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O Espectro da Papulose Fibroelastolítica: Revisão Retrospetiva

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RESUMO – **Introdução**: Existe sobreposição entre as características clínicas e histológicas da elastólise da derme papilar semelhante a pseudoxantoma elástico (EDP-PXE) e a papulose fibrosa branca do pescoço (PFBP). A interpretação destas duas entidades dentro do espetro de uma única doença, designada de papulose fibroelastolítica, foi sugerida previamente. No entanto, muitos autores continuam a diferenciá-las. **Métodos**: Realizou-se um estudo retrospetivo dos casos de papulose fibroelastolítica confirmados por exame histológico num período de 2,5 anos. **Resultados**: Identificaram-se cinco casos. Todos os doentes eram do sexo feminino, com idades compreendidas entre os 63 e os 78 anos, apresentando pápulas assintomáticas isoladas ou confluentes, brancas a amarelas, acantonadas na região cervical. Duas das doentes tinham também envolvimento extra-cervical. Em todos os casos a histopatologia demonstrou ausência ou diminuição marcada do plexo elástico da derme papilar, infiltrado linfocítico perivascular superficial ligeiro e escassos melanófagos na derme papilar sem alterações de interface. Adicionalmente, verificou-se diminuição nas fibras elásticas da derme reticular superior em quatro casos, espessamento dos feixes de colagénio em três casos, vasos da derme superficial dilatados em três casos e atrofia epidérmica ligeira num caso. **Conclusão**: Consideramos que a diferenciação entre a EDP-PXE e a PFBP é frequentemente causadora de confusão e baseada em diferenças clínicas e histológicas discretas e não significativas. Na nossa opinião, estes termos deverão ser abandonados em favor da denominação comum de papulose fibroelastolítica.
PALAVRAS-CHAVE – Dermatopatias Papuloescamosas; Doenças do Tecido Conjuntivo; Pescoço; Tecido Elástico.

The Spectrum of Fibroelastolytic Papulosis: A Retrospective Case Series

ABSTRACT – ***Introduction:*** *There is an overlap between clinical and pathological features of the entities known as pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE) and white fibrous papulosis of the neck (WFPN). Although the term fibroelastolytic papulosis has been used to encompass both entities as spectrum variants of a one and only disease, many authors still differentiate the two.* ***Methods:*** *Cases of fibroelastolytic papulosis confirmed by histopathologic examination were retrospectively reviewed within a time frame of 2.5 years.* ***Results:*** *Five cases of fibroelastolytic papulosis were identified. All patients were females aged between 63 and 78 years, presenting with an asymptomatic eruption of isolated or coalescing white to yellow papules on the neck. Two of the patients also had involvement of other anatomical areas. In all cases histology demonstrated a significantly decreased or absent papillary dermal elastic plexus, a mild superficial perivascular lymphocytic infiltrate and sparse melanophages in the papillary dermis, without interface changes. A decrease in upper reticular dermal elastic fibers was noted in four cases and thickening of dermal collagen bundles in three cases. Dilated superficial dermal vessels were present in 3 cases and mild epidermal atrophy in one case.* ***Conclusion:*** *We find the differentiation of PXE-PDE and WFPN to be somewhat theoretical, often confusing, and based on non-significant subtle histological and clinical differences. In our opinion, we should not continue to use these terms, but favor the common term of fibroelastolytic papulosis.*
KEYWORDS – *Connective Tissue Diseases; Elastic Tissue; Neck; Skin Diseases, Papulosquamous.*

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INTRODUCTION

Pseudoxanthoma elasticum-like papillary dermal elastolysis (PXE-PDE) and white fibrous papulosis of the neck (WFPN) were classically described as two separate acquired elastolytic and fibrotic disorders, usually affecting the neck, each one representing a unique entity and imposing differential diagnosis between them.[1-3] Due to overlap between clinical and pathological features,[4-6] the two entities were later proposed as spectrum variants of a single disease: fibroelastolytic papulosis (FEP).[5] Nevertheless, many authors still differentiate the two. We aimed to retrospectively review clinical and pathological features of histologically confirmed cases of FEP.

