Generalized Primary Anetoderma: A Rare Case

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Abstract: Anetoderma is a rare elastolytic disorder characterized by localized areas of slacks skins, that are reflection of a marked reduction or absence of dermal elastic fibers, that can appear as round or oval atrophic lesions, and wrinkling or sac-like protrutions. The predilection of lesions are on the trunk, thigh, and upper arms, and rarely occur on generalized distribution,. Primary anetoderma occur when there is no underlying cutaneous diseases, but could be associated with autoimmune diseases such as antiphospholipid syndrome and autoimmune connective tissue diseases. The aim of this report was to present a rare case of generalized primary anetoderma. A 19-year-old female had asymptomatic, multiple, small, circumscribed, round and oval atrophic lesions and sac-like protrution on almost all part of the body since 6 years ago without preceding cutaneous diseases. Histopathological examination with Verhoeff-Van Gieson elastin stain revealed fragmented and decreased of elastic fibers from superficial dermis until mid-dermis, and loss of elastic fibers in mid-dermis that confirmed the diagnosis of anetoderma. Laboratory test for autoimmune connective tissue diseases and antipospholipid syndrome were negative. Anetoderma is a benign disease, but can remain active for many years resulting in considerable aesthetic deformity, moreover in generalized distribution. Although no autoimmunologic abnormalities, long term follow-up is mandatory as an early warning signs of future symptoms of autoimmunity.

1 INTRODUCTION

Anetoderma is an uncommon disease characterized by focal loss of elastic tissue, resulting well-circumscribed areas of atrophic skin or sac-like protrutions (Bilen et al., 2003). The pathogenesis of anetoderma is still unknown (Staiger et al., 2008; Maari and Powell, 2012). Due to its low frequency, only isolated reports and series with few cases have been published (Staiger et al., 2008). The characteristic of lesions are circumscribed areas of slack skin with the impression of loss dermal elastic tissue forming round or oval atrophic lesions, and wrinkling or sac-like protrutions (Maari and Powell, 2012). The lesions commonly occur in young adults with the usual locations on the trunk, thighs, and upper arms, less commonly on the neck and face and rarely elsewhere (Burrows et al., 2010). According to author knowledge, there are only two cases of generalized anetoderma have been reported (Emer et al., 2013; Inamadar et el., 2003). Anetoderma lesions classified into primary and secondary types (Emer et al., 2013). Primary anetoderma develops in clinically normal skin and have been related to a variety of pathologies, mainly autoimmune diseases (Staiger et al., 2008). Primary anetoderma may be as a cutaneous sign of autoimmunity, whereas autoimmune diseases may develop later after the onset of anetoderma (Al Buainain and Allam, 2009). Secondary anetoderma arises on previous skin diseases, although not always in relation to the lesions, and could be associated with syphilis and Human immunodeficiency virus (HIV) (Bilen et al., 2003). There is no effective treatment for anetoderma (Maari and Powell, 2012), the new lesions often continue to develop for many years as the older lesions fail to resolve (Maari and Powell, 2012). The aim of this report was to present a rare case of generalized primary anetoderma.

2 CASE

A 19-year-old female was noticed to have had asymptomatic, multiple, small, circumscribed, round and oval atrophic lesions and sac-like protrution on

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almost all part of the body. The lesions started on elbows without history of skin lesion on the areas of the lesions and spread to almost all part of the body in 6 years duration. Skin lesions consisted of scattered, well-circumscribed, round and oval, skin color and white lesions, atrophic and some lesions raised above the surrounding skin level (sac-like protrutions). On palpation, a hernia orifice could be fell under the finger, and the content of the hernia sac could be pressed through this orifice, producing the "button-hole sign". Size of lesions are 0,5 until 2 centimeter in diameter with central protrusion, that were distributed on almost all part of the body with sparing in scalp, palms, and soles (figure 1). No sensory changes associated with the lesions. She did not have any history of medication consumption. No family history with the same symptoms. Skin biopsy was taken from atrophic and protruding lesions for histopathological examination and both revealed perivascular and periadnexal lymphocyte inflammatory cell infiltrate (figure 2A). Verhoeff-Van Gieson elastin stain showed fragmented and markedly decreased of elastic fibers in the superficial dermis until mid-dermis and loss of elastic fibers in mid-dermis (figure 2B) supported the diagnosis of anetoderma. Direct immunofluorescence (DIF) did not performed. Complete blood count, erythrocyte sedimentation rate, and routine chemistry were normal. The patient did not have any symptoms or show any signs of antiphospholipid syndrome (APS) and screening for antiphospholipid antibodies (anticardiolipin IgG and IgM) were negative. Bleeding time and clotting time were within normal range. Antinuclear antibody (ANA) and ANA profile were negative. Thyroid panel test did not performed. Venereal disease research laboratory (VDRL) test, Treponema pallidum haemagglutination assay (TPHA), anti-HIV were all non-reactive.

