In A Pinch

Sameen Ahmed, BSc; Mike Kalisiak, MD, BSc and Maxwell B. Rogers, MD, FRCPC

A 60-year-old female presents with a three-year history of orange discolouration and easy bruising involving her eyelids. Her basic workup reveals proteinuria of 3.7 grams in 24 hours.

What's your diagnosis?

Primary systemic amyloidosis is a disease process caused by extracellular deposition of amyloid, which is an immunoglobulin light chain fragment produced in abnormally high amounts by plasma cells. Increased amyloid production usually results from a plasma cell dyscrasia or, less often, multiple myeloma. Deposition may occur in any organ, and often affects kidneys, heart, skin, blood vessel walls, mucosal membranes, peripheral nerves and salivary glands.

Cutaneous findings include papules, nodules or plaques that are waxy, smooth and shiny. There is also the presence of purpura, especially on the eyelids, neck, axillae or in the anogenital region. The blood vessels fragility is due to amyloid deposition in vessel walls and is responsible for "pinch purpura" petechia or ecchymoses occurring after minor trauma. This is a pathognomonic sign for amyloidosis (which was inadvertently elicited in our patient).

Overall five-year survival is about 20%.

Other common physical findings are macroglossia, mucosal hemorrhage, xerostomia (due to infiltration of salivary glands), hepatosplenomegaly and neuropathy. The classic presentation of systemic amyloidosis is macroglossia accompanied by carpal tunnel syndrome. Patients may complain of dyspnea and leg edema due to cardiac and renal involvement or vague symptoms, such as fatigue, weight loss, syncopal attacks and paresthesias.

Primary systemic amyloidosis often goes undiagnosed or is misdiagnosed. It is a disease of adulthood, with the usual age of onset being older than 60 years. Visualization of amyloid in tissue is necessary for diagnosis. A biopsy can be taken from a characteristic cutaneous or mucosal lesion, rectal mucosa, gingiva or tongue, or an aspirate of subcutaneous fat can be performed. With Congo red staining, amyloid appears orange-red on light microscopy and shows characteristic apple-green birefringence under polarized light. Once the diagnosis is confirmed, further investigative studies usually include a bone marrow aspirate and biopsy in search of an underlying plasma cell dyscrasia, as well as other investigations to delineate the extent of systemic involvement.

The median survival is one to two years and varies depending on organ involvement. Overall five-year survival is about 20%. Treatment approaches include supportive measures only, chemotherapy (most commonly melphalan and prednisolone) and stem cell transplantation. Several novel therapies are under investigation.

In our patient, the skin biopsy was positive for amyloid, serum protein electrophoresis revealed monoclonal lambda chain paraproteinemia and the bone marrow aspirate showed an increase of plasma cells to 8% (normally approximately 2%). The skeletal survey and the abdominal ultrasonography were normal. Echocardiography demonstrated normal ejection fraction.

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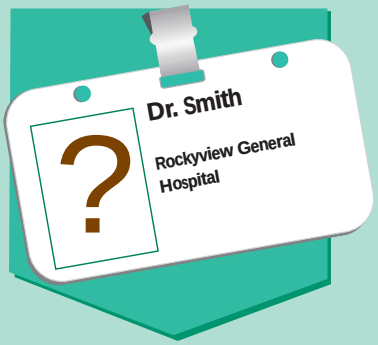
Ms. Ahmed is a fourth-year medical student, Dalhousie University, Halifax, Nova Scotia.

Dr. Kalisiak is a third-year Dermatology Resident, Edmonton, Alberta.

Dr. Rogers is a Dermatologist, Edmonton, Alberta.



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