PRIMARY SYSTEMIC AMYLOIDOSIS — A VARIANT OF PLASMA CELL DYSCRASIA

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SYNOPSIS

A case of primary systemic amyloidosis with features of plasma cell dyscrasia is presented. The patient had macroglossia and bilateral carpal tunnel syndrome. The diagnosis was confirmed by tongue and rectal biopsies. Increased bone marrow plasma cells and the presence of urinary kappa light chains were present. Serum immunoelectrophoresis and skeletal survey were normal. The concept that primary systemic amyloidosis lies within the spectrum of plasma cell disorder is supported by its association with features of plasma cell disease without overt myelomatosis and by the immunochemical similarity of its fibril to that of myeloma amyloid.

INTRODUCTION

Primary systemic amyloidosis is a rare disease. Its prevalence is unknown. The incidence based on autopsy studies is about 0.5% (1) which does not differentiate between primary and other varieties of amyloidosis. In Singapore, there has been to date, only 1 case of primary systemic amyloidosis reported (2). We present here a second case. Unlike the first case which was a diagnostic challenge, our case showed typical clinical features which led to a prompt diagnosis.

CASE REPORT

On December 17, 1980 a 54 year old Chinese man was seen in the University Department of Medicine, Singapore General Hospital for the complaint of an enlarged tongue. He had noticed it for the preceding three months and was presently experiencing difficulty in speaking. He was able to swallow and breathe comfortably. On further questioning he also admitted having weight loss, fatigue and general malaise for the past year. He had numbness of both hands and mild edema of the legs for the same period of time.

There was no past history of note. There was no family history of similar illness. He was married with five children, all of whom were well. He did not drink alcohol but smoked ten cigarettes per day for the past twenty years.

On examination, his general condition was satisfactory. The tongue was grossly enlarged and felt indurated (Fig. 1). The overlying mucosa was normal. A 2 centimetre non-tender, right submandibular lymph node was present. His hands were of normal size. There was loss of sensation to pin-prick and touch in both hands over the median nerve distribution distal to the wrists (Fig. 2). There was mild pitting edema of both legs to mid shins. In the abdomen, the liver was enlarged 3 centimetres below the right costal margin. It had a smooth, non-tender edge. The spleen and kidneys were not palpable. The skin, chest, cardiovascular and central nervous systems were normal.

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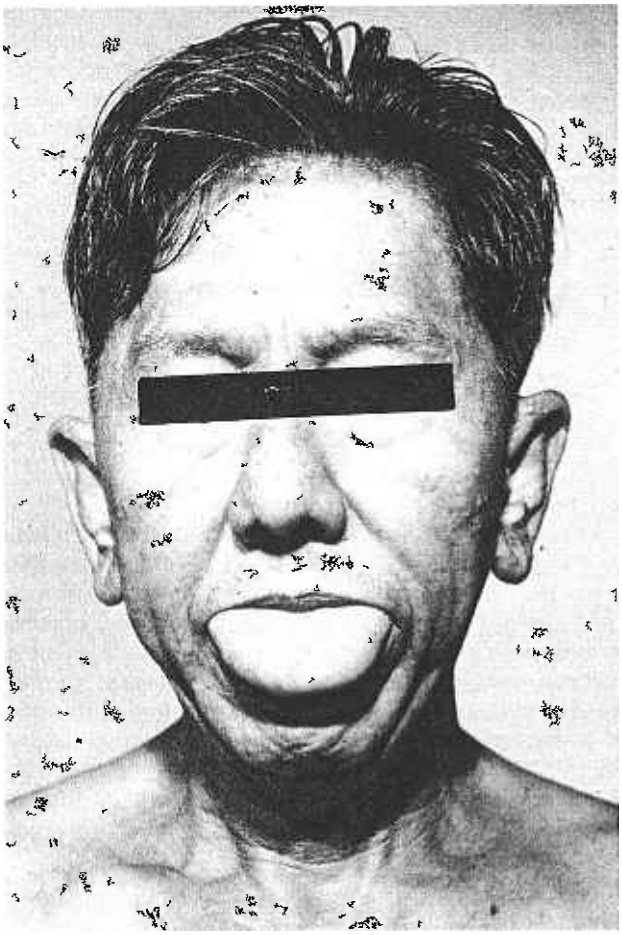

Fig. 1 Severe macroglossia in a 54 year old Chinese man producing speech difficulty.

