Dermatology Practical & Conceptual

Clinical and Dermoscopic Characteristics of Cutaneous Chondroid Syringoma: A Systematic Review

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Key words: Chondroid syringoma, Mixed tumor of the skin, Skin neoplasm, Dermoscopy

Citation: Di Guardo A, Balampanos CG, Gargano L, et al. Clinical and Dermoscopic Characteristics of Cutaneous Chondroid Syringoma: A Systematic Review. *Dermatol Pract Concept*. 2024;14(4):e2024237. DOI: https://doi.org/10.5826/dpc.1404a237

Accepted: July 31, 2024; **Published:** October 2024

Funding: None.

Competing Interests: None.

Authorship: All authors have contributed significantly to this publication.

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ABSTRACT

Introduction: Cutaneous chondroid syringoma (CS) is a rare benign mixed skin tumor originating from sweat glands. Despite its rarity, accurate diagnosis and management are crucial due to its potential for malignant transformation.

Objective: This study aimed to provide comprehensive insights into the main features of cutaneous CS, encompassing its epidemiology, clinical presentation, and particularly, dermoscopic findings.

Methods: A systematic review was conducted to identify relevant literature on CS up to November 2023. Data extraction included clinical and histopathological characteristics from case reports and small case series.

Results: The systematic review identified 347 unique CS cases, predominantly benign. Clinical features included a predilection for the head and neck region, with variations in morphology observed. Dermoscopic patterns, although limited, revealed recurrent features aiding diagnosis. Malignant CS cases constituted a notable subset, exhibiting distinct clinical and histopathological features.

Conclusion: Cutaneous chondroid syringoma presents with characteristic clinical and histopathological features, necessitating comprehensive diagnostic approaches. Dermoscopy emerges as a valuable tool, although further research is needed to establish definitive patterns. Treatment primarily involves wide local excision, with collaboration among clinicians essential for optimal management. Future studies are warranted to address existing knowledge gaps and enhance understanding of this rare skin neoplasm.

Introduction

Cutaneous chondroid syringoma is a rare benign mixed skin tumor originating from the sweat glands and belongs to the larger category of cutaneous adnexal neoplasms [1]. In 1859, Billroth described what he called a "mixed tumor of the skin," which was histologically similar to the benign mixed tumors of salivary gland origin [2]. A century later, in 1961, Hirsch and Helwig introduced the term "chondroid syringoma" to describe this tumor, characterized by the presence of sweat gland elements within a cartilage-like stroma. This nomenclature reflects the dual origin of the tumor and underscores its unique histopathological features. CS accounts for less than 0.2% of all diagnosed skin tumors [3]. Chondroid syringoma typically manifests on the head and neck area, particularly on the nose, cheek, and upper lip, although cases involving other regions such as the trunk, genital area, and extremities have also been reported. Clinically, it often presents as a solitary well-circumscribed asymptomatic painless firm-to-hard slow-growing lobulated nodule, rarely exceeding 2 cm in diameter [1, 3]. A consistent feature of chondroid syringoma is the absence of ulceration. The color of the lesion varies from skin-colored to erythematous, with rare cases exhibiting pigmentation. Malignant transformation is rare but should be suspected in cases of large-sized chondroid syringoma located on the extremities and trunk in young women. The differential diagnosis should include other adnexal tumors and non-melanoma skin cancers such as basal cell carcinoma. Histologically, chondroid syringoma presents as a well-defined multilobulated tumor mass separated by fibrous septa, situated in the dermis and/or subcutaneous tissue with epithelial and stromal components [4, 5]. The stroma may exhibit a homogeneous bluish chondroid appearance but can also be myxoid or densely collagenous, eosinophilic, and hyalinized. The epithelial component comprises cuboidal or polygonal cells forming glandular-like structures, nests, or cell strands that give rise to ducts and tubules. Immunohistochemistry may be necessary for diagnosis in rare cases where doubt exists.

Objective

The aim of this study was to comprehensively define the main epidemiological characteristics, clinical presentations, and course of cutaneous chondroid syringoma, both in its benign and malignant forms. Special attention was given to cases where the dermoscopic pattern was reported. The main limitation of this systematic review is its reliance on case reports and small case series.