METHODS

Histopathologically confirmed cases of FEP diagnosed within a 2.5-year period in the Dermatology Department of Hospital de Santo António dos Capuchos, Centro Hospitalar de Lisboa Central, were included. Clinical and pathological features of the cases were analyzed.

Previously published literature was reviewed by searching the terms "white fibrous papulosis", "papillary dermal elastolysis" and "fibroelastolytic papulosis" in *PubMed*. One published Portuguese case not indexed in *PubMed* was additionally included.

RESULTS

Five cases of FEP were identified. All five patients were females aged between 63 and 78 years (mean 67.8), presenting with an asymptomatic eruption on the neck consisting of whitish skin-colored to yellow non-follicular papules (Fig. 1). Lesions had appeared one month to nine years before. In all patients there were discrete and confluent lesions, and two of the patients also had involvement of other anatomical areas (Table 1). Four patients had important co-morbidities, though none related with PXE.

In all cases, histology demonstrated significant decrease or absence of the papillary dermal elastic plexus (Fig. 2), mild superficial perivascular lymphocytic infiltrate, and sparse melanophages in the papillary dermis without interface changes (Table 1). A decrease in the upper reticular dermal elastic fibers and substantial or mild thickening of dermal collagen bundles were observed respectively in four and three cases. Dilated superficial dermal vessels were present in three cases and mild epidermal atrophy in one case. No calcification or elastosis were observed.

DISCUSSION

WFPN was originally described in 32 Japanese patients, aged 39 to 79 years, 26 (81%) of whom were male, presenting with multiple discrete small whitish non-follicular papules, usually asymptomatic, scattered on the posterior aspect of the neck.[1] Histologically, there were circumscribed areas with thickened collagen bundles in the papillary and mid-reticular dermis and, in 40% of the specimens, also a slight decrease in elastic tissue in those areas. PXE-PDE was first reported in two 60-year-old women as yellow or skin-colored non-follicular papules coalescing into large cobblestone plaques affecting the latero-cervical and supraclavicular regions.[2] On histological examination, band-like papillary dermal elastolysis was the main feature, with a mild reduction in number of reticular elastic fibers, and no dermal fibrosis.

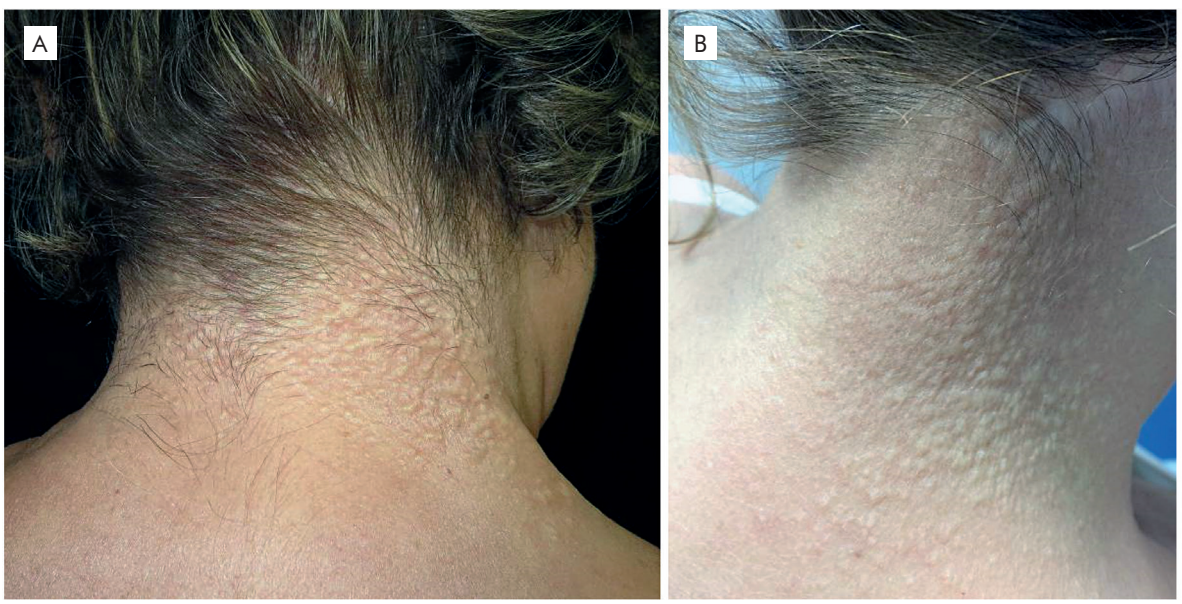

Figure 1 - Clinical presentation in cases 2 (**A**) and 4 (**B**). Whitish-yellow (**A**) to whitish skin-colored (**B**), discrete and confluent, non-follicular papules on the neck.