The clinical diagnosis of primary systemic amyloidosis was made on the basis of the macroglossia and bilateral carpal tunnel syndrome. Investigations to confirm the diagnosis and to exclude hypothyroidism were performed.

INVESTIGATION

The hemoglobin was normal (13.6 Gm%). The white cell count (7,770/c.mm) and differential counts were normal. The platelet count was also normal. The erythrocyte sedimentation rate was 2mm in the first hour which is normal. Serum thyroxine level was normal (6.1 ug%) which excluded the possibility of myxedema. To confirm the diagnosis of amyloidosis, biopsies of the tongue and rectal mucosa were carried out which revealed amyloid deposits. The clinical diagnosis of bilateral carpal tunnel syndrome was confirmed by an electromyographic study. In view of the frequent complications of the heart and kidney in primary amyloidosis, investigations to exclude their involvement were carried out. The electrocardiogram and chest x-ray were normal. The renal function was normal as shown by the blood urea of 25 mg%, serum creatinine of 1.0 mg%, normal urine microscopy and a creatinine clearance of 95.7 mls/min. As the liver was enlarged clinically, liver function tests were performed which revealed normal levels of serum alkaline phosphatase (102 units/litre), SGPT (18 units/litre), SGOT (23 units/litre), bilirubin (0.3 mg%) and albumin (3.5 Gm%). Bone marrow aspiration revealed the

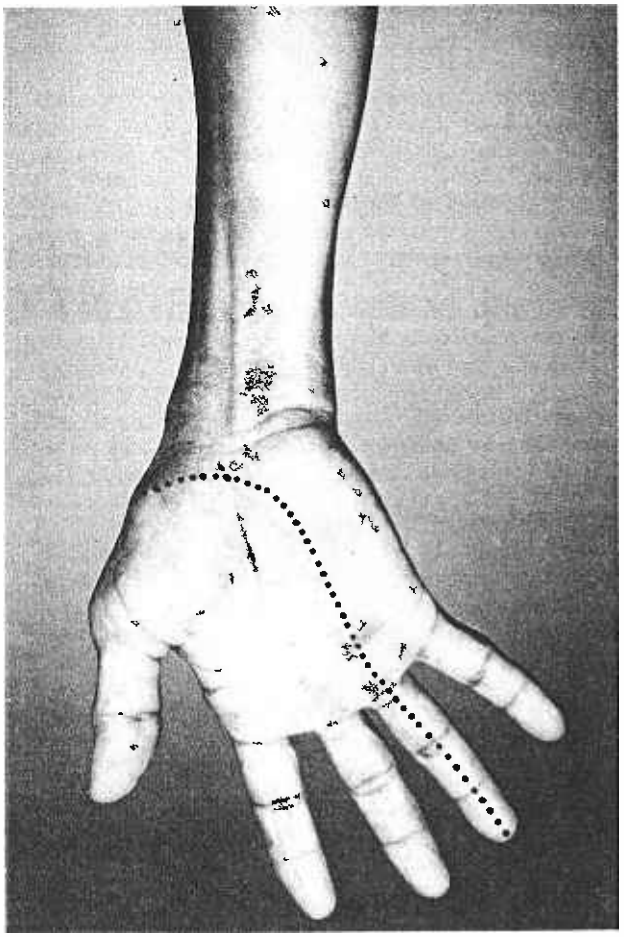

Fig. 2 Sensory loss to pinprick and touch over the median nerve distribution of each hand with wasting of the thenar muscles.

presence of approximately 16% plasma cells. There were the occasional binucleate plasma cells but the majority were normal. To exclude multiple myeloma, a full skeletal survey and serum immunoelectrophoresis were carried out. There were no osteolytic lesions or osteoporosis seen in the skeletal survey. The serum immunoelectrophoresis was normal. The urine immunoelectrophoresis revealed an M-band consisting of kappa light chains.