3 DISCUSSION

The term "anetoderma" is derived from anetos, the Greek word for slack, and derma for skin (Maari and Powell, 2012). This disease favors young adults between 15 (Maari and Powell, 2012) and 40 years (Aghaei et al., 2004). and occurs more frequently in women than men (Maari and Powell, 2012; Aghaei et al., 2004). The characteristic lesions of anetoderma are flaccid circumscribed areas of slack skin that are reflection of a marked reduction or absence of dermal elastic fiber and can appear as depressions, wrinkling or sac-like protrusions (Maari and Powell, 2012). The lesions appear as circumscribed round or oval areas of the skin with atrophic aspect (Staiger et al., 2008) and protrude from the skin and on palpation have less resistance than the surrounding skin, producing the "button-hole" sign. (James et al., 2016). The lesions can vary in number from less than five (Burrows et al., 2010) to hundreds, and they typically measure 0,5 (Aghaei et al., 2004) -2 cm in diameter (Maari and Powell, 2012). The color varies from skin color, blue, white (Maari and Powell, 2012); Burrows et al., 2010), and grey (Burrows et al., 2010). The surface skin may be slightly shiny, white, and crinkly. The patient may be totally asymptomatic or refer pruritus on the lesions (Staiger et al., 2008). In our case, the patient is a 19 years-old female, presented with asymptomatic, multiple, small, circumscribed, round and oval atrophic lesions and sac-like protrution on almost all part of the body. The lesions are 0,5 until 2 centimeter in diameter with central protrusion, skin color and white, with some had slightly shiny and crinkly surface.

The usual locations of anetoderma are the trunk, especially on the shoulder, the upper arms, and thigh (Maari and Powell, 2012; Burrows et al., 2010), less commonly on the neck and face and rarely elsewhere. The scalp, palms, and soles are usually spared (Burrows et al., 2010). There were only few reported cases of anetoderma with generalized distribution (Emer et al., 2013; Inamadar et al., 2003). Emer et al. (2013) reported one case of generalized anetoderma in a patients with secondary syphilis after being treated with intravenous penicillin. Inamadar et al. (2003) reported a case of generalized secondary anetoderma in a patient with HIV infection, pulmonary tuberculosis and lepromatous leprosy. The new lesions often continue to form for many years as the older lesions fail to resolve (Maari and Powell, 2012. The distribution of the lesions in this report are generalized, affecting almost all part of the body, and sparing on scalp, palms, and soles. The lesions started on elbows without history of skin lesion on the areas of the lesions and spread to almost all part of the body in 6 years duration.

The pathogenesis of anetoderma is still unknown (Staiger et al., 2008; Maari and Powell, 2012). The loss of dermal elastin may reflect an impaired turnover of elastin, caused by either increased destruction or decreased synthesis of elastic fibers. There are a number of proposed explanations for the focal elastin destruction such as the release of elastase from inflammatory cells, the release of cytokines such as interleukin-6, an increased

production of progelatinases A and B, and the phagocytosis of elastic fibers by macrophages (Maari and Powell, 2012).

The diagnosis of anetoderma is based on an association of clinical features, and the histopathological examination. In the routinely stained sections, the collagen within the dermis of affected skin appears normal. A perivascular inflammatory infiltrate is present that lymphocytes were the predominant cell type. There are usually some residual abnormal irregular and fragmented elastic fibers. Plasma cells and histiocytes with occasional granuloma formation can be seen (Emer et al., 2013). The predominant abnormality is a focal, more or less complete loss of elastic tissue in the papillary and/or mid-reticular dermis as revealed by elastic tissue stain such as Verhoeff-Van Gieson stain (Staiger et al., 2008; Maari and Powell, 2012). Direct immunofluorescence sometimes shows linear or granular deposits of immunoglobulins and complement along the dermal-epidermal junction or around the dermal blood vessels in affected skin. However, these findings are not helpful diagnostically (Maari and Powell, 2012). In this patient, the histopathologic examination revealed perivascular and periadnexal lymphocyte inflammatory cell infiltrate. Elastic stain (Verhoeff-Van Gieson) showed fragmented and markedly decreased of elastic fibers in the superficial dermis until mid-dermis and loss of elastic fibers in mid-dermis and the diagnosis was consistent with anetoderma. We did not perform direct immunofluorescence (DIF) examination in this patient.

