Successful Treatment of Idiopathic Plasmacytic Lymphadenopathy with Polyclonal Hypergammaglobulinemia

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A 51-year-old male was admitted because of eyelid edema and anosmia, which developed in 1985. He showed bilateral cervical lymphadenopathy, with nodes larger than 2 x 2 cm, and remarkable eyelid edema. Anemia, hyperimmunoglobulinemia with hypo-albuminemia (no M-protein) and liver dysfunction were found. Bone marrow, renal function, urine analysis and LDH level were normal. Cervical lymph node biopsy showed interfollicular proliferation of plasma cells without any malignant appearance. On day 3 of oral prednisolone (PD), anosmia abruptly improved and from day 7, eyelid swelling, cervical lymphadenopathy and gammopathy subsided gradually. Since PD was tapered off, no relapse has been observed thus far.

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Key words: Castleman’s disease, eyelid swelling, anosmia, prednisolone therapy, IPL

Introduction

Mori and associates gave a clinical and pathological review of 10 cases of idiopathic plasmacytic lymphadenopathy with polyclonal hyperimmunoglobulinemia (IPL) in 1980 (1). Although there has been some controversy concerning the relationship of IPL to Castleman’s type systemic lymphadenopathy with polyclonal hyperimmunoglobulinemia, several case reports have been published on IPL. We report successful treatment of a patient with plasmacytic lymphadenopathy with hyperimmunoglobulinemia who also showed anosmia and eyelid swelling due to a post-ocular mass. This case fulfilled the diagnostic criteria for IPL, and also showed interesting clinical manifestations.

Case Report

A 51-year-old male office worker gave chief complaints of eyelid swelling and anosmia. He had no notable history up to 1985, and there was nothing notable in his family history. The patient was well until 1985 when he noticed that his sense of smell had disappeared. He consulted an otolaryngologist but the etiology of anosmia was not elucidated. He occasionally felt epigastric discomfort; endoscopic study at a clinic revealed the presence of a gastric ulcer at stage A1. Antacid treatment eliminated his gastric symptoms. In January 1989, he noticed swelling of his eyelids, and was admitted to a hospital for evaluation. Hepatorenal function was normal. Polyclonal hyperimmunoglobulinemia (IgG 9,349 mg/dl, IgA 233 mg/dl, IgM 146 mg/dl) and low complement levels (C3 29.7 mg/dl, C4 8 mg/dl, CH50 13.7 U/ml) were found. Bone marrow survey showed no myeloma cells, and no laboratory values indicative of collagen diseases were obtained. Therefore, the patient was given no specific treatment for eyelid swelling. In May 1989, he was admitted to Nagoya National Hospital for further examination of the etiology of eyelid swelling.

On Admission, the patient was 164 cm in height and weighed 50 kg. The patient was conscious and alert and had no mental disorders. Sensation was normal except for complete anosmia. Remarkable bilateral swelling of the eyelids was found. The conjunctivae were not anemic or icteric. Multiple lymphadenopathy, with nodes measuring from 0.5 x 0.5 cm to 3 x 3 cm was observed in the neck region. The chest was normal on auscultation and percussion. No organomegaly was observed on abdominal palpation.

The laboratory findings are shown in Fig. 1. Chest X-ray film showed mild hilar lymphadenopathy with no mediastinal mass. Abdominal CT scan showed no specific findings such as organomegaly or retroperitoneal lymphadenopathy. Brain CT scan is shown in Fig. 2 (orbital

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Tanabe et al

WBC 6,800 /μl (Seg 39%, Stb 8%, Mono 4%, Eos 2%, Lym 47%)
RBC 354×10^6/μl
Hb 10.8 g/dl
Ht 34.6 %
Pit 38.0×10^4/μl
TP 12.4 g/dl
Alb 2.1 g/dl
α₁-glb 1.3 % (normal: 0.80~1.80)
GOT 59 IU/I
α₂-glb 4.0 %
GPT 97 IU/I
β-glb 2.2 % (normal: 0.80~1.60)
LDH 244 IU/I
γ-glb 74.1 % (normal: 1.00~1.50)
γ-GTP 143 IU/I
ALP 805 IU/I
ChE 0.33 ApH
BUN 18 mg/dl
Cr 1.2 mg/dl
T-chole 92 mg/dl
TG 40 mg/dl
Na 130 mEq/l
K 4.3 mEq/l
Cl 96 mEq/l
UA 8.7 mg/dl
CPK 15 IU/I
viscosity (whole blood) 5.6 cp
(serum) 2.4 cp
RA 15 IU/ml
ds-DNA 0 U/ml
Cold Agg ×8
SS-DNA 1.6 U/ml
Toxoplasma ×256
CH₅₀ <6 U/ml
EBNA ×8
ANA (−)
EB-VCA-IgM ×4
Urine analysis: RBC (−), Protein (−)
Bone marrow: TCC 7.5×10⁶/μl, Meg 2×31.2/μl, Plasma 3%

Fig. 1. Laboratory findings on admission.

