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CASE REPORT

Late-Onset Eruptive Clear Cell Syringoma: A Case Report and Literature Review

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Abstract: Eruptive syringoma, a rare subtype of syringoma, is a benign adnexal tumor arising from the eccrine sweat glands. It is characterized by multiple asymptomatic, flat-topped, brown-pigmented papules. The disease typically occurs during adolescence and young adulthood. The clear cell variant of syringoma, which histologically features ductal epithelial cells with clear cytoplasm, is relatively rare, while eruptive clear cell syringoma is even more infrequent. In this report, we present a case of a 64-year-old Thai woman who developed multiple erythematous to brownish papules on her right cheek, which eventually spread to the periorbital region, face, neck, and chest over five years. The diagnosis of late-onset eruptive clear cell syringoma was made based on the patient's clinical manifestations and confirmed by histopathological examination. Notably, the patient was found to have impaired fasting plasma glucose upon screening, highlighting the potential association between clear cell syringoma and glucose metabolism abnormalities. This case report emphasizes the importance of considering this diagnosis in elderly patients presenting with eruptive papular dermatoses and underscores the need for metabolic screening in affected individuals.

Keywords: adnexal tumor, benign neoplasm, diabetes mellitus, eccrine sweat gland, histopathology, widespread papular eruption

Introduction

Syringoma is a benign neoplasm that originates in the eccrine ductal epithelium of the skin. The term "syringoma" is derived from the Greek word "syrinx", which means pipe or tube and refers to their histological appearance.[1–3] The condition, which affects 1% of the population, is most common in women and often appears on the face, particularly in the periorbital area.[2,3] Eruptive syringoma, first identified by Jacquet and Darier in 1887, represents an uncommon variant of syringoma characterized by a sudden emergence of numerous lesions appearing on various areas of the body, including the chest, neck, abdomen, and limbs.[1–3] This subtype typically appears before or during puberty.[4,5] In 1972, Headington et al were the first to describe the clear cell variant of syringoma, an exceedingly rare type distinguished histologically by the presence of ductal epithelial cells that exhibit clear cytoplasm.[6]

Late-onset eruptive clear cell syringoma is exceptionally rare, with only a handful of cases reported in the literature.[4,5] This variant is of particular interest due to its potential association with metabolic disorders, especially diabetes mellitus.[7] In this report, we present a case of late-onset eruptive clear cell syringoma in an elderly woman and review previously published articles, detailing cases of this uncommon entity.

Case Presentation

A 64-year-old Thai woman presented with a five-year history of multiple erythematous to brownish papules. The lesions initially appeared on her right cheek and progressively spread across her periorbital region, face, neck, and chest over time. The patient's medical history included essential hypertension and female pattern hair loss. The lesions were asymptomatic, with the exception of mild itching during sweating. The patient reported no family history of similar skin conditions.

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Upon dermatological examination, multiple small erythematous to brownish papules were identified on periorbital region, face, neck, and chest (Figure 1A–C). A skin biopsy was performed from a lesion on the right cheek, histopathological examination revealed an acanthotic epidermis with dermally-located numerous well-circumscribed tubular and cystic structures embedded in the dense fibrous stroma. These structures were lined with one to two layers of cuboidal epithelial cells, the majority of which exhibited pale-to-clear cytoplasm (Figure 2A and B). Some ducts