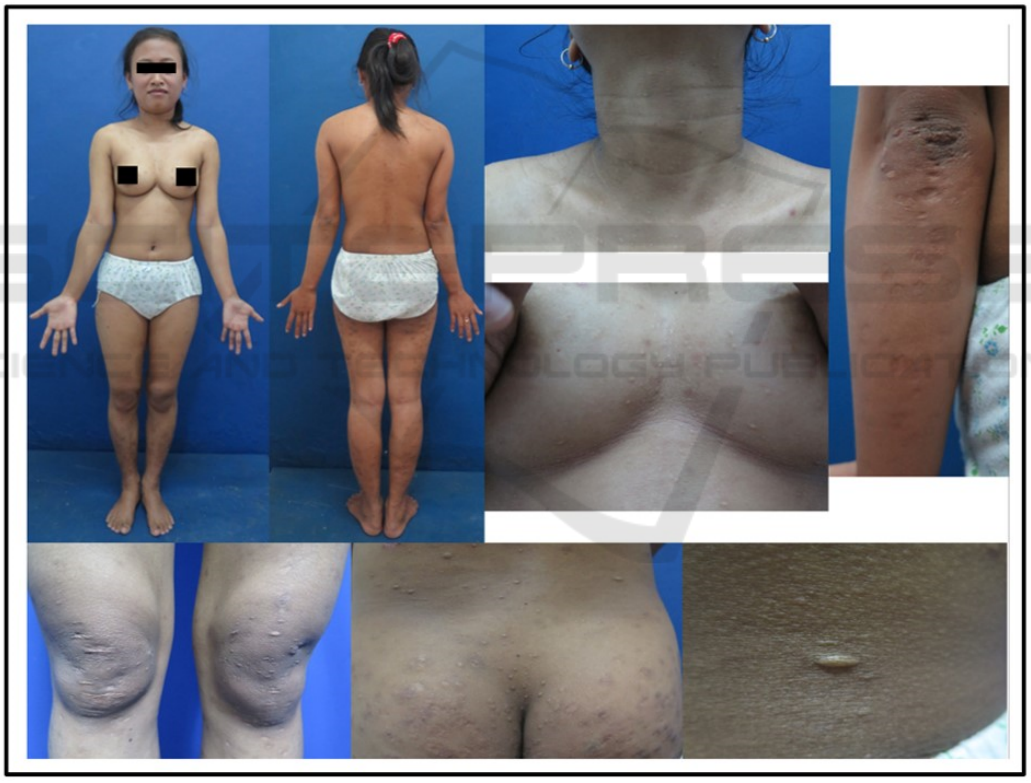

Figure 1. Multiple, small, circumscribed, round/oval, skin color and white, atrophic lesions and sac-like protrutions on almost all part the body with “button-hole sign” on palpation.