Methods

For the case described herein, we collected pertinent data including sex, age, personal medical history, and dermoscopic features of the cutaneous lesion (Heine DELTA30, 10 × magnification). Additionally, a comprehensive histological description of the specimen was provided. Subsequently, a thorough review of both benign and malignant chondroid syringomas reported in the existing literature was conducted. The data for this review adhered to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6, 7], as detailed in Supplementary file - Figure S1. Given the nature of the available literature, which primarily consisted of case reports and small case series, no formal methods were employed to assess the risk of bias in study design or reporting. When necessary, authors of the articles were contacted, and reference sections were meticulously examined to ensure inclusion of all relevant reports, including unpublished data.

Search Strategy

A systematic literature search was conducted from inception to November 24th, 2023, encompassing the PubMed, EMBASE, and Cochrane CENTRAL databases. The search terms "chondroid syringom*" and "mixed tumour AND cutaneous" were employed across all databases. A detailed search strategy for PubMed is outlined in Supplementary File. Chondroid syringomas were categorized into two groups based on reported histopathological and clinical features: benign/atypical and malignant, as delineated in Supplementary File.

Data Extraction

Clinical information retrieved from the case reports and small series encompassed sex, age, ethnicity, past medical history, description of clinical lesions, imaging, histopathology, treatment modalities, and disease outcomes. All statistical analyses were conducted using R (ver. 4.0.2) and RStudio (ver. 1.2.5033) [8], with descriptive statistics, including frequencies and percentages, computed for all variables.

Results

Systematic Review

In this review, a total of 387 relevant articles were initially identified using the specified search criteria. Additionally, 27 supplementary articles were obtained from the reference lists of review publications and subsequently included in this review. After the removal of 54 duplicate records, 241 articles remained following the initial screening based on title and abstract. Subsequent full-text assessment led to the exclusion of 34 studies due to unavailability, irrelevance to the topic, or being categorized as a review/meta-analysis. Out of the 207 remaining articles, five were further excluded due to reporting collisions between different adnexal tumors (4/5) or collision

Table 1. Epidemiology, Clinical Morphology, Dermoscopic Features, and Histology of Benign and Atypical Chondroid Syringomas.

Cases/ Articles	M/F	Ages (K-Means) (n = 229)	Site (n = 287)	Max Diameter (n = 287)	Clinical Morphology (n = 164)	Dermoscopic Features (n = 5)	Histology (n = 297)
297/155	**179/118** M: 60.27% F: 39.73%	**0-2**: 1 (0.4%) **3-5:** 0 (0%) **6-13**: 1 (0.4%) **14-18**: 3 (1.3%) **19-33:** 29 (12.7%) **34-48**: 60 (26.2%) **49-64:** 71 (31%) **65-78**: 52 (22.7%) **79 and over**: 12 (5.2%) **- NP**: 68 Media: 52.4 yrs Median: 54 yrs Range: 0.5 – 88 yrs	**Head and neck**: 208 (72.5%) Scalp: 15 Forehead/ glabella: 8 Ear/External ear canal: 12 Eyelid/Periocular: 40 Nose/Perinasal: 34 Cheek: 18 Lip/philtrum: 17 Neck: 4 Chin: 3 **Trunk**: 23 (8%) Chest/Breast: 7 Abdomen: 1 Axilla: 6 Back: 5 Gluteus: 1 Genitalia: 2 (scrotum), 2 (vulva) **Limbs**: 54 (18.8%) Arm/elbow: 7 Forearm: Hand/Wrist: 14 Thigh: 4 Leg: 3 Foot/Ankle: 20 **Multiple sites**: 4 (1.4%) **NP:** 8	**≤ 0.5 cm**: 17 (5.9%) **0.6- 0.9 cm:** 34 (11.8%) **1.0-1.9 cm**: 67 (23.3%) **2.0– 2.9 cm:** 33 (11.5%) **3.0– 3.9 cm:** 23 (8%) **≥ 4.0 cm**: 27 (9.4%) **Median diameter**: 1.9 cm **Range:** 0.3-13 cm **NP:** 100	**Firm superficial nodule/ mass (with or without skin involvement)**: 82 (50%) **Deep subcutaneous lesion (with intact overlying skin)**: 42 (25.6%) **Protruding/pedunculated mass**: 40 (24.4%) Additional clinical features (records yet included in previous classification) Periocular mobile lesion: 15 (9.1%) Pseudo-cystic appearance: 9 (5.5%) Telangiectasias: 8 (4.9%) Giant mass (>8 cm): 7 (4.3%) Ulceration and bleeding: 6 (3.7%) Multiple lesions: 4 (2.4%) Keloid-like: 1 (0.6%) **NP**: 133	White structures/ streaks and "cotton-white" area: 4/5 Telangiectatic vessels: 3/5 Homogenous erythematous background: 3/5 Milia-like cysts: 2/5 "Crown" of vessels: 1/5 Erythematous rim at periphery: 1/5 Curved vessels: 1/5 Homogeneous whitish-blue color pattern: 1/5 Brown blotches: 1/5 "Marble" appearance (mixture of with and red structure)	Benign: 290 Atypical: 7