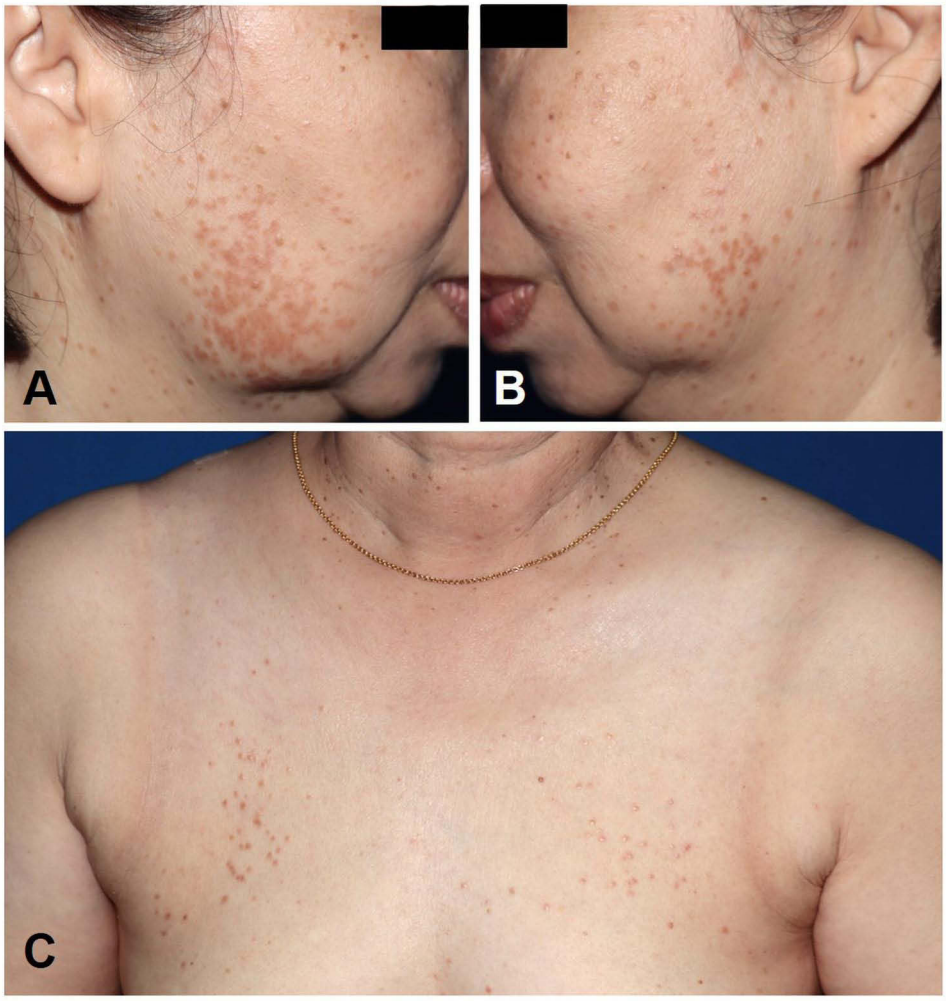

Figure 1 Clinical presentations: multiple small erythematous to brownish papules on periorbital region, face, neck **(A and B)**, and chest **(C)**.

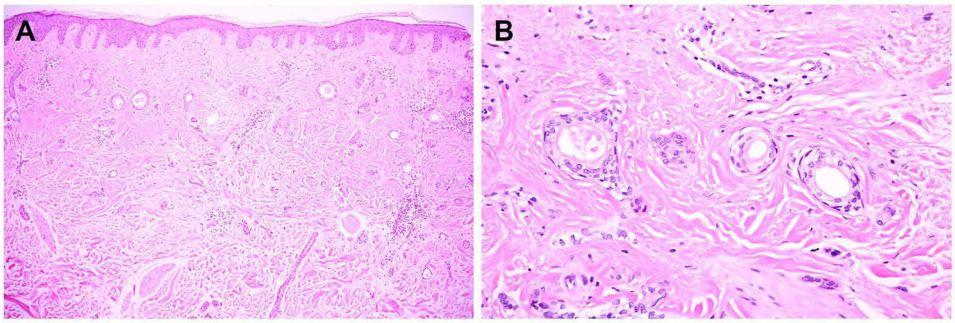

Figure 2 Histopathological findings: **(A)** an acanthotic epidermis with dermally-located numerous well-circumscribed tubular and cystic structures embedded in the dense fibrous stroma (H&E; original magnification x100); **(B)** multiple small ducts and strands of clear to pale cuboidal cells. Some of which exhibited a comma-shaped or "tadpole" appearance. Amorphous materials are noted in some of the ductal luminas (H&E; original magnification x400).

displayed elongated tails of epithelial cells, producing a characteristic comma-shaped or "tadpole" appearance. The ductal lumina contained amorphous material. No significant atypia or mitotic activity was observed.

Based on the clinical and histopathological findings, a diagnosis of late-onset eruptive clear cell syringoma was established. Given the reported association between clear cell syringoma and diabetes mellitus, the patient underwent metabolic screening. Results showed an HbA1c level of 6.4% and a fasting plasma glucose level of 119 mg/dL, leading to a diagnosis of impaired fasting plasma glucose. Following a discussion of treatment, the patient declined treatment due to the benign nature of the condition and concerns about scarring risk. The patient was also advised on lifestyle modifications and scheduled for regular follow-up to monitor her glucose levels.