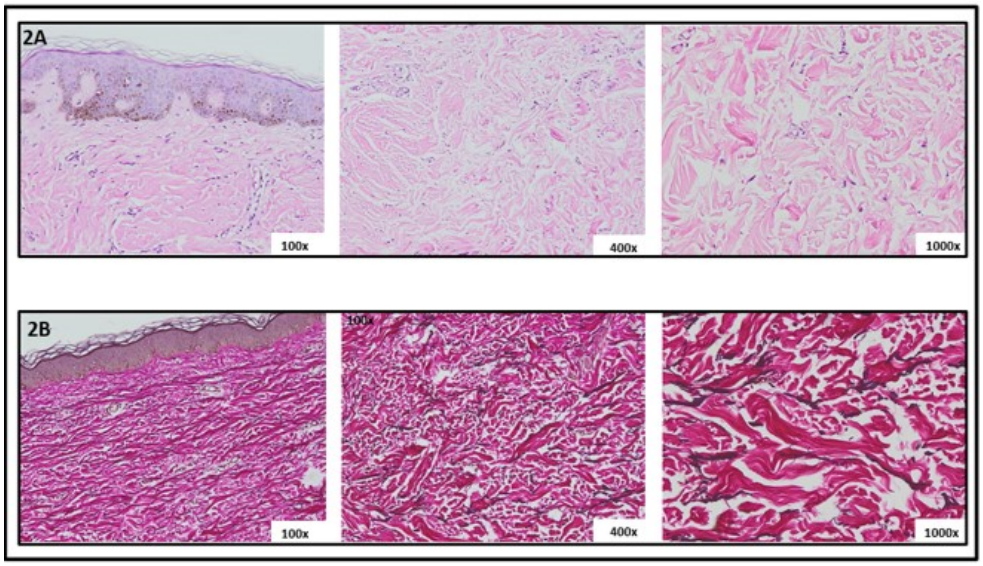

Figure 2. Histopathological examination. 2A. Hematoxilin-Eosin stain 2B. Verhoeff-Van Gieson elastin stain

Two forms of anetoderma are traditionally distinguished, primary and secondary (Staiger et al., 2008; Persechino et al., 2011). The lesions of primary anetoderma occur in clinically normal skin (Maari and Powell, 2012; Persechino et al., 2011) although there could be an association with other dermatological or systemic diseases or conditions, without a well-established relationship (Persechino et al., 2011). Some author classified primary anetoderma into two major forms, Jadassohn-Pellizzari type which is preceded with inflammatory lesions, and Schweninger-Buzzi type without preceding inflammatory lesions. This clinical classification is primarily of historical interest, since the two types of lesions can coexist in the same patient and their histopathology is often the same and not related to prognosis (Maari and Powell, 2012). In the secondary anetoderma the lesions can occurs on the same site as another skin lesions (Persechino et al., 2011), including acne, insect bites, varicella, syphilis, leprosy, tuberculosis, granuloma annulare, and urticarial pigmentosa, but no always in relation to the lesions (Emer et al., 2013). The diagnosis of primary anetoderma can be established only by excluding the presence of any of the diseases known to be associated with secondary atrophy (Burrows et al., 2010). We diagnosed this patient as primary anetoderma because the patient did not noticed any signs of inflammatory lesions or skin diseases preceded the lesions. We performed laboratory test for syphilis and HIV infection which could be the etiology of secondary anetoderma, and the results were all non-reactive.

Primary anetoderma has been related to multiple diseases. For some time, its association with autoimmune pathologies has been highlighted, mainly systemic lupus erythematosus and antiphospholipid syndrome (Staiger et al., 2008). There are some evidence to consider primary anetoderma as a cutaneous sign of positive antiphospholipid antibodies with or without fulfilling the criteria antiphospholipid antibodies syndrome (Al Buainain and Allam, 2009). Several studies have subsequently linked anetoderma with concurrent Grave's disease (autoimmune thyroiditis), autoimmune hemolysis, systemic sclerosis, and alopecia areata (Emer et al., 2013). Xia et al. (2016) reported a case of anetoderma in a patient with SLE, who around the time of anetoderma presentation was negative for antiphospholipid antibody but who later went on to develop antiphospholipid antibody (IgM anticardiolipin). They suggest that anetoderma can precede antiphospholipid antibody serologic conversion and continued monitoring of antiphospholipid serology regardless of initial serology will be important. Bergman et al. (1990) described a case of primary hypothyroidism that developed 3 years after the onset of anetoderma. From some literature suggested to think of primary anetoderma as a cutaneous sign of autoimmunity and patients should be examined and carefully tested for autoimmune diseases, especially for antiphospholipid antibodies, lupus erythematosus and also thyroid antibodies. Patients should also be followed up because associated autoimmune

diseases may develop later in the course of the disease (Al Buainain and Allam, 2009). Evaluation for the presence of antiphospholipid antibodies should be performed before patients with idiopathic anetoderma are labeled as having true primary anetoderma (Maari and Powell, 2012). Laboratory examinations for autoimmune connective tissue diseases and antipospholipid syndrome in this patient were negative. There were no sign and symptoms of autoimmunity diseases confirmed the diagnosis of idiopathic primary anetoderma. In this patient, we plan long-term follow-up to monitor if there will develop any signs and laboratory abnormalities suggest to autoimmunity diseases.

