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Case Report

Primary Systemic Amyloidosis

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Abstract: Primary systemic amyloidosis is a rare entity. We report a case of primary systemic amyloidosis without any associated hematological abnormality who presented with macroglossia and hemorrhagic lesions around eyes and sub mammary region. There were soft lobulated masses around perianal region, labia majora and on external auditory meatus obstructing auditory canal. She was also operated for carpel tunnel syndrome in thepast. Urine and serum electrophoresis were negative. Diagnosis was confirmed by biopsy of submammary skin lesion using haematoxylin and eosin and Congo red stain. Polarized microscopy was used to see birefringence of amyloid.
Key words: *Amyloidosis, Primary systemic amyloidosis, macroglossia, carpal tunnel syndrome, electrophoresis.*

Introduction

Amyloidosis is a broad and complex class of diseases that comprises several etiologies, many manifestations, and a diversity of outcomes. It is a generic term that refers to extracellular deposition of fibrils composed of low molecular weight subunit of variety of normal serum proteins. Despite more in-depth assessment and accurate classification, survival for patients with primary systemic disease remains poor.

Case Report

In June 2012, a 61years old Pakistani female presented to our dermatology unit with complaint of lobulated outgrowths from both sides of tongue, perianal region and external auditory meatus for last 2 years. There was history of papules and plaques on periorbital and submammary regions for 2 years. Skin lesions were not associated with itch or burning sensation. There was history of occasional hematuria, hematochazia and bruises on different sites of body without associated trauma. She had been operated recently for carpel tunnel syndrome. She was nonsmoker and there was no history of any substance abuse.

On examination, her pulse and blood pressure were normal. Pitting type pedal edema was present. There were soft lobulated swellings with bluish tinge on both sides of tongue having tooth indentations along its lateral borders (Figure 1).There were hemorrhagic papules coalescing to form plaques on purpuric base in periorbital an submammary areas, (Figures 2&3) A lobulated outgrowth from external auditory meatus obstructing the canal was noted (Figure 4). A similar 4 cm long lobulated soft swelling from perianal region (Figure 5) and another one on labia majora were documented. Nails showed longitudinal splitting and ridging (Figure 6). Rest of systemic examination was normal.

Her laboratory workup showed normal blood picture, liver and renal functions. Urinalysis revealed significant proteinuria and microhematuria. Serum and urine protein electrophoresis were negative for Bence Jones proteins. Skin biopsy from sub mammary lesions showed classic homogenous, faintly eosinophilic deposits in papillary dermis along with thinning of rete ridge (Figure 7). The Congo Red showed birefringence.

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Discussion

Systemic amyloidosis is classified as primary systemic amyloidosis (usually with no evidence of preceding or coexisting disease, paraproteinemia, or plasma-cell dyscrasia), amyloidosis associated with multiple myeloma and secondary systemic amyloidosis with evidence of coexisting previous chronic inflammatory or infectious conditions[1].

Primary systemic amyloidosis involves the deposition of insoluble monoclonal immunoglobulin light chains or fragments in various tissues[1]. Unlike the normal L-chain and the usual form seen in patients with myeloma, these L-chains undergo partial lysosomal proteolysis within macrophages and are extracellularly deposited as insoluble amyloid filaments attached to a polysaccharide[2].

