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Amyloidosis - A rare case report in Bangladesh

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ABSTRACT

CASE REPORT

Amyloidosis is a disorder where there is extracellular deposition of insoluble protein in different tissues and organs. AL amyloidosis is the commonest type where monoclonal immunoglobin light chain secreted by plasma cells is deposited as amyloid fibrils in tissues which can lead to multiorgan failure. This disorder is a rare and complex condition characterized by the deposition of amyloid proteins in tissues, leading to their dysfunction. The condition may be localized or systemic, with a wide range of clinical manifestations depending on the organs involved, such as the heart, kidneys, liver, gastrointestinal tract, and nervous system. We report a 50-year-old lady with multiple joint pain and multiple papulovesicular lesion around oral cavity, eye, around anus and macroglossia. She was diagnosed as a case of AL amyloidosis by clinical features and skin biopsy. She was put on oral lenalidomide and dexamethasone. This type of papulovesicular lesion is rare form of skin manifestation in AL amyloidosis. The importance of early recognition, multidisciplinary management, and improved healthcare resources in addressing rare diseases like amyloidosis in low-resource settings such as Bangladesh. Awareness campaigns and capacity building in healthcare systems are vital for timely diagnosis and intervention.

INTRODUCTION:

Amyloidosis is a disorder where there is extracellular deposition insoluble misfolded protein in different tissues and organs. AL amyloidosis is the commonest type where monoclonal immunoglobin light chain secreted by plasma cells is deposited as amyloid fibrils in tissues which can lead to

multiorgan failure. [1] Petechiae, purpura and ecchymoses are the usual form of skin involvement due to infiltration of blood vessel walls by amyloid deposit. [2] Here we are reporting a case with multiple joint pain and papulovesicular skin lesion.

Amyloidosis is a type of protein conformational disorder caused by specific proteins' capacity to adopt an unstable tertiary structure, resulting in polymerization into insoluble amyloid fibrils in the extracellular space of diverse tissues. Twenty-seven proteins have been identified as amyloidogenic precursors. Immunoglobulinic amyloidosis, commonly known as AL or "primary" amyloidosis, is the most frequent and severe kind of amyloidosis. It is characterized by fibrils composed of a monoclonal immunoglobulin (Ig) light chain. [3] AL amyloidosis is usually a systemic illness that affects several organs and tissues. Less frequently, it presents as a local disease, limited to a single tissue or organ, caused by focal infiltration of a plasma cell clone secreting amyloid-forming LC, which does not develop to multi-system involvement. As a result, the disease spectrum of AL amyloidosis is broad, ranging from mild symptoms in some patients with localized AL amyloidosis that can be managed with local therapy to life-threatening disorders in those with multiple organ deposition that necessitate prompt diagnosis and aggressive therapy to ensure survival. [4]

AL amyloidosis is thought to be 5 to 10 times less common than multiple myeloma, but it is the most common type of systemic amyloidosis in Western countries, with an incidence of approximately 9 cases per million inhabitants per year, whereas the frequency of AA amyloidosis has significantly decreased due to improved treatment of chronic infectious and inflammatory diseases. [5] AL amyloidosis affects men slightly more than women. The average age of diagnosed patients is 65 years, with around 10% being under 50 years old.

Amyloidosis is a rare localized and systemic condition caused by the extracellular deposition of various fibrillar proteins, resulting in alterations in tissue architecture or function. There are numerous forms of amyloidosis based on their precursor proteins. The most frequent kind of systemic amyloidosis is immunoglobulin light chain (AL). [4] The signs and symptoms of amyloidosis are determined by the kind of amyloid protein accumulation and the organs affected. The heart, kidney, liver, skin, gastrointestinal tract (GIT), autonomic and peripheral nerve systems are the most commonly affected organs. Amyloid protein may accumulate in the joints, joint capsules, and articular cartilage. Amyloid arthropathy refers to the arthroscopic symptoms of amyloidosis. Amyloid arthropathy is a very uncommon form of amyloidosis. [5] This may be the only presenting feature of systemic amyloidosis. Most patients with this ailment may experience pain and swelling in various joints, as well as morning stiffness, which might mimic rheumatoid arthritis. [5] Polyarthropathy occurs more frequently in b2-microglobulin-derived amyloidosis, which exacerbate chronic renal failure with haemodialysis, but is infrequent in amyloid light-chain (AL) amyloidosis. [6]

With the exception of the central nervous system, systemic AL amyloidosis can impact every organ. Asthenia and dyspnea are the most common presenting symptoms; nevertheless, they are not very specific and may be the cause of delayed diagnosis. The 2010 International Society of Amyloidosis meeting in Rome modified the agreed criteria for defining organ involvement in systemic AL amyloidosis. [9]

CASE PRESENTATION:

A 50-year-old lady was admitted to our hospital with history of pain in multiple joints for 2 years and skin lesion in different parts of

body for 1 year. Joint pain was insidious in onset, gradually progressive, involved all the small and large joints, inflammatory in nature, associated with joint deformity and morning stiffness for about 2 hours.