Abbreviations: F: female; M: male; n: records included in every column; NP: not published.

of chondroid syringoma with other lesions (1/5). Consequently, a total of 202 publications were utilized, collectively representing 347 unique patients. It is noteworthy that all the publications included in this review were either single case reports or small case series, with no cohort studies or randomized controlled trials identified. A comprehensive summary of data derived from reported cases of benign and atypical chondroid syringomas in the literature is presented in Table 1, while cases of malignant chondroid syringomas are delineated in Table 2. The list of publications included in this systematic review is presented in Table 3. Among the included 347 cases, 290 were histopathologically categorized as benign (83.6%), 50 as malignant (14.4%), and seven as atypical (2%). Age and maximum diameter variables were categorized into groups, with the number of cases considered for each variable varying based on availability within the studied works.

Benign/Atypical CSs

Of the 297 listed cases of benign and atypical chondroid syringomas (CS), 179 were male (60.27%) and 118 were female (39.73%), resulting in a male-to-female ratio of 1.5:1. The average age at diagnosis was 52.4 years, with a median age of 54 years and an age range from 0.5 to 88 years. The highest incidence was observed in the age group ranging from 49 to 64 years (71/229 - 31%), followed by the age group from 65 to 78 years (52/229 – 22.7%). The incidence was relatively low in the age group from 0 to 18 years (4/229 - 1.75%). Regarding anatomical site, the majority of CS cases were located on the head and neck (208/287, 72.5%), specifically on the eyelid and periocular area (40/287), nose and perinasal area (34/287), and lips (17/287). Additionally, 54 cases (18.8%) were noted on the limbs, with frequent locations including the sole and foot (20/287) and the

Table 2. Epidemiology, Clinical Morphology, and Metastatic Behavior of the Malignant Chondroid Syringomas.

Cases/ Articles	M/F	Ages (n = 50)		Site (n = 50)	Max Diameter (n = 35)	Clinical Morphology of Primitive Lesion (n = 47)	Metastasis, Local Invasion and Recurrences (at Time of Diagnosis) (n = 47)
50/47	22/28 M: 44% F: 56%	13 14 18 22 24 25 31 32 32 33 33 34 37 40 40 41 44 44 46 48 49 50 51 52 52 53	54 55 57 60 60 61 61 61 63 64 72 72 75 77 78 79 81 81 82 83 84 86 89 93 Media: 52.9 yrs Median: 52 yrs	**Head and neck:** 19 (38%) - Scalp: 6 - Forehead/glabella: 1 - Ear/External ear canal: 1 - Eyelid/ Periocular: 1 - Nose/Perinasal: 3 - Cheek: 4 - Neck: 3 **Trunk:** 8 (16%) - Chest/Breast: 1 - Abdomen: 2 - Axilla: 1 - Back: 3 - Gluteus: 1 **Limbs:** 23 (46%) - Arm/elbow: 3 - Forearm: - Hand/Wrist: 5 - Thigh: 3 - Leg/knee: 3 - Foot/Ankle: 9 - **Multiple sites** (records yet included in previous classification): 2 (4%)	- ≤ **0.5 cm:** 0 (0%) - **0.6- 0.9 cm:** 1 (2%) - **1.0-1.9 cm:** 6 (12%) - **2.0– 2.9 cm:** 5 (10%) - **3.0– 3.9 cm:** 6 (12%) - ≥**4.0 cm:** 17 (34%) **Median diameter:** 4.0 cm **Range:** 0.7-19 cm **NP:** 15	- **Firm superficial nodule/ mass (with or without skin involvement):** 15 (31.91 %) - **Deep subcutaneous lesion (with intact overlying skin):** 19 (40.43 %) - **Protruding/pedunculated mass:** 8 (19.15 %) - **Infiltrative lesion:** 5 (10.64 %) Additional clinical features (records yet included in previous classification) - Ulceration: 8 (17.02%) - Periocular mobile lesion: 1 - Pseudo-cystic appearance: 1 (2.13%) - Telangiectasias: 2 (4.26%) - Giant mass (>8 cm): 14 (29.79%) - **NP:** 3	- **Distant metastasis:** 9 (19.15%) Lung and pleura: 6/9 Brain: 4/9 Bone: 3/9 Liver: 2/9 Spinal cord: 1/9 Kidney: 1/9 Thyroid: 1/9 - **Nodal metastasis:** 14 (29.79%) - **No metastasis:** 27 (57.45%) - **Unknown staging:** 3 - **Local Recurrence:** 9 (19.15%) - **Local invasion:** 5 (10.64%)

