A Possible New Variants of Familial Syringoma: Case Reports and Review of Literature

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ABSTRACT:

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Syringoma is a benign tumor of the intraepidermal portion of eccrine sweat ducts with distinct histopathology features, including the characteristic comma (tadpole)-shaped tail comprised of dilated, cystic eccrine ducts. Syringoma was classified into four main clinical variants: localized, familial, a variant associated with Down syndrome, and a generalized form with multiple and eruptive syringoma.

In familial eruptive syringoma is a rare form of syringoma. The clinical presentations are firm, smooth, skin-colored to pigmented, discrete papules that appear as successive crops on the anterior body surface of individuals who also have one or more family members with similar eruptive or localized lesions. Treatment of these benign conditions is a cosmetic purpose by destructive methods, medical therapies or a new treatment modality such as botulinum toxin A.

This report presents two cases of familial eruptive syringoma at the Institute of Dermatology in Thailand and literature reviews of familial eruptive syringoma: The first case, a 15-year-old Thai female

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presented with eruptive syringoma on the left lower eyelid, neck, antecubital fossae, groins, and mon pubis and her mother also had syringoma on the lower eyelids. In the second case, a 15-year-old Thai female presented with eruptive syringoma on the face, trunk, back, and extremities, as well as her father and uncle.
Key words: Familial eruptive syringoma, adnexal tumor, tadpole, eccrine sweat duct, botulinum toxin

Introduction

Syringoma is a benign adnexal neoplasm with mostly ductal differentiation. The clinical features represent small, firm, skin-colored papule(s) that occur at any site on the body but are prone to appear on the periorbital area, especially the eyelids[1]. Sometimes, lesions involved the upper trunk or genital skin. Familial eruptive syringoma is an uncommon clinical variant that combines the familial and generalized eruptive form. There are 8 type variants of familial syringoma (Table 1)[2]. To literature reviews, there are reports of patients with familial eruptive syringoma in which eruptive syringoma occurred in one family member, whereas at least one family member only had localized periorbital syringoma. In our report described two cases of familial eruptive syringoma at the Institute of Dermatology, Thailand.

Table 1 Classification of familial syringoma

Type	Description
1	Familial cases of syringoma can be localized, usually on periorbital area in two or more family members
2	A clinical variant of this localized type of familial syringoma present with milia-like lesions in two or more family members
3	Eruptive syringoma occurred in one family member, whereas at least one different family member had only localized periorbital syringoma
4	Eruptive syringoma and localized periorbital syringoma in one family member and localized periorbital syringoma in one or more different family members
5	Eruptive syringoma in two or more family members and localized periorbital syringoma in one or more different family members
6	Eruptive syringoma without periorbital syringoma in two or more of the same family members
7	Eruptive syringoma and localized periorbital syringoma in two or more of the same family members
8	Eruptive syringoma in two or more family members and localized periorbital syringoma in one or more of the same patients with eruptive syringoma and localized periorbital syringoma in one or more different family members

Case 1

A 15-year-old Thai female presented with multiple small, firm, brownish papules on the neck for six years. The biopsy was performed on the left side of the neck in October 2016. The biopsy showed ductal forming epithelial islands in the upper dermis (Figure 1A). No atypia was seen. The lesion does not infiltrate into the deep dermis. Therefore, syringoma was confirmed by histology. She preferred to try topical treatment. Unfortunately, topical retinoids; 0.05% retinoic acid could not make any improvement. After that, she lost to follow up for two years. She came back again with progressive multiple discrete and confluent monomorphous skin-colored papules on the left lower eyelid, neck, antecubital fossae, groins, and mon pubis. Her mother has some skin-colored papules on the lower eyelids. Though, the diagnosis is familial eruptive syringoma. After CO_2 laser on the small area of the neck for trial, the patient was not satisfied, so she decided no active intervention. We classify the diagnosis of this case into a new variant of familial syringoma which is eruptive syringoma and localized periorbital syringoma in one family member and localized periorbital syringoma in one or more of the same family members.

Case2

A 15-year-old Thai female has had multiple discrete skin-colored papules on the face, trunk, back, and extremities for eight years. The biopsy was done at the forehead. Her father and the 5th uncle have the same skin lesions. Her father has had lesions since the age of 6 years and her uncle has had lesions since the age of 30 years. There were multiple discrete skin-colored papules on the forehead, periorbital area, trunk, back and extremities, normal hair and nail, and no mucosal lesion on physical examination. The biopsy showed small ducts with narrow lumen lined by two-layer thick cuboidal epithelium and milia in the upper dermis (Figure 1B). She was diagnosed familial eruptive syringoma and three sessions of CO_2 laser for syringoma removal were performed. The results were satisfying. The diagnosis of this case was familial eruptive syringoma in a new variant type which is eruptive syringoma and localized periorbital syringoma in one or more family member and eruptive syringoma with localized periorbital syringoma in one or more of the different family members.

