Evaluation and management of the patient with multiple syringomas: A systematic review of the literature

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Syringomas are benign adnexal tumors with distinct histopathologic features, including the characteristic comma ("tadpole") shaped tail comprised of dilated, cystic eccrine ducts. Clinically, syringomas typically present in adolescent females predominantly in the periorbital region. They may present as solitary or multiple lesions, and more rare sites of involvement include the genitals, palms, scalp, and the chest. Over the past 50 years, there have been >800 reported cases of syringoma either alone or in conjunction with a systemic syndrome, most commonly Down syndrome. The primary aim of this systematic review is to discuss the clinical features and associations of syringomas with a focus on the patient with multiple syringomas. Its secondary aims are to explore pathophysiology with a focus on multiple syringomas and provide comprehensive data on both traditional and novel treatments. Importantly, multiple syringomas present across a broad clinical spectrum. Though noted in many textbooks to be related to tumor syndromes, the association of syringomas with inherited tumor syndromes is only rarely reported in the literature. Despite multiple reported cases of syringoma, the pathophysiology remains poorly understood and treatment continues to pose a significant challenge. (J Am Acad Dermatol 2016;74:1234-40.)

Key words: eruptive syringoma; familial syringoma; multiple syringomas; syringoma; syringoma syndromes; syringoma treatment.

Syringomas are benign adnexal tumors with characteristic histopathologic features deriving from intraepidermal eccrine ducts. Clinically, lesions appear as small, firm, flesh-colored or yellow asymptomatic papules, 1 to 3 mm in diameter, often in multiples with symmetric distribution. Syringomas typically present in early adulthood, with a female predominance. Although the most common site of localized involvement is periorbital, other affected sites have been reported, including the vulva, penis, scalp, and axillae (Fig 1). Less commonly, eruptive distributions (a form of generalized syringoma) that occur in successive crops, including the anterior chest, axillae, neck, abdomen, and extremities, have also been reported.[1]

The clinical differential diagnosis of syringomas includes milia, xanthoma, hidrocystoma, trichoepithelioma, and xanthelasma, especially for lesions on the eyelids; additional diagnostic considerations include cutaneous mastocytosis, fibrofolliculomas, vellus hair cysts, angiofibromas, and fibroelastic papulosis. Diagnosis is confirmed by distinct histopathologic features (ie, the presence of multiple small ducts and epithelial cords within the dermis, and cystic eccrine ducts with a characteristic comma-shaped tail).

Abbreviations used:

DM: diabetes mellitus
DS: Down syndrome
TCA: trichloroacetic acid

A syringoma classification criterion proposed by Friedman and Butler[1] is based on clinical features and consists of 4 variants: localized, familial, a form

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associated with Down syndrome (DS), and a generalized variant, including multiple and eruptive syringomas. Lau et al[2] recently proposed the classification of familial syringomas based on hereditary pattern and clinical presentation, including factors such as distribution, syringoma type, and anatomic location.

Multiple syringomas are seen in several clinical contexts, including familial syringomatosis and tumor syndromes, but little is known about the clinical spectrum of syringoma presentations and effective treatments. The aim of this review is aim to describe the clinical features, systemic associations, and effective treatment strategies for multiple syringomas.

CAPSULE SUMMARY

- Syringomas are benign adnexal tumors deriving from intraepidermal eccrine ducts.
- Multiple syringomas occur in several clinical contexts, including familial syringomatosis, and rarely as a feature of tumor syndromes.
- This review outlines an evidence-based approach to the diagnosis and management of a patient presenting with multiple syringomas.

METHODS

Search strategies

A systematic literature search was conducted on the PubMed and Scopus databases using the following search terms: "familial syringoma," "hereditary syringoma," "familial eruptive syringoma," "hereditary eruptive syringoma," "syringoma," "familial generalized syringoma," "generalized syringoma," "multiple syringoma," "eruptive syringoma," "vulvar syringoma," "periorbital syringoma," "penile syringoma," "scalp syringoma," "axilla syringoma," "milia AND syringoma," "lichen AND syringoma," "plaque AND syringoma," "syringoma AND syndrome," "syringoma AND diabetes mellitus," "syringoma AND Down syndrome," "syringoma AND Nicolau–Balus," "syringoma AND Brooke–Spiegler," "syringoma treatment," "syringoma laser," "syringoma removal," "syringoma destruction," "syringoma argon," "syringoma CO_2," "syringoma isotretinoin," and "syringoma Accutane." Bibliographies of select publications were reviewed for additional eligible studies. Based on available data, cases were grouped as "comprehensive," "familial cases," or "treatment cases," as described in Supplemental Fig 1 (available online at http://www.jaad.org). Please note that additional references appear online only and include results of the search criteria described. Papers containing comprehensive data, including age, sex, anatomic involvement, family history, and treatments were included as "comprehensive"; a diagnosis of syringoma confirmed by biopsy specimen or clinical presentation was also used as inclusion criteria. Two hundred thirty-nine comprehensive cases were included in this review. For familial cases, the reported patient needed to have clinical or biopsy-confirmed syringoma with a reported family history of similar lesions in ≥1 family members; 29 familial cases were included in this review. For treatment cases, reports needed to provide data on method of treatment, number of cases, anatomic sites treated, and results of treatment; 215 cases met the inclusion criteria.

Data sources

Case reports, systematic reviews, and research letters published in PubMed and Scopus between 1964 and 2013 were included.

Data extraction

Comprehensive data, including age, age at presentation, sex, anatomic involvement, family history, and treatments were obtained from 46 reports. Percentages were calculated from available reported data from these select cases. Anatomic location and syndrome association demographics were obtained from 826 cases from 204 reports.

RESULTS

Eight hundred twenty-six cases of syringomas were reported in the literature between 1964 and 2013. Comprehensive data were obtained from 239 cases of syringoma identified from 46 reports[2-47] that met the inclusion criteria. Two hundred fifteen cases described treatment,[17-47] 24 cases were familial,[2-17] and 5 cases were familial with reported treatment attempts.[18,19] Of the 239 cases, 92% were women, and 70%, 20%, and 10% presented during adolescence, childhood, and adulthood, respectively. Localized syringoma—defined as multiple syringomas confined to 1 anatomic site—was more commonly reported than the eruptive form. Specifically, 212 (88.7%) cases were localized, with the most frequent type being located in the periorbital region (81%), followed by the vulva (17%) and face (2%). Ten (5.8%) of the localized periorbital cases were plaque type. Eruptive cases (11.3%) were largely distributed over the trunk, neck, and extremities (92.6%), with some distributed over the face and neck (7.4%).

Case reports of familial syringomatosis (ie, multiple syringomas present in familial cohorts) were rare, with only 29 reported cases[2-19] that are summarized in Supplemental Table I (available online at http://www.jaad.org). Of the 29 cases described, 15