Abbreviations: F: female; M: male; n: records included in every column; NP: not published.

hand (14/287). The trunk and genitalia accounted for 8% of cases (23/287), with two cases reported on the scrotum and two cases on the vulva. Multiple sites were observed in four cases of benign CS (1.4%). In terms of maximum diameter, a significant portion of reported cases measured between 1.0 to 1.9 cm in size (67/287; 23.3%), followed by lesions ranging from 0.6 to 0.9 cm (34/287; 11.8%). Notably, 9.4% (27/287) of the studied cases were large in size (≥ 4 cm). The median size of benign/atypical CSs was 1.9 cm, ranging from 0.3 to 13 cm. The most common clinical morphology observed was a firm superficial nodule or mass, with or without skin involvement, accounting for 82 records (50%). Other frequently encountered clinical types included a deep subcutaneous lesion with intact overlying skin (42/164; 25.6%) and a protruding or pedunculated mass (40/164; 24.4%). Pseudo-cystic appearance was reported in nine cases (5.5%). Superficial macroscopic telangiectasias were observed on the surface of eight lesions (4.9%), while seven records (4.3%) presented as "giant" masses (≥ 8 cm). Additionally, one case was described with a keloid-like clinical appearance. Dermoscopy descriptions were available for only five cases. Most benign CS lesions presented with white structures or the so-called "white-cotton" area (4/5), followed by telangiectatic vessels (3/5). A homogeneous erythematous background and milia-like cysts were observed in more than one case. Moreover, unique dermoscopic patterns such as a "marble" appearance, erythematous rim at the periphery, and a vascular "signet ring" (as seen in our case) were described.

Malignant CSs

Out of the 50 listed cases of malignant chondroid syringomas (MCS), 28 cases were female (56%), and 22 cases were male (44%). The average age at MCS diagnosis was 52.4 years, with ages ranging from 13 to 93 years. A substantial number of these cases were located on the limbs (23/50;

Table 3. List of Publications Included in This Systematic Review.

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Halpert	1933	60	M	Bridge of the nose	1	1) the shape of the "end of a sausage", measured 3 x 2 x 2 cm	NP	Benign
Rabinovitch	1948	36	M	Bridge of the nose	1	Irregular raised nodular deformity over the bridge of the nose of a maximum diameter of 1.2 cm	NP	Benign
Mark	1951	37	F	External auditory meatus	1	Firm mobile circumscribed nodule	NP	Benign
Lennox	1952	26, 69, 53, 23, Adult	F, M, F, NP, M	Glabella, Nose, Finger, Foot, Thigh	5	Lump or nodule	NP	Benign
Klein	1956	Adult	F	Vulva	1	NP	NP	Benign
Greeley	1956	50	M	Cheek	1	Firm non-tender freely moveable tumor	NP	Benign
Rosborough	1963	83	F	Upper arm	1	Painful, mobile mass 3 cm	NP	Malignant (with nodal metastasis)
Khoo	1964	51	M	Middle toe	1	Firm and tender mass with superficial ulceration and sinus discharge (3 x 2 cm)	NP	Benign
Matz	1969	80	F	Parieto-occipital region of the scalp	1	Firm elevated irregular oval-shaped skin lesion, 5 x 3.5 x 2.5 cm	NP	Malignant (with local recurrence and nodal metastasis)
Hilton	1973	14	F	Arm	1	A recurrent lump with cystic appearance	NP	Malignant (with local recurrence)
Webb	1975	52	F	Medial aspect of the right thigh	1	Firm freely mobile swelling measuring 10 x 4 cm with cystic appearance	NP	Malignant (with local recurrence)
Hernandez	1976	39, 40	F, M	Scalp, Chest	2	1) Subcutaneous, well-circumscribed gray-white, firm, glistening nodule measuring 0.8 cm in diameter (suspected diagnosis: sebaceous cyst) 2) Well-circumscribed nodule measuring 1 cm in diameter	NP	Benign
Silva	1976	39	F	Sole	1	Painful ulcerated nodule simulating a poroma	NP	Benign
Dissanayake	1980	79, 33	F, M	Sacrum, Sole	2	1) Well circumscribed mass, 8 x 6 x 5 cm, with intact overlying skin; 2) Plantar nodule	NP	Malignant (1. pulmonary metastasis, 2. multiple lung metastasis)
Gupta	1982	48	M	Left thigh and left leg	1	Fungating growth of 15 x 10 cm in size on the anteromedial aspect of left leg with multiple hard grayish nontender nodules on left thigh	NP	Malignant (with multiple lesions and local recurrence)