Discussion

Syringoma is a benign appendage tumor typically seen in adolescents and young adult females. The incidence of syringomas appears to be higher in Asians and African-Americans[3]. Syringoma often presents as multiple, 1-3 millimeters, skin-colored, sometimes yellow, papules commonly on the face, especially the periorbital region. They can also show on the scalp, vulva, penis, chest, and axilla. Friedman and Butler proposed a classification of syringoma

into four main clinical variants such as localized, familial, a variant associated with Down syndrome, and a generalized form with multiple and eruptive syringomas[4].

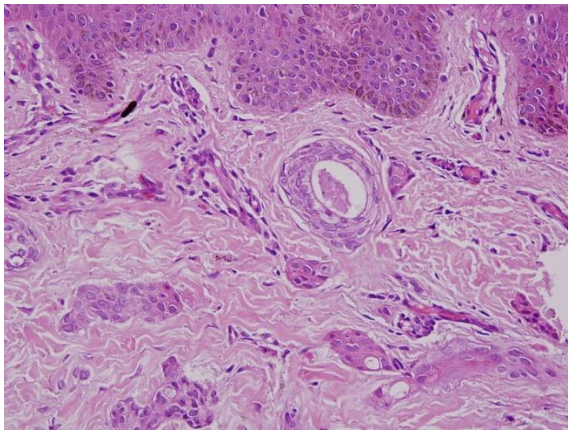

Figure 1A Ductal forming epithelial islands in upper dermis (X40)

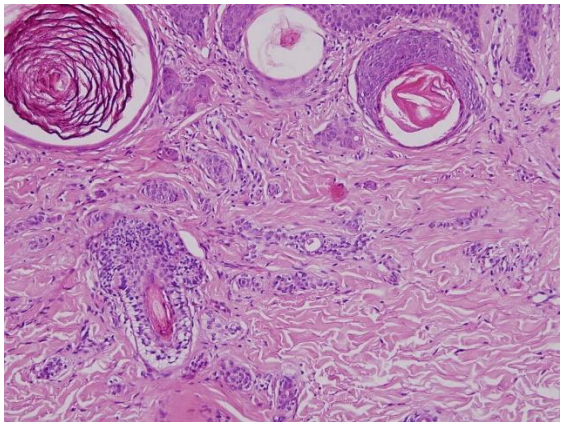

Figure 1B Small ducts with narrow lumen lined by two layer thick cuboidal epithelium and milia in upper dermis (X20)

Eruptive syringoma was first described in 1887 by Jacquet and Darier[5]. The firm, skin-colored to yellow papules appear in large numbers and in crops on the affected person's anterior chest, neck, axilla, and trunk that are usually symmetrical and appear in clusters during childhood and puberty. Familial forms are the cases with familial history of syringoma. Familial eruptive syringoma is a rare variant of syringoma which combines between eruptive type and familial type. In addition, the familial eruptive syringoma is a linkage of autosomal dominant on chromosome 16q22, but the genetic basis of eruptive syringoma is unknown[6]. There are many systemic diseases associated in syringoma, such as Down syndrome, diabetes mellitus, Brooke-Spiegler syndrome, Nicolau-Balus syndrome, and Costello syndrome[7-9].

In medical literature, only 16 published studies described the clinical entity affecting people in the family (Table 2)[10-24].

The pathogenesis of familial eruptive syringoma is controversial. The most accepted theory in syringoma is a benign neoplasm derived from the intraepidermal portion of eccrine ducts. Hashimoto and colleagues suggested that eruptive syringoma is formed by eccrine germ-like budding from the epidermis. They used antibody staining with monoclonal antikeratin antibodies epidermolytic hyperkeratosis 4 (EKH4) and epidermolytic hyperkeratosis 6 (EKH6) to show

that syringoma originates from the basal layers of the epidermis and eccrine secretory and ductal structures. The third theory proposed that syringoma may result from a localized or generalized hamartomatous process in case there is a familial history of eruptive lesions[11].

Histologic characteristics of syringoma present with convoluted and cystic ducts collections in the upper half of the dermis. Most are lined by a double layer of cells similar to normal eccrine ducts. The lumina contains amorphous debris. A characteristic feature is the tail-like strand of cells projecting from one side of the duct into the stromal, resembling a tadpole or comma[1,25].

There are many different potential treatment modalities for syringoma. The goal of treatment is the improvement of cosmetic appearance. Destructive methods (lasers, chemical peel, and electrodessication) and surgical excision are associated with postprocedural adverse events such as scarring and dyspigmentation. Medical treatment options include topical retinoids, dermabrasion, and topical atropine have been successful modalities in a case report or small case series. Moreover, intradermal botulinum toxin A injection is an alternative treatment for multiple syringomas in periocular and lip area which is affects the autonomic control of eccrine sweat gland but it still unknown exact mechanism[26]. However, no single treatment has proven to be a consistently effective treatment[25-26].