Table 1 - Cases of fibroelastolytic papulosis reviewed.

CLINICAL PRESENTATION		PATHOLOGY						
		Epidermis	Melano-phages	Infiltrate	Superficial dermal vessels	Dermal collagen bundles	Elastic fibers	
							Papillary dermis	Upper reticular dermis
1	Skin-colored Neck, Axillae, Abdomen, Thighs	Normal	Yes	MSPL (+ some eosinophils) (+ periadnexal lym-phocytes)	Dilated	Thickened	Complete loss	Slightly ↓
2	Whitish-yellow Neck, Axillae, Antecubital fossae	Normal	Yes	MSPL	Normal	Mildly thickened	Significantly ↓	Slightly ↓
3	Whitish-yellow Neck	**Normal**	Yes	MSPL	Dilated	Mildly thickened	Significantly ↓	Slightly ↓
4	Whitish skin-colored Neck	Normal	Yes	MSPL	Dilated	Normal	Significantly ↓	Significantly ↓
5	Whitish skin-colored Neck	Mild epidermal atrophy Mild hyperkeratosis	Yes	MSPL	Normal	Normal	Significantly ↓	Normal

MSPL: mild superficial perivascular lymphocytic infiltrate.

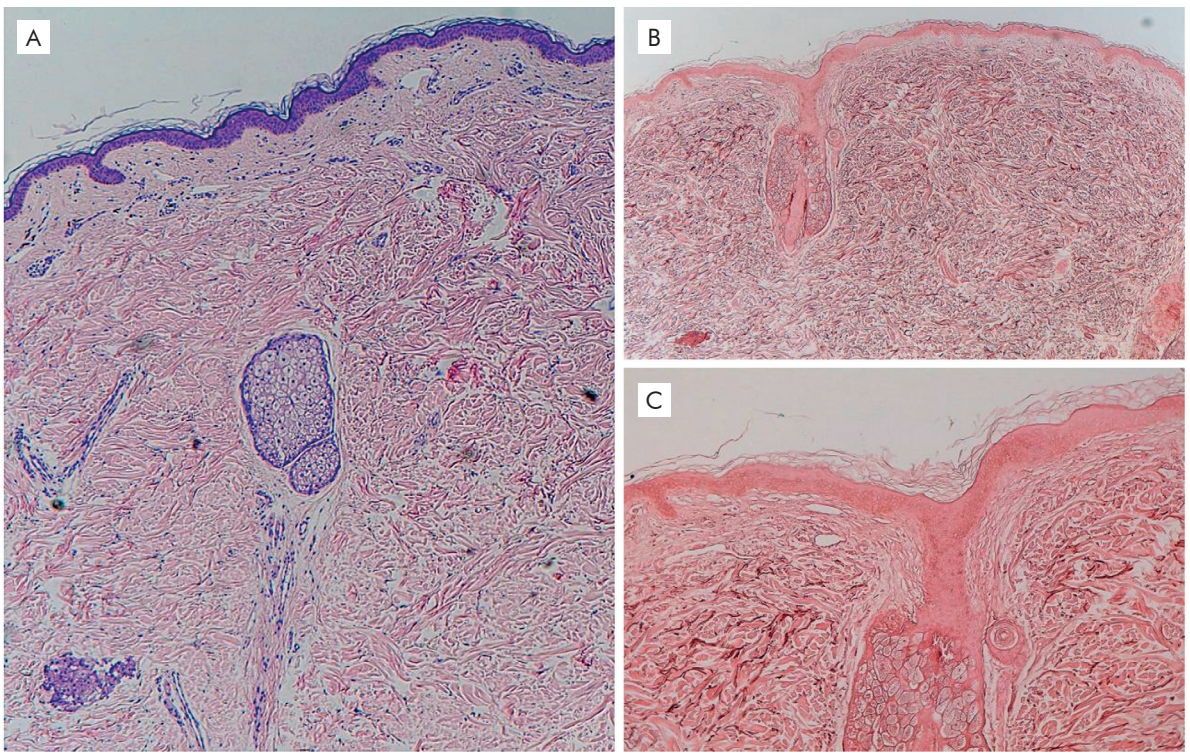

Figure 2 - Histological examination of case 4. A mild superficial perivascular lymphocytic infiltrate and dilated superficial dermal vessels could be observed in hematoxilin-eosin staining (**A**, x40). Significant reduction of papillary and reticular dermal elastic fibers was observed with orcein staining (**B**, x40; **C**, x100).

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Rongioletti *et al* first classified these entities as two fibroelastolytic syndromes.[7] Some years later, Balus *et al*[4] reviewed all the cases published in the meantime (12 and four additional cases of WFPN and PXE-PDE) and their own 20 cases, and observed a significant clinical and pathological overlap, proposing that these two entities could be variants of a single disease: FEP of the neck. The simpler term of FEP was proposed by Jagdeo *et al* in 2004, when reporting six additional cases with overlapping features, highlighting additional anatomical areas sometimes involved.[5] However, several authors still differentiate and perpetuate the terms of WFPN and PXE-PDE, and some only recognize the term FEP for cases with clear overlapping features, as an additional clinicopathological entity.[8-10]

Concerning pathogenesis, although a prominent role has been attributed to intrinsic aging, it remains poorly understood and is probably multifactorial.[6,8,11] The most important differential diagnosis is PXE, caused by a mutation in the ABCC6 gene and associated with systemic complications. Skin lesions are very similar, but calcified fragmented dermal elastic fibers observed after staining with von Kossa stain and the beginning of the lesions during the first or second decade of life support the difference. FEP is not associated with systemic complications and usually appears late in life. This should be recognized to avoid unnecessary investigations.[8] Moreover, the correct histological diagnosis requires clinicopathological correlation with special microscopic stains (elastic tissue and calcium salts) as the routine hematoxylin-eosin stain is not specific.[8]