Table 3 continues

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Redono	1982	61	F	Sole	1	2.5-cm firm, tender nodule with intact overlying skin	NP	Malignant (with local invasion and nodal metastasis)
Manni	1983	29	M	Tip of the nose	1	Firm semi-mobile nodular tumor (2 cm in size)	NP	Benign
Ishimura	1983	73	M	Back	1	Firm protruding slow-growing tumor measuring approximately 7 X 5 cm in size	NP	Malignant (with local recurrence, nodal and widespread metastasis)
Devine	1984	72	M	Sole	1	Slowly enlarging mass	NP	Malignant (with bone metastasis)
Shvili	1986	44	F	Gluteal region	1	Tender mass with a maximum diameter of 5 cm	NP	Malignant (with nodal metastasis and multiple visceral metastasis)
Terrill	1987	65, 29	M, F	Dorsum of the hand, index finger	2	1) 8 cm, irregular, lobulated, nontender, rubbery firm mass; 2) 1 cm, firm and rubbery, not adherent to flexor tendons or skin	NP	Benign
Scott	1988	61	M	Back of the neck	1	Soft ulcerated pedunculated nodule measuring 5 x 4 x 3 cm	NP	Malignant (nodal metastasis)
Sánchez Yus	1988	72	F	Nose	1	Firm pedunculated 3 cm mass	NP	Malignant
Steinmetz	1990	59	M	Scapula	1	Large scapular subcutaneous mass (4.0 X 2.5 X 1.6 cm)	NP	Malignant (nodal and distant metastasis)
Watson	1991	25	F	Dorso-lateral aspect of the foot	1	Tender swelling	NP	Malignant (local secondary deposit in the foot bone)
Stromberg	1991	Adult	M	Face	1	NP	NP	Atypical
Wenig	1992	13	F	Septum of the nose	1	Obstruction and epistaxis	NP	Malignant (metastasis - 31 yrs.)
Martorina	1993	81	M	Lower eyelid	1	Painless well-demarcated roughly polypoid lesion approximately 18 x 15 x 15 mm in size	NP	Benign
Gottschalk-Sabag	1994	82	F	Axilla	1	Subcutaneous mass	NP	Benign (cytology)
Trown	1994	22, 89	M, M	Sole, Neck	2	1) Circumscribed nodular mass of maximum diameter 3.5 cm, with a cystic and hemorrhagic surface 2) Pale slightly raised lesion with a well-defined erythematous edge	NP	Malignant (with eccrine differentiation)