Conclusion

Familial eruptive syringoma is a rare clinical variant that combination of familial and generalized eruptive form. Histologic examination is helpful for confirmation. Treatments for syringoma, including topical retinoids, lasers, chemical peel, botulinum toxin A injection, electrodessication, surgical excision, mostly focus on sweat gland destruction. We report 2 cases of familial eruptive syringoma. Physicians may underestimate the diagnosis of familial eruptive syringoma. Dermatologists should perform skin examination throughout patient's entire body and consider the history of syringoma in family members. Genetic testing still needs to be researched.

Table 2 Case reports of familial eruptive syringoma

No.	Authors	Year of publication	Nation	Age/ Sex	Age of onset	Site of lesions in the patient	Affected family members	Site of lesions in affected family members	Type of familial syringoma
1	Yesudian, et al.[10]	1975	India	19 M	18	Periorbital, neck	Brother (21M)	Periorbital, neck	7
2	Hashimoto, et al.[11]	1985	Iran	55 M	5-10	Eyelids, chest, back	Father Sister Two daughters	Eyelids Eyelids Eyelids, anterior neck, chest	- (Should be eruptive syringoma with or without localized periorbital syringoma in one or more family members with localized periorbital syringoma in one or more family member)
3	Ribera, et al.[12]	1989	Spain	14 F	12	Lower eyelids (Milia-like)	Mother	Infraorbital	- (Should be localized milia-like syringoma in one or more family members with localized periorbital syringoma in one or more family member)
4	Patrizi, et al.[13]	1998	N/A	N/A	N/A	N/A	N/A	N/A	N/A
5	Metze, et al.[14]	2001	N/A	52 F	N/A	Forehead, periorbital, neck, axilla, mon pubis	Mother Daughter	Eyelids Eyelid, chin, neck, abdomen, sacral, thigh	- (Should be eruptive syringoma with or without localized periorbital syringoma in one or more family members with localized periorbital syringoma in one or more family member)
6	Smith, et al.[15]	2001	N/A	19 M	Adolescence	Anterior trunk	Mother	Anterior trunk	6
7	Soler-Carrilo, et al.[16]	2001	Spain	33 F	10	Neck, eyelids	Father Brother	N/A N/A	N/A
				16 F	12	Neck, trunk	Father	N/A	N/A

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8	Bautista, et al.[17]	2003	N/A	32 M	N/A	Face, neck, anterior chest, arm, thigh	Mother	Eyelids, forehead, retroauricular	7
9	Elsayed, et al.[18]	2009	Egypt	23 F	N/A	Neck, axilla, abdomen	Father Two Sisters (27 F, 36 F) Two Brother (22 M, 32 M)	Eyelids, cheek, anterior neck Forearm, chest, axilla Axilla, neck, chest, abdomen	- (Should be eruptive syringoma with or without localized periorbital syringoma in two or more family members)
10	Marzano, et al.[19]	2009	USA	36 F	N/A	Neck, chest, arms	Son (17M) Mother Two brothers Two sisters Two nephews	Anterior chest, ankle, upper and lower extremities N/A N/A N/A N/A	N/A
11	Lau, et al.[20]	2013	Asia	16 F	13	Axilla, abdomen	Mother Brother (19M)	Infraorbital Infraorbital, arm, axilla, abdomen, groin	- (Should be eruptive syringoma with or without localized periorbital syringoma in one or more family members with localized periorbital syringoma in one or more family member)
12	Singh SK, et al[21]	2013	India	60 F	20	Eyelids, cheek, forehead, chin	Daughter (38F) Daughter (35F)	Forehead, eyelids, cheek, chin Eyelids, cheek	7

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13	Ibekwe, et al[22]	2016	Nigeria	13 F	11	Periorbital, forearm, chest	Mother	Periorbital	- (Should be eruptive syringoma with or without localized periorbital syringoma in one or more family members with localized periorbital syringoma in one or more family member)
14	Yaldiz, et al.[23]	2018	N/A	20 F	16	Neck, supraclavicular	Brother (25 M)	Upper chest, back	6
15	Mahaisavariya, et al.[24]	2020	Thailand	20 F	18	Face, axilla, trunk, groins	Mother	Cheeks, lower eyelids	7
16	Srimuang, et al. (our patients)	2021	Thailand	15F	9	Eyelids, neck, antecubital fossae, groins, mon pubis	Mother	Periorbital	- (Should be eruptive syringoma with or without localized periorbital syringoma in one or more family members with localized periorbital syringoma in one or more family member)
				15F	7	Periorbital, forehead, chin, neck, trunk, forearm	Father Uncle	Periorbital, forehead anterior trunk Periorbital, trunk	- (Should be eruptive syringoma with or without localized periorbital syringoma in two or more family members with eruptive syringoma in one or more different family member)

