Journal of Korean Medical Science
Vol. 10, No. 6, 453-456 December 1995

Xanthoma of the Liver in a Patient with Multiple Myeloma Associated with Hyperlipidemia

— A Case Report —

Hyunee Yim, M.D., Hee Jeong Ahn, M.D.,* Chanil Park, M.D.,* Jae-Yoon Cheon, M.D.**

Department of Pathology, Ajou University College of Medicine, Suwon, Korea
Departments of Pathology, and Internal Medicine,***
Yonsei University College of Medicine, Seoul, Korea

A case of xanthoma of the liver in a 61-year-old Korean woman with multiple myeloma, hyperlipidemia and xanthoma of the skin is described. Microscopically, the liver showed a multiple xanthomatous collection of foamy histiocytes as well as diffuse sinusoidal infiltration of the foam cells. This hepatic accumulation of foam cells seems to be related to hyperlipidemia of the patient. The mechanism of hyperlipidemia in multiple myeloma is discussed.

Key Words : *Multiple myeloma, Hyperlipidemia, Xanthoma of liver*

INTRODUCTION

Multiple myeloma (MM) is a malignant neoplasm of plasma cells, involving primarily the bone marrow, although other organs such as spleen, liver and lymph nodes can be secondarily involved(Kapadia, 1980). The serum lipid level is low in most patients with multiple myeloma, but in about 6 % of patients, hyperlipidemia is present, and the latter situation usually accompanies xanthoma of the skin(Lewis and Page, 1954 ; Lennard-Jones, 1960 ; Levin et al., 1964 ; Ozer et al., 1970). In those cases, histologic findings of xanthoma of the skin are well described. Infiltrations of foamy histiocyte in bone marrow, lungs, pleura and lymph nodes have also been described in the findings of autopsy of patients with multiple myeloma(Lennard-Jones, 1960 ; Levin et al., 1964 ; Thomas et al., 1973), but congestion and fatty infiltration are the only changes as yet described in the liver(Short, 1964). We herein describe a case of hepatic xanthoma occurring in a patient with multiple myeloma. To our knowledge, this report might be the first document on such a case.

Address for correspondence : *Chanil Park, M.D., Department of Pathology, Yonsei University College of Medicine, ShinChon-dong 134, SeoDaeMoon-gu, Seoul, Korea.*
Tel : 361-5254, Fax : 362-0860.

CASE PRESENTATION

A 61-year-old female had dizziness and headaches for several years, which had become aggravated during the last four months. She had a history of pyogenic arthritis of the right knee 5 years ago. She did not consume alcohol and was not diabetic. She complained of general weakness, easy fatigue, anorexia, nausea, indigestion and epistaxis. Physical examination revealed a blood presure of 120 /70 mmHg and a pulse of 78/min. The skin was slightly icteric and there were several small yellowish papules on abdomen and upper extremities. Her conjunctivae were pale and the liver and spleen were not palpable. Blood examination showed anemia (hemoglobin 8.5 mg/dl and hematocrit 24 %). The laboratory studies demonstrated an elevated serum protein (total protein 9.8 g/dl and albumin 2.1 g/dl) and mild elevation of the hepatic enzymes (SGOT 89 IU/L, SGPT 23 IU/L). All markers for hepatitis B and

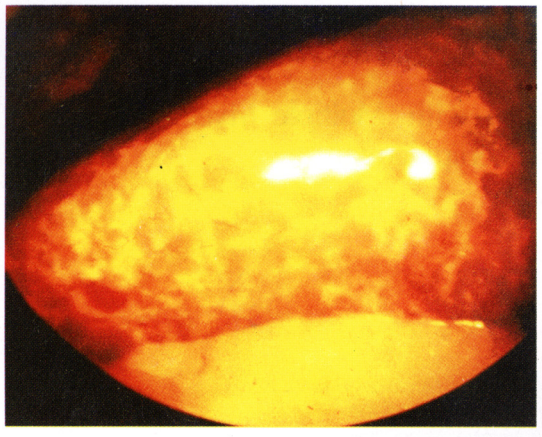

Fig. 1. Peritoneoscopic finding : The liver is diffusely enlarged with blunt margin. Surface reveals diffusely scattered yellowish pigmentation of reticulate pattern.