Discussion

Late-onset eruptive clear cell syringoma represents a significant diagnostic challenge due to its rarity and atypical age of onset. Our case adds to the limited literature on this entity and highlights several important aspects of the condition. Eruptive syringoma typically develops during adolescence or early adulthood, with a marked female predominance (68.9% of cases).[4,8–10] Late-onset cases, particularly those presenting after the fifth decade of life, are exceedingly rare. Our patient's age of onset at 59 years is among the oldest reported in the literature for eruptive clear cell syringoma. This underscores the importance of considering this diagnosis even in elderly patients presenting with eruptive papular dermatoses. Table 1 summarizes previously reported cases of eruptive clear cell syringoma.[7,11–20]

The clinical presentation of eruptive clear cell syringoma is similar to that of typical eruptive syringoma, characterized by multiple small (1–4 mm), firm, flat-topped papules.[1,3,9] However, the clear cell variant may have a more pronounced brownish coloration due to increased melanin in the basal layer of the epidermis and pigmentary incontinence.[1,9] This distinctive coloration can serve as a clinical clue for dermatologists when evaluating patients with eruptive papular dermatoses. Histopathologically, the hallmark of clear cell syringoma is the presence of cells with abundant cytoplasmic glycogen and multivesicular bodies, resulting in pale-to-clear-appearing tumor cells. This feature distinguishes it from typical syringoma, which exhibits only small amounts of intracellular glycogen deposits.[7] This unique histological feature not only gives rise to a unique variant of syringoma but also raises intriguing questions about the underlying pathophysiology of these lesions.

The exact etiology of late-onset eruptive clear cell syringoma remains unclear, but several factors have been proposed to contribute to its development. Hormonal factors likely play a role but cannot fully explain all cases. Immunohistochemical studies have shown that clear cell syringoma expresses estrogen and progesterone receptors, suggesting a potential hormonal influence on their development.[8,21,22] This finding may partially explain the female predominance observed in syringoma overall. However, it does not fully account for the late onset in our patient, given that estrogen levels typically decline post-menopause. This discrepancy highlights the complex and multifactorial nature of the pathogenesis of late-onset eruptive clear cell syringoma. Some researchers propose that eruptive syringoma may represent a hyperplastic response of eccrine ducts to inflammatory stimuli rather than true neoplasms.[23] This theory is supported by reports of eruptive syringoma developing following episodes of contact dermatitis or other inflammatory skin conditions.[24,25] The inflammatory hypothesis is particularly intriguing in the context of late-onset cases, as it suggests that cumulative inflammatory insults over time could potentially trigger the eruption of these lesions in older individuals.

Genetic factors may also contribute to the development of syringoma. While familial cases of syringoma have been reported, suggesting a genetic component in some instances, our patient had no family history of similar lesions.[9] This lack of familial involvement in our case supports the notion that late-onset eruptive clear cell syringoma may have a distinct pathogenesis compared to earlier-onset or familial cases. Further genetic studies on sporadic late-onset cases could potentially reveal novel insights into the molecular mechanisms underlying this condition. Immunological factors have also been implicated in the development of eruptive syringoma. Cases have been reported in patients with autoimmune conditions, eg, alopecia areata and vitiligo, and in kidney and liver transplant recipients on immunosuppressive therapy.[4,8,26] These observations suggest that immune dysregulation may contribute to the development of eruptive syringoma. The potential role of the immune system in late-onset cases is particularly interesting, as age-related changes in immune function could potentially contribute to the delayed onset of these lesions. The pathogenesis of late-onset eruptive syringoma may also involve a correlation between underlying medical conditions and specific medications

Table 1 Previously Reported Cases of Eruptive Clear Cell Syringoma

Author(s), Year	No.	Age	Sex	Age of Onset	Area of Involvement	Diabetes mellitus/ impaired glucose tolerance	Treatment	Outcome
Diestelmeier and Rodman, 1983[11]	1	40	Female	15	Face, neck, chest, abdomen, axillae, arms, forearms, and thighs	+	Light electrodesiccation	Hypopigmented scars
Kudo et al, 1989[12]	2	63	Male	60	Trunk and extremities	+	NR	NR
Honma, 1990[13]	3	16	Male	N/A	Trunk and thighs	–	No treatment	NR
Fujise et al, 1992[14]	4	27	Male	N/A	Face, breasts, and axillae	–	NR	NR
Yajima and Kumakiri, 1996[15]	5	75	Male	N/A	Trunk, upper extremities, breasts, and abdomen	–	Cryotherapy	NR
Ohhashi et al, 1996[16]	6	27	Female	N/A	Face, axillae, breasts, and abdomen	–	No treatment	NR
Timpanidis et al, 2003[7]	7	55	Male	45	Face, arms, and trunk	+	NR	NR
Wen-Yuan, 2008[17]	8	47	Female	17	Face and trunk	-	NR	NR
Yoshimi et al, 2011[18]	9	70	Female	61	Upper extremities, breasts, and abdomen	+	No treatment	NR
Lentini and Schepis, 2011[19]	10	32	Female	32	Abdomen and pubic area	-	NR	NR
Ortega et al, 2019[20]	11	72	Male	42	Trunk, axillae, chest, and upper abdomen	+	No treatment	NR
The present case	12	64	Female	59	Face, neck, and chest	+	No treatment	NR

