Skin and Mucosal Hemorrhage of Prolonged Duration in Systemic Amyloidosis

By Jacob Amir, Elena Kessler and André de Vries

A patient with primary systemic amyloidosis is described in whom skin and mucosal hemorrhages constituted the sole clinical manifestation for a period of 3 yr. The cause of the hemorrhagic disorder was widespread vascular deposition of amyloid. Characteristic features of amyloid purpura are emphasized.

The presently reported patient with systemic amyloidosis is clinically remarkable in that she had skin and mucosal purpura for about 3 yr as the sole manifestation of this disorder.

Case Report

E.S., a 56-yr-old housewife, mother of two healthy children, first admitted in May 1966, had for a year noted pinpoint red spots around the eyes, ears, mouth, and chin, appearing spontaneously or following even gentle scratching, and preceded by a peculiar sensation in the skin.

Physical examination revealed small crops of petechiae around the eyes, ears, and mouth, and on the gums and oral mucosa. Laboratory studies showed normal hematological values with a platelet count of 200,000/cu mm. Extensive studies of coagulation factor and platelet functions were normal. Capillary fragility test according to Rumpel-Leede was positive. Serum protein was 6.7 g/100 ml with globulin 2.7 g/100 ml, and a normal electrophoretic pattern on acetate cellulose. A skin punch biopsy from a petechial area was normal. After discharge, regular follow-up examinations, including hemostatic tests, erythrocyte sedimentation rate (ESR), and serum protein paper electrophoresis, were normal for 2 yr except for the continuous appearance of petechiae in the same areas.

In April 1968 the patient was readmitted because of the sudden appearance of an extremely fast ESR, 110 mm in the first hour. A walnut sized non-tender firm lymph node was palpated in the left axilla. Purpura and hemostatic studies were as previously. Following a routine ear, nose, and throat examination, severe subcapsular hematomas appeared on the tongue. Serum protein was 6.2 g/100 ml with globulin 2.9 g/100 ml. Paper and cellulose acetate electrophoresis showed a dense band in the gamma globulin region. Immunoelctrophoresis demonstrated an IgG "M" protein with gamma G-2 heavy chains and L light chains. Extensive X-ray studies were negative. A sternal bone marrow aspirate showed normal morphology. Rectoscopy revealed numerous petechial hemorrhages of the mucosa. A skin punch biopsy from a purpuric lesion in the neck did not reveal vascular changes. The excised axillary lymph gland showed slight reticular hyperplasia. The patient died in May 1969 following a cerebrovascular accident.

Autopsy showed numerous hemorrhages on the face and chin, and a large hematoma of the lower lip. The heart weighed 320 g. The liver and spleen were not enlarged.

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Hemorrhage in Systemic Amyloidosis

Fig. 1.—Arterial wall with amyloid deposit. Congo red stain. × 200.

weighing 1000 g and 70 g, respectively. Submucosal hemorrhages were seen in the large intestine. The brain showed small foci of softening. Amyloid deposits were found virtually in all organs, particularly in the blood vessels of the tongue, heart, lungs, kidneys, and skeletal muscles. Both larger (Figs. 1 and 2) and smaller blood vessels were involved. In the skin amyloid deposits were present in the derma and blood vessel walls. A review of the lymph gland biopsy made in 1968 with amyloid stain revealed amyloid deposits in the blood vessel walls and connective tissue. Similar reviews of the skin biopsies obtained in 1966 and 1968 were negative.

Comments

Hemorrhages are a common cutaneous and mucosal manifestation of amyloidosis1-7 and may rarely precede its other clinical symptomatology.3-7 Our patient had skin and mucosal purpura as an isolated phenomenon for about 3 yr prior to other clinical manifestations of amyloidosis.

Fig. 2.—The same vessel as in Fig. 1 viewed under polarized light.
Amyloid purpura is preferably localized in the upper part of the body, mainly on the face, neck, and upper extremities, and often on the eyelids and the sides of the nose. The lesions, which may appear spontaneously, may also be elicited by external pressure and even by gentle scratching. Mucosal hemorrhages in amyloidosis occur mainly in the mouth and rectum, but may manifest as gross gastrointestinal bleeding. In our patient, as in others reported, the striking features were the spontaneous and traumatic hemorrhages in the tongue. Remarkably, these occurred in the absence of macroglossia, a common sequel of amyloid involvement of the tongue.

In a few patients with primary systemic amyloidosis the hemorrhagic tendency has been found associated with blood-clotting abnormalities, such as factor X deficiency, decrease in factor V and VII, fibrinolysis, and hypofibrinogenemia. Such abnormalities were not detected in our patient. Furthermore, the purpura preceded the paraproteinemia. Amyloid deposition in the vessel wall, invoked in the pathogenesis of the hemorrhagic tendency in systemic amyloidosis, appears to furnish a sufficient explanation of the purpura in this patient.

REFERENCES

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