References

1. Timothy H, Laura B. Adnexal Neoplasm. In: Bolognia JL, Schaffer JV, Cerroni L, et al. editors. Bolognia Dermatology. 4th ed. Edinburgh: Elsevier; 2018:1944-5.
2. Lau J, Haber RM. Familial eruptive syringomas: case report and review of the literature. J Cutan Med Surg 2013;17:84-8.
3. Singh S, Tewari R, Gupta S. An unusual case of generalised eruptive syringoma in an adult male. Med J Armed Forces India 2014;70:389-91.
4. Friedman SJ, Butler DF. Syringoma presenting as milia. J Am Acad Dermatol 1987;16:310-4.
5. Jacquet L, Darier J. Hiydradénomes éruptifs, épithéliomes adénoides des glandes sudoripares ou adénomes sudoripares. Ann Dermatol Syph 1887;8:317–23.
6. Wu WM, Lee YS. Autosomal dominant multiple syringomas linked to chromosome 16q22. Br J Dermatol 2010;162:1083-7.
7. Uede K, Yamamoto Y, Furukawa F. BrookeeSpiegler syndrome associated with cylindroma, trichoepithelioma, spiradenoma and syringoma J Dermatol 2004;31:32-8.
8. Dupré A, Carrère S, Bonafé JL, Christol B, Lassère J, Touron P. Syringomes éruptifs généralisés, grains de milium et atrophodermie vermiculée. Syndrome de Nicolau et Balus [Eruptive generalized syringomas, milium and atrophoderma vermiculata. Nicolau and Balus' syndrome (author's transl)]. Dermatologica 1981;162:281-6.
9. Nguyen V, Buka R, Roberts BJ, Eichenfield LF. Cutaneous manifestations of Costello syndrome. Int J Dermatol 2007;46:72-6.
10. Yesudian P, Thambiah A. Familial syringoma. Dermatologica 1975;150:32-5.
11. Hashimoto K, Blum D, Fukaya T, Eto H. Familial syringoma. Case history and application of monoclonal anti-eccrine gland antibodies. Arch Dermatol 1985;121:756–60.
12. Ribera M, Servitje O, Peyri J, Ferrándiz C. Familial syringoma clinically suggesting milia. J Am Acad Dermatol 1989;20:702-3.
13. Patrizi A, Neri I, Marzaduri S, Varotti E, Passarini B. Syringoma: a review of twenty-nine cases. Acta Derm Venereol 1998;78:460-2.
14. Metze D, Wigbels B, Hildebrand A. Familial syringoma: a rare clinical variant. Hautarzt 2001;52:1045-8.
15. Smith KJ, Skelton HG. Familial syringomas: an example of gonadal mosaicism. Cutis 2001;68:293-5.
16. Soler-Carrillo J, Estrach T, Mascaró JM. Eruptive syringoma: 27 new cases and review of the literature. J Eur Acad Dermatol Venereol 2001;15:242–6.
17. Bautista ST, Orrego GV, Salas MLT. Siringoma eruptivo familiar. Dermatol Peruana 2003;13:227-30.
18. Elsayed M, Assaf M. Familial eruptive syringoma. Egyptian Dermatology Online Journal 2009;5:1-6.
19. Marzano AV, Fiorani R, Girgenti V, Crosti C, Alessi E. Familial syringoma: report of two cases with a published work review and the unique association

with steatocystoma multiplex. J Dermatol 2009;36:154–8.
20. Lau J, Haber RM. Famililal eruptive syringomas: case report and review of the literature. J Cutan Med Surg 2013;17:84-8.
21. Singh SK, Rai T. Familial syringomas. Indian J Dermatol 2013;58:412.
22. Ibekwe P. Familial eruptive syringoma in a Nigerian girl. Clin Exp Dermatol 2016;41:383-5.
23. Yaldiz M, Cosansu C, Erdem MT, Dikicier BS, Kahyaoglu Z. Familial eruptive syringoma. Hong Kong Med J 2018;24:200-2.
24. Mahaisaviriya P, Techapichetvanich T. Familial Eruptive Syringoma in a Thai Women: Case Report and Literature Review. Thai J Dermatol 2020;36:7-14.
25. Williams K, Shinkai K. Evaluation and management of the patient with multiple syringomas: A systematic review of the literature. J Am Acad Dermatol 2016;74:1234-40.
26. Zaldivar-Fujigaki JL, Achell Nava L. Botulinum toxin A as monotherapy for syringoma. J Cosmet Dermatol 2021;20:1393-5.