Abbreviation: NR, no report.

that cause inflammatory changes in the eccrine sweat ducts.[4,27] Korekawa et al reported a case where the lesions of late-onset eruptive syringoma worsened after the patient experienced a cerebral infarction and began taking the anti-epileptic medication, carbamazepine.[27]

The most intriguing aspect of clear cell syringoma is its strong association with diabetes mellitus. Approximately 80% of reported cases of clear cell syringoma have been associated with diabetes or impaired glucose tolerance.[7,18] Our patient's diagnosis of impaired fasting glucose corroborates this association and highlights the importance of metabolic screening in patients presenting with clear cell syringoma. The mechanism underlying the accumulation of glycogen in clear cell syringoma is not fully understood. It has been hypothesized that a deficiency or decreased activity of the enzyme phosphorylase may play a role in this process.[7] The association with diabetes suggests that systemic metabolic alterations may influence the development of these lesions. This relationship raises the possibility that clear cell syringoma could serve as a cutaneous marker for underlying metabolic disturbances, potentially allowing for early detection and intervention in cases of undiagnosed diabetes or pre-diabetic states. However, we acknowledge that this finding cannot definitively establish causation. Instead, this observation is presented as a possible association that requires further investigation.

The diagnosis of late-onset eruptive clear cell syringoma can be challenging due to its rarity and similarity to other eruptive papular dermatoses. The differential diagnosis includes eruptive xanthomas, disseminated granuloma annulare, cutaneous mastocytosis, lichen planus, flat warts, and eruptive vellus hair cysts.[28–31] Histopathological examination is

crucial for definitive diagnosis. The presence of clear cells in the biopsy specimen should prompt consideration of clear cell syringoma and initiate screening for diabetes mellitus or impaired glucose tolerance. This diagnostic approach not only confirms the dermatological condition but also provides an opportunity for early detection and management of potential metabolic abnormalities.

Treatment of eruptive clear cell syringoma is generally undertaken for cosmetic reasons, as the lesions are typically asymptomatic. Options include topical retinoids, chemical peels, cryotherapy, electrodesiccation, laser therapy, ie, carbon dioxide or erbium-doped yttrium aluminium garnet lasers, and surgical excision.[4,5,28] However, these treatments often yield unsatisfactory results due to the dermal location of the tumors thereby carry a risk of scarring.[4,5,28] Additionally, oral tranilast (N-[3,4-dimethoxycinnamoyl]-anthranilic acid), a medication that inhibits the release of histamine and prostaglandins from mast cells, has demonstrated positive outcomes in some cases.[32] It is important to consider the potential risks and benefits of each treatment option before making a decision.

Our patient declined treatment due to the benign nature of the condition and concerns about potential scarring. The natural history of late-onset eruptive clear cell syringoma is not well-documented due to its rarity. Long-term follow-up studies are needed to determine if these lesions continue to develop over time or if they remain stable after the initial eruptive phase. Such studies could provide valuable insights into the progression of the condition and inform management strategies for affected individuals.

Conclusion

This case of late-onset eruptive clear cell syringoma in a 64-year-old woman emphasizes the importance of considering this rare entity in the differential diagnosis of eruptive papular dermatoses, even in elderly patients. The association with impaired glucose tolerance in our patient underscores the need for metabolic screening in individuals diagnosed with clear cell syringoma. Future research should focus on elucidating the pathogenesis of clear cell syringoma, particularly their relationship with glucose metabolism. Additionally, long-term follow-up studies of patients with late-onset eruptive clear cell syringoma are needed to better understand the natural history and prognosis of this condition. As our understanding of this rare entity grows, we may uncover new insights into the complex interplay between the skin and systemic metabolic processes, potentially opening new avenues for both dermatological and endocrine research.

Ethics Approval and Consent to Participate

This article was performed in accordance with the principles of Declaration of Helsinki. Ethical review and approval was not required to publish the case details in accordance with the local legislation and institutional requirements. Written informed consent was obtained from the patient for publication of this case report and any accompanying images as per our standard institutional rules.

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