Skin lesions were raised, fluid filled, around her mouth, upper lip, around eyes, around her anus, painless, not itchy, no abnormal sensation. There was no history of photosensitivity, skin rash, oral ulcer, alopecia, chest pain, eye problem, frothy or scanty urine. Her bowel and bladder habit were normal. She is non-diabetic, normotensive, no history of any heart disease. She has a history of total abdominal hysterectomy.

On general examination, she was moderately built and poorly nourished, conscious and well oriented, pulse and temperature were normal. BP-120/80 mm Hg. She was moderately anaemic but there was no jaundice, oedema, koilonychia, leukonychia or lymphadenopathy. Examination of skin reveals multiple papulovesicular lesion around oral cavity, eye, around anus, non-tender, no abnormal sensation, no discharge or crusting.

Examination of abdominal system reveals macroglossia but no organomegaly. Other systemic examination including cardio-respiratory system, nervous system was unremarkable.

Laboratory investigation reveals Hb-11.8 gm/dl, normal WBC and platelet count, ESR 35 mm in 1st hour. PBF shows normocytic normochromic red blood cells, CRP- 132 mg/L, RBS 8.0 mmol/L, S. creatinine- 0.66 mg/dl, S. electrolytes: Na-132 mmol/L, K-5.1 mmol/L, Cl-105 mmol/L, S. Ca- 9.5 mg/dl, iPTH-3.0 mg/dl, Normal Urine RME, 24 hours urinary protein was 0.17 gm, S. albumin- 37 gm/L, autoantibodies: ANA 5.71 AU/ml, Anti-ds DNA 0.64 AU/ml, RA test- 9.31 IU/ml, Anti CCP- <0.40 U/ml.

CXR was normal. Echocardiography revealed no regional wall motion abnormality at rest. EF-65%, USG of whole abdomen shows right kidney 9.3cm and left kidney 9.7cm, cortical echogenicity is raised, corticomedullary differentiation was poor suggesting bilateral renal parenchymal disease, Urine for Benes Protein-absent. Serum protein electrophoresis shows Alpha-2 region raised, normal immunofixation study.

Skin biopsy and histopathology from lower lip shows epidermis hyperkeratosis and few follicular plugs containing demodex folliculorum. The superficial and upper part of dermis revealed organophilic deposits of amyloid like material. It shows apple green birefringence in polarized microscopy. A diagnosis of AL Amyloidosis was made and patient was put on oral lenalidomide and dexamethasone as the patient did not agree on any parenteral drugs.

DISCUSSION:

AL amyloidosis is a rare condition which has a peak incidence in the 7th to 8th decade of life. It affects men slightly more than women. [10] Incidence of AL amyloidosis is about 4.5/100000 population, but the actual incidence may be a lot higher as significant portion of this disease remain undiagnosed. It can occur with multiple myeloma, lymphoma or Waldenstrom's Macroglobulinemia. [1] Amyloidosis presents with nonspecific symptoms like fatigue and weight loss until symptoms of specific affected organ develops. Kidney is the most commonly affected organ, heart being the second commonest. It can also affect the liver, spleen, nerves, joints and skin. Macroglossia is a pathognomonic sign of AL amyloidosis. [11] In amyloid arthropathy there is thickening of synovial membrane. It most commonly affects the wrist and shoulders. [1]

Chemotherapy, which suppresses the underlying plasma cell clone secreting amyloid-forming Ig LC, is the primary treatment for systemic AL amyloidosis. A balance between amyloid formation and deposit clearance leads to AL amyloidosis. The treatment shifts the balance in favor of tissue breakdown of deposits by reducing or

stopping the generation of amyloidogenic proteins. [12] Individual factors and the affected organ determine the extent of monoclonal protein secretion reduction needed for amyloid deposit regression. While amyloid infiltration of the heart muscle takes years to reverse, hepatic deposits can often be reduced in 3–4 months, even if the reduction in serum free LC levels is incomplete.