Fig. 2. Brain CT scan at the orbital line. Bilateral Mm. rectus lateralis are swollen, and have the density of soft tissue. Pseudotumor was suspected from the radiological findings. Other slices did not reveal space-occupying lesions in the cranium. A cervical lymph node was biopsied and the histological sections are shown in Fig. 3 (hematoxylin-eosin staining and Unna Pappenheim staining for plasma cells). The pathological features and clinical findings supported the diagnosis of IPL. Oral prednisolone therapy was then started. The subsequent decrease in polyclonal immunoglobulin and other aspects of the clinical course are illustrated in Fig. 4. Prednisolone was very effective in reducing hyperimmunoglobulinemia; on day 3 of prednisolone treatment, the patient’s sudden and complete recovery from anosmia was obtained. Brain CT scan at the orbital line revealed complete remission of the paraorbital pseudotumor. In approximately one and a half years afterwards, no relapse of symptoms has occurred without prednisolone treatment, and hyper immunoglobulinemia is well controlled.

Discussion

Mori and associates (1) reviewed cases of IPL and adopted the following diagnostic criteria for this disease: 1) polyclonal hyperimmunoglobulinemia without M-protein (Ig-G must exceed 4,500 mg/dl); 2) systemic lymphadenopathy with the biggest lymph node exceeding 1.8 cm in diameter, pathologically, high plasmacytic infiltration without deterioration of the basic structure; 3) the absence of other diseases including infection, collagen and autoimmune diseases, hepatitis and liver cirrhosis, malignancies and immunoblastic lymphadenopathy. The present case showed polyclonal hyperimmunoglobulinemia with a serum IgG level of 9,349 mg/dl at the time of diagnosis, and no M-component was detected. Multiple cervical lymphadenopathy with a node diameter of 3 cm and a post-ocular mass were observed. The lymph node specimen showed plasmacytic infiltration with normal structure. Infection was ruled out because of the rapid improvement with corticosteroid therapy over several months. Collagen disease was ruled out because of the absence of the characteristic clinical symptoms and autoimmune antibodies. Liver disease was unlikely as indicated by biochemical tests. Therefore this case was diagnosed as IPL. In the report of Mori et al (1) and in other case reports (2), IPL was characterized as a chronic but resistant disease in spite of the efficacy of corticosteroid therapy. The present case followed the same clinical course as the others with the exception that, in this case, the administration of only 5~10 mg of oral prednisolone therapy successfully controlled total protein and peripheral lymphadenopathy and completely eliminated anosmia and eyelid swelling.

IPL has been distinguished from plasma cell type Castleman’s disease (3) which is characterized as follows: 1) solitary lymphadenopathy with specific histopathological findings, 2) rapid improvement of systemic symptoms and hyperimmunoglobulinemia with the removal of the mass. Moreover, systemic type Castleman’s disease
IPL with Eyelid Swelling and Anosmia

Fig. 3. Pathological findings of the biopsied specimen of cervical lymphadenopathy. Left: Hematoxylin and eosin staining (upper ×100, lower ×400); Right: Unna-Pappenheim stain. Marked infiltration of plasma cells without conspicuous deterioration of the structure of the lymph nodes was observed.

CLINICAL COURSE

![Clinical course graph]

Fig. 4. Clinical course is illustrated. Oral prednisolone therapy was very effective for reducing hyperimmunoglobulinemia and clinical symptoms over several months.

has been termed “angiofollicular and plasmacytic polyadenopathy” (4), “multicentric giant lymph node hyperplasia” (5), “multicentric angiofollicular lymph node hyperplasia” (6) and “multicentric Castleman’s disease” (7). These have been considered to be the same disease entity as IPL by some authors. However, Frizzera (8) reported the co-existence of malignant neoplasm in his accumulated cases and Weisenberger (9) reported that multicentric angiofollicular lymph node hyperplasia could be divided into four groups as follows: 1) stable, 2) chronic, 3) relapsing and 4) lymphoma (25% of his cases progressed to lymphoma). Thus, careful follow-up of
this type of patient is necessary. In addition, Yoshizaki and associates recently reported that IL-16 plays an important role in Castleman's disease (10). Although we did not study the presence of IL-6 pathologically or the serum IL-6 level, it should be considered in future studies.

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References