C viruses were negative. Serum levels of lipid were as follows ; total cholesterol 142 mg/dl (Ref ;120-220 mg /dl), triglyceride 644 mg/dl (Ref ; 44-166 mg/dl), and HDL-cholesterol 6 mg/dl (Ref ;30-80 mg/dl). Serum immunoelectrophoresis revealed monoclonal gammopathy of IgG, -light chain type, which strongly suggested the possibility of multiple myeloma. Soon thereafter, a bone marrow biopsy was performed, which showed packed marrow by diffuse infiltration of plasma cells, and the diagnosis of multiple myeloma was confirmed. To rule out possible chronic liver diseases which were suspected from the elevated hepatic enzymes, a peritoneoscopic liver biopsy was done. The liver on peritoneoscopy (Fig. 1) was diffusely enlarged with a blunt margin. The surface of the liver showed diffusely scattered areas of reticulate yellowish discoloration. Sections of the liver were examined with hematoxylin and eosin stain, Masson's trichrome stain and periodic acid Schiff stain with and without diastase treatment.

Microscopically, there were infiltrates of foamy histiocytes both as xanthomatous aggregates(Fig. 2) and diffusely in sinusoids(Fig. 3). The lobular architecture of the liver was partially disrupted by the xanthomatous lesion. The cytoplasm of histiocytes was not stained by periodic acid-Schiff stain with and without diastase treatment, but showed positive reaction for lysozyme by immunohistochemical stain using the LSAB method. Some hepatocytes showed nuclear glycogenosis. There was no evidence of amyloid deposit or infiltration of plasma cells.

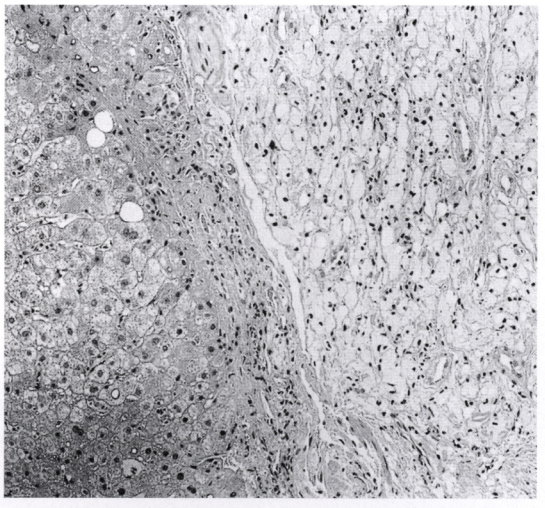

Fig. 2. Dense infiltration of foamy histiocytes forming xanthoma (H&E, ×100).

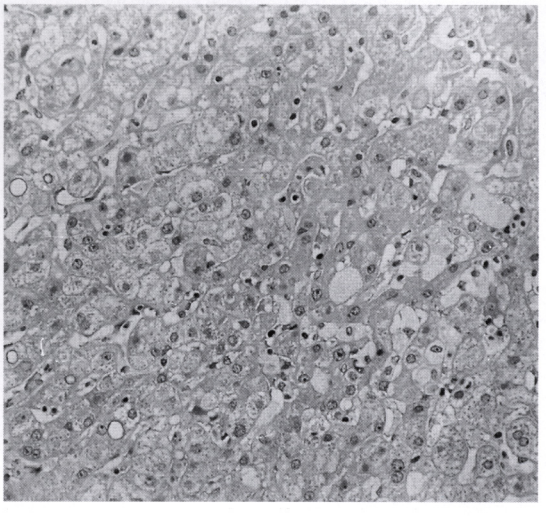

Fig. 3. Foamy histiocytes also infiltrate along the sinusoid. A few hepatocytes show nuclear glycogenosis (H&E, ×400).