Until this moment/ At present, a total of 55,[4,9,10,12-21] 54,[11,22-28] and 32[4-6,29-33] cases were reported as WFPN, PXE-PDE and FEP respectively. Concerning WFPN, 60% of the reported patients are males and cases in other countries in Asia, Europe, Middle East and South America have been reported. Additional features beyond the ones originally described are the presence of confluent lesions,[4,18] involvement of the inferior axillae, upper arms, the trunk's upper third, central mid-back, and abdomen,[3,4,9,18,19] a higher loss of papillary and reticular elastic tissue including the complete absence of oxytalan and elaunin fibers in some lesions and smaller fragmented reticular elastin fibers,[3,4,11,12] decrease of epidermal melanin,[16] slight epidermal atrophy,[12] and mild hyperkeratosis.[10] In cases of PXE-PDE, lesions may be more pale than originally described,[11,27] discrete,[11,25] and involve the flexor aspect of the forearms, axillae, the lower abdomen, and the inframammary folds.[3-5,11] All patients were female, three younger than 40 years-old. Additional histological features reported in some cases are epidermal atrophy, mild superficial perivascular lymphocytic infiltrate, papillary dermal melanophages, papillary dermal fibrosis and/or papillary dermal telangiectasia.[3,4,8,11] Therefore, dermal fibrosis has also been reported in PXE-PDE, and important loss of elastic tissue has also been reported in WFPN. Lesions in PXE-PDE may sometimes be paler and more discrete.

Considerable overlap and variation of clinical and histological features is also observed in our series. All the patients presented pale (whitish, yellowish, flesh-coloured) papules and plaques, confluent and discrete at different areas in the same patient. Thickened collagen bundles, a classic feature of WFPN, were observed in cases with features mostly reported in PXE-PDE like important elastic tissue loss in papillary dermis, mild superficial perivascular lymphocytic infiltrate and dilated superficial vessels (cases one to three). There were no clear clinical differences between cases with or without dermal fibrosis, and two of those three cases were the only cases with additional involvement of other anatomical areas, a feature, in its turn, described for PXE-PDE.