Amyloidosis treatment is frequently quite complicated, frequently combining chemotherapy, transplantation, and research procedures. Treatment choices will depend on the type of amyloid, the degree of organ involvement, and the specific mutation; these can only be developed in a specialized unit with the necessary knowledge. [13]

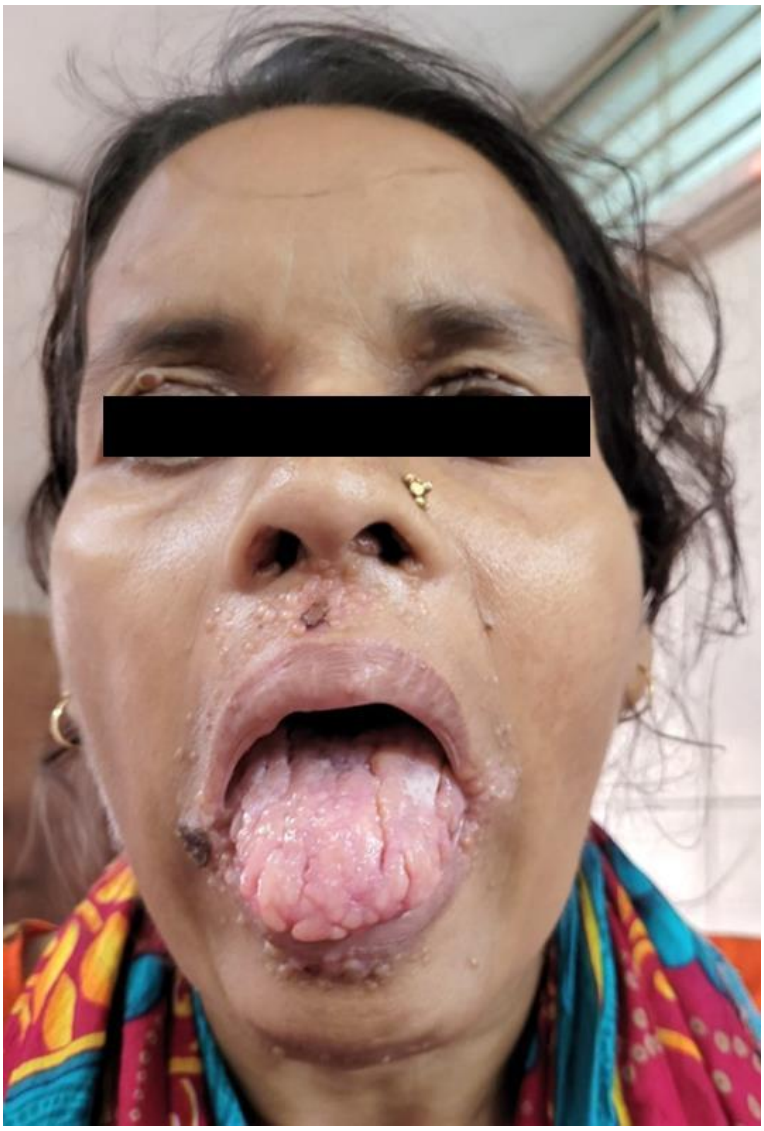
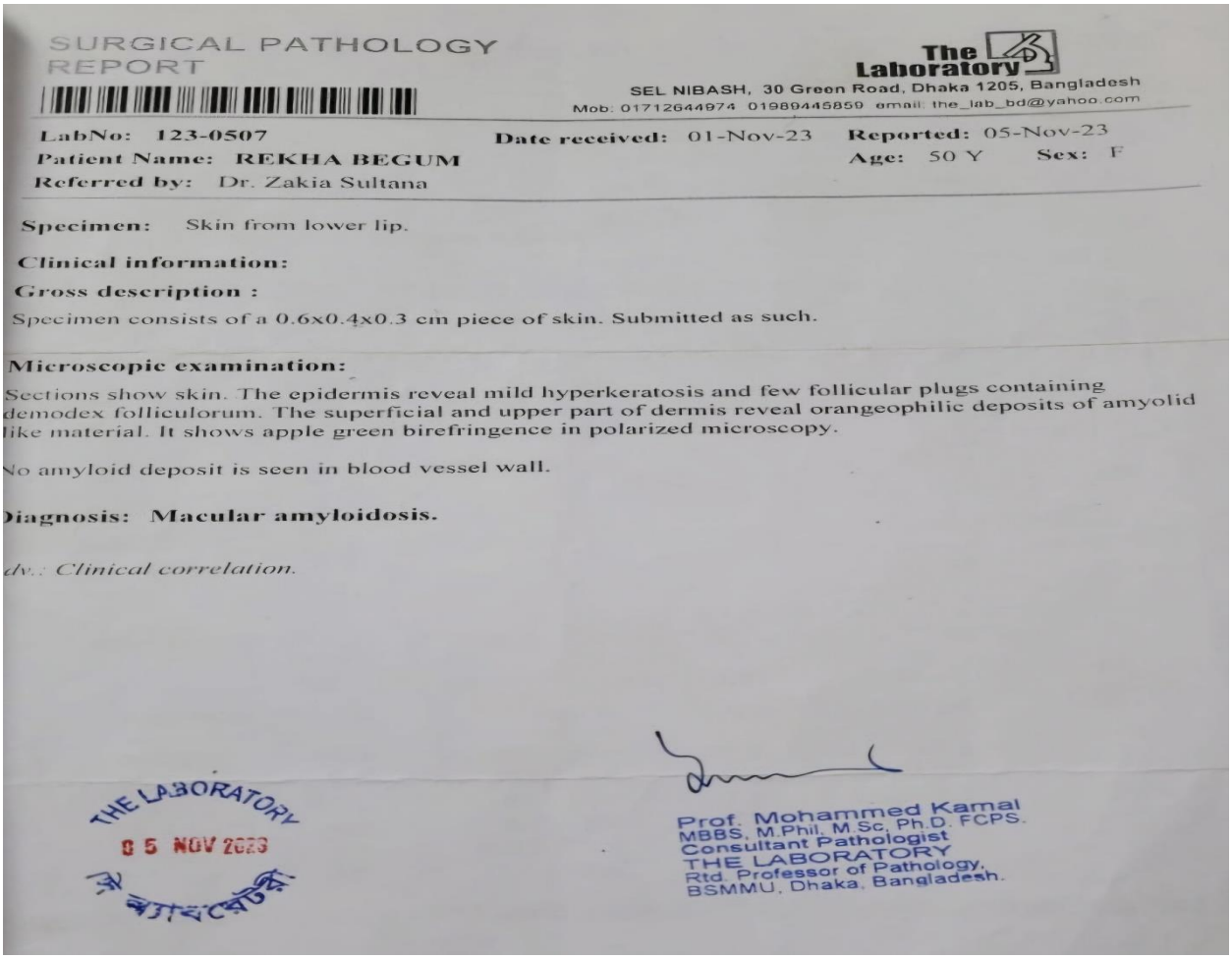