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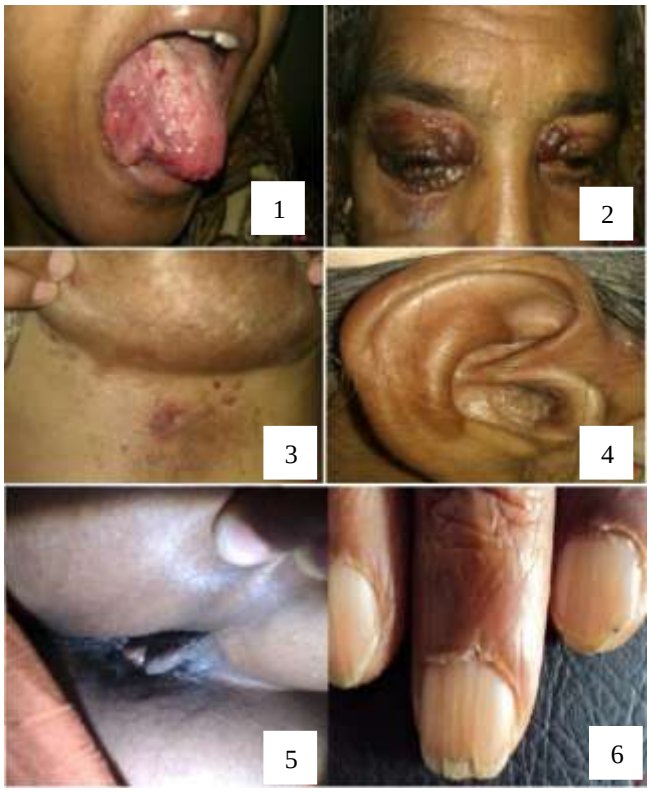

Figure 1. Soft lobulated swellings with bluish tinge on both sides of tongue having tooth indentations along its lateral borders

Figures 2&3. Hemorrhagic papules coalescing to form plaques on purpuric base in periorbital an submammary areas

Figure 4. A lobulated outgrowth from external auditory meatus obstructing the canal was noted

Figure 5. 4 cm long lobulated soft swelling from perianal region

Figure 6. Nails showed longitudinal splitting and ridging.

The incidence of primary systemic amyloidosis is estimated to be 5.1-12.8 cases per million person-years with no sex or racial predilection[3,4]. It usually presents in seventh or eighth decade of life. Clinical presentation includes fatigue, weight loss, paresthesias, hoarseness, mucocutaneous lesions, carpel tunnel syndrome, hepatomegaly and edema Clinically evident mucocutaneous involvement occurs in 30-40% of patients with primary systemic amyloidosis while secondary systemic amyloidosis does not involve the

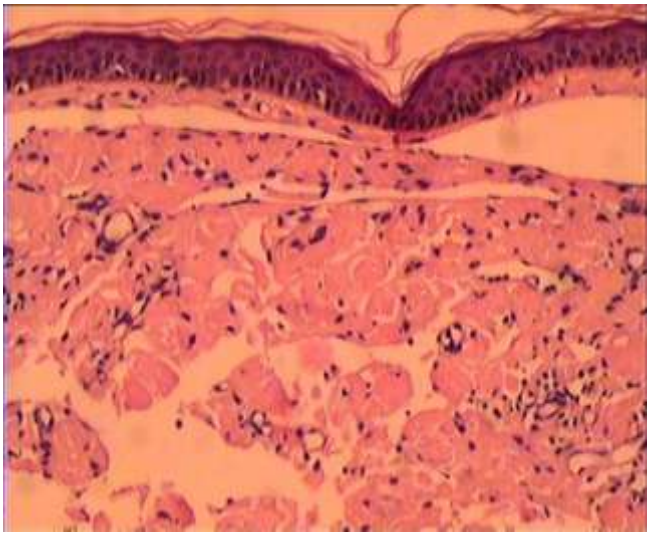

Figure 7: Eosinophilic deposits of amyloid in the dermis (H&E X 100)

Figure 8. Birefringence (Congo Red X 100)

skin. Petechiae and ecchymoses are the most common skin findings.The face is most commonly affected (pinch purpura or raccoon eyes sign). Purpuric lesions are found in flexural regions such as the nasolabial folds, neck, and axillae. The most characteristic skin lesion consists of waxy papules, nodules, or plaques that may be evident in the eyelids, retroauricular region, neck, or inguinal and anogenital regions. Plaques may coalesce to form large tumors[5]. Dystrophic nail changes include brittleness, crumbling, and subungual striation. Macroglossia is a classic feature of primary systemic amyloidosis. The presence of amyloid in the oral cavity is often revealed by localized, soft, elastic papules[6,7]. Amyloid deposition in the smooth and striated muscles, connective tissue, blood vessel walls, and

peripheral nerves may result in myocardial insufficiency, which is the most common cause of death in this fatal disease. Renal amyloidosis usually manifests as proteinuria, often resulting in nephrotic syndrome. Edema is frequently found and may be the result of cardiac failure or nephrotic syndrome. Amyloid infiltration of the gastrointestinal tract may result in hemorrhage or malabsorption. Hepatomegaly occurs in about 50% of patients with primary systemic amyloidosis, but splenomegaly is present in less than 10% of patients. Autonomic and sensory neuropathies are relatively common features.