DISCUSSION

Multiple myeloma is a neoplastic proliferation of plasma cells which arises almost exclusively in the bone marrow, although extraosseous reticuloendothelial organs such as liver, spleen and lymph node are involved in two-thirds of the patients with multiple myeloma at autopsy (Hayes et al., 1952 ; Pasmantier

and Azar, 1969 ; Kapadia, 1980). Signs of liver involvement are usually absent, although some series have reported that about 20 % of patients have hepatomegaly at the time of diagnosis (Kapadia, 1980). Mild elevation of liver enzymes, jaundice, and signs of portal hypertension as ascites and splenomegaly can also be seen as evidences of liver involvement (Droz et al., 1984 ; Peretz-Soler et al., 1985). Because the symptoms and signs of liver dysfunction are not a part of the classical clinical manifestations of multiple myeloma and the liver involvement in multiple myeloma is known not to have a prognostic significance, biopsies of liver are rarely performed even though the patients with multiple myeloma have signs of liver disease. So most of the histologic findings described on liver are from the autopsy or necropsy. The histologic findings of liver involvement include diffuse infiltration of plasma cells in the liver, either sinusoidal, portal or both, myeloid metaplasia, amyloid deposition, toxic hepatitis in association with medical treatment, congestion, and fatty change of hepatocytes. The incidence of plasma cell infiltration in the liver is in about 40 % of cases. Well defined tumor formation is rare, but present in 12 % of cases (Kapadia, 1980).

But in the case under reporting, there was neither dense infiltration of plasma cells nor atypical plasma cells, instead nodular and diffuse infiltration of foamy histiocytes was observed.

Such hepatic infiltration of lipid laden foam cells can be observed in hyperlipoproteinemia, Fabry's disease and mucolipidosis. Although the serum lipid levels in multiple myeloma are generally low, a few patients revealed hyperlipidemia and xanthomatosis(Lewis and Page, 1954 ; Lennard-Jones, 1960 ; Levin et al., 1964 ; Ozer et al., 1970). The patient under discussion had hyperlipidemia showing markedly increased serum triglyceride and decreased HDL-cholesterol. Other conditions causing hyperlipidemia such as diabetes, alcoholism and familial disorders were ruled out by the patient's history. Xanthoma of the skin and xanthomatosis of such visceral tissues as the lungs, pleura, kidneys and lymph nodes have been described in autopsies of the hyperlipidemic patients with multiple myeloma(Lennard-Jones, 1960 ; Levin et al., 1964 ; Thomas et al., 1973). But the liver, when not involved by the myeloma cells, appears to have only chronic passive congestion and fatty change (Short 1964). So the present report is of the first case of hepatic xanthoma in a patient with hyperlipidemia associated with multiple myeloma.

Hyperlipidemia in multiple myeloma can occur in a familial trait that is purely coincidental. In our case, there was no familial history of hyperlipidemia. Some authors detected lipid inclusions in myeloma cells and thus they claimed that lipoprotein might be synthesized by the myeloma cells, which is not convincing as yet and requires further investigation(Levin et al. 1964). Another explanation of hyperlipidemia in multiple myeloma is the possibly unusual affinity of serum lipoprotein to the newly formed myeloma protein(Lewis and Page, 1965). Beaumont(1970) suggested that the lipoprotein-paraprotein complex might occur due to an autoantibody activity of the paraprotein against serum lipoprotein, thus forming an immune complex, which in turn interrupts the normal metabolism of lipoprotein and resulting in hyperlipidemia. The lipoprotein-paraprotein complex has been demonstrated in many cases of cutaneous xanthoma associated with multiple myeloma by Taylor et al (1980). By the way, Baudet et al.(1980) have reported that human fibroblasts lead to a decreased degradation of the low-density lipoprotein and thus lose their regulatory function of intracellular cholesterol synthesis, when cultured with anti-lipoprotein IgA extracted from hyperlipidemic patients with multiple myeloma and xanthomatosis. Some investigators have proposed an alternative mechanism, in that the circulating myeloma protein might bind itself to heparin, blocking the activation of lipoprotein lipase(Glueck et al., 1972 ; Kilgore et al., 1985). It is very interesting that multiple myeloma could induce hyperlipidemia and xanthomatosis elsewhere. The liver could be also a victim for the xanthomatous involvement, regardless of myeloma cell infiltration.