Figure-1: Photograph showing multiple papulovesicular lesion around oral cavity and eye with macroglossia


SURGICAL PATHOLOGY REPORT

The Laboratory
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LabNo: 123-0507 Date received: 01-Nov-23 Reported: 05-Nov-23
Patient Name: REKHA BEGUM Age: 50 Y Sex: F
Referred by: Dr. Zakia Sultana

Specimen: Skin from lower lip.

Clinical information:

Gross description :

Specimen consists of a 0.6x0.4x0.3 cm piece of skin. Submitted as such.

Microscopic examination:

Sections show skin. The epidermis reveal mild hyperkeratosis and few follicular plugs containing demodex folliculorum. The superficial and upper part of dermis reveal orangeophilic deposits of amyolid like material. It shows apple green birefringence in polarized microscopy.

No amyloid deposit is seen in blood vessel wall.

Diagnosis: Macular amyloidosis.

dv.: Clinical correlation.

THE LABORATORY
05 NOV 2023

Prof. Mohammed Kamal
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Figure-2: Histopathology of skin from lower lip shows amyloid like material in superficial and upper part of dermis which shows apple green birefringence in polarized microscopy

Our patient had no organomegaly, no significant proteinuria, no suggestive finding of cardiac involvement in echocardiography. Protein electrophoresis and immunofixation also revealed no significant abnormality. But our patient had macroglossia which is a pathognomonic sign of AL amyloidosis.

Cutaneous manifestation in AL amyloidosis depends on where the amyloid deposition occurs. If the deposition is in the superficial dermal layer, it can manifest as shiny waxy translucent papules. [14] Amyloidosis has a predilection to flexural sites including the neck, axillae, eyelids, retroauricular area, inflammatory area, umbilicus, inguinal and anogenital area. It can also affect the lips, central face, tongue, buccal mucosa. [2]

Our patient presented with multiple papulovesicular lesion around oral cavity, eye, around anus. Skin biopsy and histopathology from lower lip shows epidermis hyperkeratosis and few follicular plugs containing demodex folliculorum. The superficial and upper part of dermis revealed organophilic deposits of amyloid like material. It shows apple green birefringence in polarized microscopy. All of these confirms the diagnosis of amyloidosis. Though Petechiae, purpura and ecchymoses are the usual form of skin involvement due to infiltration of blood vessel walls by amyloid deposit, our patient had none of these. [2]

CONCLUSION:

This case demonstrates uncommon type of skin manifestations of AL amyloidosis in the form multiple papulovesicular lesion around oral cavity, eye, around anus without any evidence of liver, spleen, heart involvement. Skin biopsy and histopathology from lower lip confirmed the diagnosis of amyloidosis.

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