Kyle and Bayrd reported that laboratory studies revealed anemia in less than 50% of the cases[3]. The white cell count was usually within the reference range, and the erythrocyte sedimentation rate was higher than 50 mm/h in one half of the cases. Hepatic function was abnormal, and the serum creatinine level was increased in 50% of patients. Proteinuria was present in more than 90% of the cases.

Immunoelectrophoresis of serum and concentrated urine samples is essential[4]. Echocardiography usually reveals a concentrically thickened left ventricle and often a thickened right ventricle, with a normal-to-small cavity.

Biopsy of a cutaneous lesion has the advantage of safety and a high diagnostic yield. Routine hematoxylin-eosin staining may show a homogenous, faintly eosinophilic mass if enough amyloid is present as seen in our case (Figure 7). The best way to identify amyloid is to stain paraffin-embedded sections with alkaline Congo red and to examine them with polarized light to elicit a green fluorescence. (Figure 8)

The treatment of primary systemic amyloidosis is directed toward the affected organ and the specific type of the disease. In studies different regimens of intermittent oral melphalan and prednisone have been used[8,9]. The prognosis of primary systemic amyloidosis is generally poor. Cardiac failure and renal failure are the major causes of death. The median survival in most reported cases is as long as 14.7 months. The prognosis depends on the response to therapy and the extent of disease[10].

Our case showed characteristic mucocutaneous lesions, macroglossia, dystrophic nails and heavy deposits of eosinophilic material in papillary dermis. There was typical birefringence on Congo Red stains. She was prescribed oral steroids and is under regular follow up till date. Primary systemic amyloidosis should always be suspected in such scenario when macroglossia and new mucocutaneous lesions are observed in the elderly with signs of systemic involvement.

References

1. Hayman SR, Bailey RJ, Jalal SM, Ahmann GJ, Dispenzieri A, Gertz MAet al. Translocations involving the immunoglobulin heavy-chain locus are possible early genetic events in patients with primary systemic amyloidosis. Blood 2001;98:2266-8
2. Divry P, Florkin M, Firket J. Sur les proprietesotiques de l'amiloide. *C R Soc Biol*.1927;97:1808-10
3. Kyle RA, Bayrd ED. Amyloidosis: Review of 236 cases. *Medicine*1975;54:271-299
4. Kyle RA, Greipp PR. Amyloidosis (AL). Clinical and laboratory features in 229 cases. *Mayo Clin Proc*.1983;58:665-83
5. Lutz ME, Pittelkow MR. Progressive generalized alopecia due to systemic amyloidosis. *J Am AcadDermatol*. 2002;46:434-6
6. Moura CG, Moura TG, Duraes AR, Souza SP. Exuberant macroglossia in a patient with primary systemic amyloidosis. *ClinExpRheumatol*. 2005;23:428
7. Xavier SD, Bussoloti IF, Muller H. Macroglossia secondary to systemic amyloidosis: case report and literature review. *Ear Nose Throat J*. 2005;84:358-61
8. Skinner M, Anderson J, Simms R, Falk R, Wang M, Libbey C et al. Treatment of 100 patients with primary amyloidosis: a randomized trial of melphalan, prednisone, and colchicine versus colchicine only. *Am J Med*. 1996;100:290-8
9. Kyle RA, Gertz MA, Greipp PR, Witzig TE, Lust JA, Lacy MQet al. A trial of three regimens for primary amyloidosis: colchicine alone, melphalan and prednisone, and melphalan, prednisone, and colchicine. *N Engl J Med*. 1997;336:1202-7
10. Roy A, Roy V. Primary systemic amyloidosis. Early diagnosis and therapy can improve survival rates and quality of life. *Postgrad Med*. 2006; 119: 93-9