Reflecting this overlap, FEP, as defined by Jagdeo *et al*,[5] is characterized by whitish-yellow papules that may coalesce into cobblestone plaques and may involve the neck, supraclavicular region, scalp, axillae, lower aspect of the abdomen/inguinal region, and antecubital fossa. Histologically there may be normal, decreased, or absent elastic fibers in the papillary dermis, sometimes accompanied by a thickening of collagen fibers.[4,5] In 2009,[34] yet another term was coined and described in a case having similar features, but presenting alternating areas of elastic fiber clumping and loss of these fibers – papillary dermal elastosis. In our opinion, this is not a novel elastic tissue disorder, but another spectrum variant of FEP. Recently, Patterson *et al*[6] reported a single case with histopathologic findings of PXE-PDE, WFPN and papillary dermal elastosis, further supporting the theory that these entities are spectrum variants of FEP.

Thus, we find the differentiation of PXE-PDE and WFPN to be somewhat theoretical, oftentimes confusing, and based on non-significant subtle histological and clinical differences. In our opinion, we should try to favor the common term of FEP.

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Protecção de pessoas e animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial

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REFERENCES

1. Shimizu H, Kimura S, Harada T, Nishikawa T. White fibrous papulosis of the neck: A new clinicopathologic entity? J Am Acad Dermatol. 1989;20:1073–7.
2. Rongioletti F, Rebora A. Pseudoxanthoma elasticum-like papillary dermal elastolysis. J Am Acad Dermatol. 1992;26:648–50.
3. Lewis KG, Bercovitch L, Dill SW, Robinson-Bostom L. Acquired disorders of elastic tissue: Part II. decreased elastic tissue. J Am Acad Dermatol. 2004;51:165–85.
4. Balus L, Amantea A, Donati P, Fazio M, Giuliano MC, Bellocci M. Fibroelastolytic papulosis of the neck: a report of 20 cases. Br J Dermatol. 1997;137:461–6.
5. Jagdeo J, Ng C, Ronchetti IP, Wilkel C, Bercovitch L, Robinson-Bostom L. Fibroelastolytic papulosis. J Am Acad Dermatol. 2004;51:958–64.
6. Patterson AT, Beasley KJ, Kobayashi TT. Fibroelastolytic papulosis: histopathologic confirmation of disease spectrum variants in a single case. J Cutan Pathol. 2016;43:142–7.
7. Rongioletti F, Rebora A. Fibroelastolytic patterns of intrinsic skin aging: pseudoxanthoma-elasticum-like papillary dermal elastolysis and white fibrous papulosis of the neck. Dermatology. 1995;191:19–24.
8. Rongioletti F, Izakovic J, Romanelli P, Lanuti E, Miteva M. Pseudoxanthoma elasticum-like papillary dermal elastolysis: A large case series with clinicopathological correlation. J Am Acad Dermatol. 2012;67:128–35.
9. Castilla C, Kim RH, Meehan SA, Pomerantz R. White fibrous papulosis of the neck. Dermatol Online J. 2016;22:43–4.
10. Kandhari R, Kandhari S, Jain S. White fibrous papulosis of the neck. Indian J Dermatol Venereol Leprol. 2015;81:224.
11. Vázquez-Osorio I, Rosón E, Suárez-Peñaranda JM, Vázquez-Veiga H. Pseudoxanthoma elasticum-like papillary dermal elastolysis. Actas Dermosifiliogr. 2015;106:333–6.
12. Zanca A, Contri MB, Carnevali C, Bertazzoni MG. White fibrous papulosis of the neck. Int J Dermatol. 1996;35:720–2.
13. Siragusa M, Batolo D, Schepis C. White fibrous papulosis of the neck in three Sicilian patients. Australas J Dermatol. 1996;37:202–4.
14. Wang D, Zhu W. White fibrous papulosis of the neck: a chinese case. J Dermatol. 2005;32:497–9.
