous adenopathies. I. Immunoblastic and plasmocytic lymphadenopathies]. Ann Anat Pathol (Paris). 1977; 22: 41-60.
7. Kitamura K, Tamura N, Hatano H, et al. [A case of plasmacytosis with multiple peculiar eruptions]. Japanese Journal of Clinical Dermatology. 1979; 33: 891-899.
8. Kahn LB, Ranchod M, Stables DP, King H, Yudelman I. Giant lymph node hyperplasia with haematological abnormalities. S Afr Med J. 1973; 47: 811-816.
9. Sethi G, Kepes JJ. Intrathoracic angiomatous lymphoid hamartomas. A report of three cases, one of iron refractory anemia and retarded growth. J Thorac Cardiovasc Surg. 1971; 61: 657-664.
10. Notomi A, Iwamoto Y, Kikuchi M. Giant lymph node hyperplasia with fever, anemia, hypergammaglobulinemia and jaundice. Nihon Ketsueki Gakkai Zasshi. 1976; 39: 11-19.
11. Yu GSM, Carson JW. Giant lymph-node hyperplasia, plasma cell type, of the mediastinum, with peripheral neuropathy. Am J Clin Pathol. 1976; 66: 46-53.
12. Uchida T, Shikata T, Sakurai I, et al. [A case of systemic plasma cell dysplasia]. Japanese Journal of Cancer Clinics. 1979; 25: 731-740.