Anetoderma is a benign condition (Persechino et al., 2011), and the disease can remain active for many years resulting in considerable aesthetic deformity (Zaki et al., 1994). Venencie et al. (1984) studied 16 patients and found that no treatment was beneficial once the depressed lesions had developed. Various therapeutic modalities have been tried, but have not resulted in improvement of existing atrophic lesions, these include intralesional injections of triamcinolone and systemic administration of aspirin, dapsone phenytoin, penicillin G, vitamin E, and inositol niacinate. Surgical excision of limited lesions may be helpful, with consideration the possibility of scars formation (Maari and Powell, 2012).

4 CONCLUSION

Anetoderma is rarely occur in generalized distribution. In each case of anetoderma, it is important to determine the case of primary or secondary, and patients should be examined, carefully tested, and followed up for autoimmune diseases. This is a benign condition, no effective treatment, and the new lesions often continue to form as the older lesions fail to resolve results in aesthetic deformity.

REFERENCES

Aghaei S, Sodaifi M, Aslani FS, Mazharinia N. An unusual presentation of anetoderma: a case report. BMC Dermatol. 2004;4(1):9.

Al Buainain H, Allam M. Anetoderma: Is It a Sign of Autoimmunity? Case Rep Dermatol. 2009;1(1):100-4.

Bergman R, Friedman-Birnbaum R, Hazaz B, Cohen E, Munichor M, Lichtig C. An immunofluorescence study of primary anetoderma. Clin Exp Dermatol. 1990;15(2):124-30.

Bilen N, Bayramgürler D, Şikar A, Ercin C, Yilmaz A. Anetoderma associated with antiphospholipid syndrome and systemic lupus erythematosus. Lupus. 2003;12(9):714-6.

Burrows NP, Lovell CR. Anetoderma. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rook's textbook of dermatology.8th ed. Oxford: Willey-Blackwell; 2010. h. 45.17-45.18.

Emer J, Roberts D, Sidhu H, Phelps R, Goodheart H. Generalized Anetoderma after intravenous penicillin therapy for secondary syphilis in an HIV Patient. The Journal of clinical and aesthetic dermatology. 2013;6(8):23.

Inamadar AC, Palit A, Athanikar S, Sampagavi V, Deshmukh N. Generalized anetoderma in a patient with HIV and dual mycobacterial infection. Lepr Rev. 2003;74(3):275-8.

James WD, Berger TG, Elston DM, Isaac MN. Anetoderma (macular atrophy). In: James WD, Berger TG, Elston DM, Isaac MN, editors. Andrews' diseases of the skin clinical dermatology.12th ed. Philadelphia: Elsevier-Book Aid International; 2016. p. 507.

Maari C, Powell J. Atrophies of connective tissue. In: Bolognia JL, Jorizzo JL, Schaffer JV, Editors. Dermatology. 3rd ed. New York: Elsevier Saunders; 2012. p. 1631-40.

Maari C, Powell J. Antoderma and other atrophic disorders of the skin. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffel DJ, Wolff K, editors. Fitzpatrick's dermatology in general medicine.8th ed. New York: McGraw-Hill; 2012. p. 718-24.

Persechino S, Caperchi C, Cortesi G, Persechino F, Raffa S, Pucci E, et al. Anetoderma: evidence of the relationship with autoimmune disease and a possible role of macrophages in the etiopathogenesis. Int J Immunopathol Pharmacol. 2011;24(4):1075-7.

Staiger H, Saposnik M, Spiner RE, Schroh RG, Corbella MC, Hassan ML. Primary anetoderma and antiphospholipid antibodies. Dermatología Argentina. 2008;14(SE):2008; 14 (5): 372-378.

Venencie PY, Winkelmann R, Moore BA. Anetoderma: clinical findings, associations, and long-term follow-up evaluations. Arch Dermatol. 1984;120(8):1032-9

Xia FD, Hoang MP, Smith GP. Anetoderma before development of antiphospholipid antibodies: delayed development and monitoring of antiphospholipid antibodies in an SLE patient presenting with anetoderma. Dermatol Online J. 2016;23(3).

Zaki I, Scerri L, Nelson H. Primary anetoderma: phagocytosis of elastic fibres by macrophages. Clin Exp Dermatol. 1994;19(5):388-90.