15. Byun JY, Do MO, Kim SH, Choi HY, Myung KB, Choi YW. Pseudoxanthoma elasticum-like papillary dermal elastolysis developed in early middle age. J Dermatol. 2007;34:709–11.
16. Minagawa A, Koga H, Saida T. Dermoscopy of white fibrous papulosis of the neck. Arch Dermatol. 2010;146:220.
17. Moreira AP, de Souza AL, Quevedo Filho LP, Rochael MC, Amaral V. White fibrous papulosis of the neck: the first South American case. Dermatol Online J. 2009;15:9.
18. Mitoma C, Takahara M, Takeshita T, Kiryu H, Moroi Y, Furue M. White fibrous papulosis on the trunk and upper arms. Int J Dermatol. 2013;52:337–8.
19. Schaffer PR, Tran K, Kaplan J, Patel R, Kamino H, Ramachandran S, et al. White fibrous papulosis of the neck. Dermatol Online J. 2014;20.
20. Gencoglan G, Ceylan C, Kazandi AC. White fibrous papulosis of the neck. Cutan Ocul Toxicol. 2011;30:69–71.
21. Lueangarun S, Panchaprateep R. White fibrous papulosis of the neck treated with fractionated 1550-nm erbium glass laser: a case report. J Lasers Med Sci. 2016;7:256–8.
22. Pitarch G, Torrijos A, García-Melgares ML, Roche E, Calatayud A, Fortea JM. Elastolisis dérmica papilar similar a pseudoxantoma elástico. Actas Dermosifiliogr. 2006;97:131–3.
23. Lopes L, Reis M, Gouveia A, Vasconcelos J, Soares-Almeida L, Filipe PL. Elastólise da derme papilar semelhante a Pseudoxantoma Elástico - Uma entidade sub-diagnosticada. Rev Soc Port Dermatol Venereol. 2014;72:223–6.
24. Gambichler T, Reininghhaus L, Schaller J. Early-onset pseudoxanthoma elasticum-like papillary dermal elastolysis. J Eur Acad Dermatology Venereol. 2016;30:448–9.
25. Valbuena V, Assaad D, Yeung J. Pseudoxanthoma elasticum–like papillary dermal elastolysis: a single case report. J Cutan Med Surg. 2017;21:345–7.
26. Foering K, Torbeck RL, Frank MP, Saedi N. Treatment of Pseudoxanthoma elasticum-like papillary dermal elastolysis with non-ablative fractional resurfacing laser resulting in clinical and histologic improvement in elastin and collagen. J Cosmet Laser Ther. 2017 (in press). doi: 10.1080/14764172.2017.1358457
27. Fukuda H, Mukai H, Otani A, Oharaseki T, Takahashi M. Dermoscopic findings of pseudoxanthoma elasticum-like papillary dermal elastolysis. Eur J Dermatol. 2017;27:99–100.
28. Alves R, Ferreira L, Vale E, Bordalo O. Pseudoxanthoma elasticum papillary dermal elastolysis: A case report. Dermatol Res Pract. 2010;2010:4–7.
29. Song YC, Oh BH, Ko JH, Kim JY, Hwang YJ, Won Lee Y, et al. A case of fibroelastolytic papulosis on the neck of a young man. Ann Dermatol. 2011;23:193–7.
30. Chong SP, Woodley DT, Kim GH, Shim EK. Treatment of fibroelastolytic papulosis with fractionated carbon dioxide laser. J Cosmet Laser Ther. 2015;17:90–2.
31. Oiso N, Kato M, Kawada A. Fibroelastolytic papulosis in an elderly woman with a 30-year history: Overlapping between pseudoxanthoma elasticum-like papillary dermal elastolysis and white fibrous papulosis of the neck. Eur J Dermatology. 2014;24:688–9.
32. Maione V, Errichetti E, Stinco G, Orsaria M, Patrone P. Fibroelastolytic papulosis of the neck treated with

topical tretinoin. J Dermatol. 2014;41:758–9.
33. Ho D, Jagdeo J. Fractionated carbon dioxide laser treatment of fibroelastolytic papulosis with excellent cosmetic result and resolution of pruritus. J Drugs Dermatol. 2015;14:1354–7.
34. Wang AR, Lewis K, Lewis M, Robinson-Bostom L. Papillary dermal elastosis: A unique elastic tissue disorder or an unusual manifestation of pseudoxanthoma elasticum-like papillary dermal elastolysis? J Cutan Pathol. 2009;36:1010–3.