REFERENCES

Baudet MF, Dachet C, Beaummt JL. *Interaction between fibroblasts, lipoprotein and three antilipoprotein IgA kappa. Clin Exp Immunol 1980 ; 39 : 455-60.*

Beaumont JL. *Autoimmune hyperlipidemia : An atherogenic metabolic disease of immune origin. Rev Europ Etudes Clin Biol 1970 ; 15 : 1037-41.*

Droz D, Noel LH, Carnot F, Degos F, Ganeval D, Grunfeld JP. *Liver invlvement in nonamyloid light chain deposits disease. Lab Invest 1984 ; 50 : 683-9.*

Glueck HJ, MacKenzte MR, Glueck CJ. *Crystalline IgG protein in multiple myeloma : identification of effts on coagulation and on lipoprotein metabolism. J Lab Clin Med 1972 ; 79 : 731-44.*

Hayes DW, Bennet WA, Heck FJ. *Extramedullary lesions in multiple myeloma : Review of literature and pathologic studies. Arch Pathol 1952 ; 53 : 262-72.*

Kapadia SB. *Multiple Myeloma : A clinicopathologic study of 62 consecutively autopsied cases. Medicine 1980 ; 59 : 380-92.*

Kilgore LL, Patterson BW, Parenti DM, Fisher WR. *Immune complex hyperlipidemia induced by apolipoprotein reactive immunoglobulin A paraprotein from a patient with multiple myeloma : Characterization of this immunoglobulin. J Clin Invest 1985 ; 76 : 225-32.*

Lennard-Jones JE. *Myelomatosis with lipidemia and xanthomata. Br Med J 1960 ; 1 : 781-3.*

Levin WC, Aboumrad MH, Rotzamm SE, Brantly C. *Y-type I myeloma and xanthomatosis. Arch Intern Med 1964 ; 114 : 688-93.*

Lewis LA, Page IH. *Serum proteins and lipoproteins in multiple myelomatosis. Am J Med 1954 ; 17 : 670-3.*

Lewis LA, Page IH. *An unusual serum lipoprotein-globulin complex in a patient with hyperlipidemia. Am J Med 1965 ; 38 : 286-97.*

Ozer FL, Telatar H, Telatar F, Muftuoglu E. *Monoclonal gammopathy with hyperlipidemia. Am J Med 1970 ; 49 : 841-4.*

Pasmantier MW, Azar HA. *Extraskeletal spread in multiple plasma cell myeloma : A review of 57 autopsied cases. Cancer 1969 ; 23 : 167-74.*

Peretz-Soler R, Esteban R, Allende E, Salomo CT, Julia A, Guardia J. *Liver involvement in multiple myeloma. Am J Hematol 1985 ; 20 : 25-7.*

Short JH. *Multiple Myeloma with xantoma formation : A report of a case. Arch Pathol 1964 ; 77 : 400-5.*

Taylor JS, Lewis LA, Battle JD, Butkus A, Robertson AL, Deodhar S, Roenigk H. *Plane xanthoma and multiple myeloma, with lipoprotein-paraprotein complexing. Arch Dermatol 1980 ; 114 : 425-31.*

Thomas FB, Clausen KP, Greenberger NJ. *Liver disease in multiple myeloma. Arch Intern Med 1973 ; 132 : 195-202.*