DISCUSSION

The clinical manifestations of primary systemic amyloidosis is highly variable. In one large series it was found that purpura, ankle edema and fatigue are the most common presenting symptoms (3). The same study found that the triad of purpura, macroglossia and bilateral carpal tunnel syndrome was pathognomonic of the disease. Specific organ dysfunction depends on the distribution and extent of amyloid deposition. The heart, kidney and gastrointestinal tract are commonly involved. Thus the cause of death is frequently intractable heart failure or renal failure.

Our patient presented with the classical features of macroglossia and bilateral carpal tunnel syndrome. The tongue and rectal biopsies confirmed the diagnosis of primary systemic amyloidosis. It is of interest that his bone marrow showed increased plasma cells and his urine showed kappa light chains. The normal skeletal survey and normal serum immunoelectro-

phoresis excluded overt multiple myeloma.

The relationship of primary systemic amyloidosis and multiple myeloma is an interesting one. About 15% of patients with overt myelomatosis develop amyloidosis which has clinical features and a distribution pattern indistinguishable from primary systemic amyloidosis. The association of primary systemic amyloidosis with increased bone marrow plasma cells was reported by Spitz in 1940. Since then the concept of primary amyloidosis as a varying aspect of plasma cell dyscrasia has gained general acceptance. The finding of increased plasma cells and the demonstration of serum M-type globulin or urinary light chains in patients with primary systemic amyloidosis are dependent on the rigorousness with which these associations are looked for (3), (6). That it is a variant of plasma cell disorder is further supported by immunochemical evidence. Whereas the composition of the amyloid fibril in the secondary and other forms of amyloidosis has no identifying amino acid sequence, that of the primary and the myeloma varieties consists of well defined fragments of immunoglobulin light chains (9). Immunochemically therefore, primary systemic amyloidosis and amyloidosis occurring with multiple myeloma are identical. This knowledge represents an important advancement in the understanding of amyloidosis. Inherent in this new information lies, perhaps, the therapeutic future of this condition which to date has received negligible impetus.

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REFERENCES

1. Cohen AS: Amyloidosis. N. Engl. J. Med. 277: 522-530, 1967.
2. Tay CH: Primary systemic amyloidosis presented as a diagnostic problems in one case. Sing. Med. J. 11: 193-199, 1970.
3. Kyle RA and Bayrd ED: "Primary" systemic amyloidosis and myeloma. Arch Int. Med. 107: 344-353, 1961.
4. Akin RK, Barton K and Walters PJ: Case report of amyloidosis. Macroglossia with myeloma in a 53 year old man. J. Oral Surg. 33: 690-692, 1975.
5. Barth WF, Glenner GG, Waldmann TA and Zelis RF: Primary amyloidosis. Ann. Int. Med. 69: 787-805, 1968.
6. Barth WF, Wilkerson JT, Walmann TA and Decker JL: Primary amyloidosis: clinical, immunochemical and immunoglobulin metabolism studies in fifteen patients. Amer. J. Med. 47: 259-273, 1969.
7. French JM, Hall G, Parish DJ and Smith WT: Peripheral and automatic nerve involvement in primary amyloidosis associated with uncontrollable diarrhoea and steatorrhoea. Amer. J. Med. 39: 277-284, 1965.
8. Glenner GG, Ein D and Terry WD: The immunoglobulin origin of amyloid. Amer. J. Med. 52: 141-147, 1972.
9. Glenner GG: Immunoglobulin and amyloid fibril proteins. Brit. J. Haematol 24: 533-537, 1973.