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Tang	1994	39	M	external auditory canal	1	Freely movable firm polypoid mass	NP	Benign
Zumdick	1995	85	M	Upper lip	1	Firm papillomatous nodule	NP	Benign (with apocrine differentiation)
Hong	1995	40	M	Suprapubic region	1	Well-circumscribed nodular mass measuring 7.0 x 3.5 x 2.5 cm	NP	Malignant
Torii	1995	52	F	Wrist	1	Hemispherically elevated elastic hard subcutaneous nodule	NP	Benign
Nakayama	1996	52	M	Neck	1	Firm discrete partially cutaneous and partially subcutaneous nodule (2 cm in size)	NP	Benign (hyaline cell-rich CS)
Kim	1996	45, 35, 53	F	Forehead	3	1) Numerous rice-sized skin colored papules; 2) Skin-colored papules; 3) Multiple skin-colored papules	NP	Benign
Chen	1996	60	F	Nasofacial groove	1	Asymptomatic mass	NP	Benign
Poku	1996	65	M	Scrotum	1	3–3.5. cm firm, subcutaneous mass	NP	Benign
Shimizu	1996	68	F	Upper lip	1	Firm mass measuring 3 x 2 x 2 cm	NP	Benign (with marked ossification)
Kakuta	1996	35	M	Cheek	1	Skin-covered relatively firm bottom-adhered tumor approximately 6 cm in diameter	NP	Benign
Tyagi	1996	41	M	Upper eyelid	1	Firm nodular mass	NP	Benign
Sun	1996	18	M	Foot	1	Protruding mass on the sole surface	NP	Malignant
Kiely	1997	50	F	Hand	1	Primitive lesion is not described	NP	Malignant (lung metastasis due CS resected 17 yrs previously)
Bisceglia	1997	64	M	External ear	1	NP	NP	Benign (hyaline cell-rich CS)
Akasaka	1997	58	M	Chin	1	Slightly reddish, 18 x 21 mm, dome-shaped nodule with telangiectasia on the surface	NP	Benign (ossification, hair matrix, and sebaceous ductal differentiation)
Bhargava	1997	29	M	Nasal tip	1	Round intradermal nodule	NP	Benign
Nakamura	1998	72	M	2 lesions in maxillary region and ear lobe	1	Both skin tumors were firm, light brown in color, dome-shaped; their sizes were 25 x 30 mm and 30 x 40 mm in diameter	NP	Benign (multiple and recurrent CS)

Table 3 continues

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Bates	1998	Adult	M, M, F	Toe, Foot, Finger	3	Size (longest length in cm): 3, 2, 2	NP	Atypical CS
Nakayama	1998	55, 36, 45, 42, 39, 55, 60, 52, 70	6 M, 3 F	Shoulder (1), Face (6), Neck (2)	9	Diameter (cm): 3.5, 0.7, 1.5, 1.5, 0.7, 1 .0, 0.7, 2.0, 2.0.	NP	Benign
Agrawal	1998	40	F	Scalp (occipital region)	1	Recurrent subcutaneous 6 cm x 4 cm, soft swelling adherent to the operative scar	NP	Malignant (with recurrence)
Hardisson	1998	64	M	Axilla	1	Painless subcutaneous tumor measuring 8.3 x 7.3 x 6.5	NP	Benign
Kitazawa	1999	84	F	Canthal region	1	Firm well-demarcated, polypoid tumor, approximately 2.5 x 1.5 cm	NP	Benign
Yamamoto	1999	45, 80, 68, 44, 73, 25, 77, 35	2 F, 6 M	Upper lip, cheek, nose, ear, eyebrow	8	NP	NP	Benign
Park	2000	55	F	Medial aspect of the right proximal leg	1	Well-circumscribed egg-sized mass with a protrusion in the central area but with no ulceration (3 × 3 × 4 cm in size)	NP	Malignant
Sheik	2000	28	F	Thigh	1	Well-circumscribed 2.5 cm firm-to-hard nodule with a shiny smooth white cut surface	NP	Benign
Barnett	2000	24	M	Foot	1	Recurrent nodules on sole	NP	Malignant
De Fata Chillón	2001	76	M	Scrotum	1	Solid scrotal mass (4.2 cm in diameter)	NP	Benign
Hasson	2001	55	F	Cheek	1	Multifocal rounded mobile solid tender lesions with intact overlying skin	NP	Benign
Nicolaou	2001	54	M	Thenar eminence	1	Firm lobulated 4.5 cm × 3.5 cm lesion. Some dilated veins were visible beneath the surface.	NP	Malignant (low-grade)
Mencía-Gutiérrez	2001	71, 60	M, F	Upper eyelid, upper eyelid	2	1) Smooth firm rounded well-circumscribed elevated lesion of polypoid appearance, measuring 1.3 cm in diameter 2) Mass of verrucose aspect, rounded, well-circumscribed, measuring 0.4 cm in diameter	NP	Benign
Medina Henriquez	2001	37	M	Hand	1	2 cm hard subcutaneous nodule which was adherent to the skin	NP	Malignant (nodal metastasis)
Rege	2001	45, 40	M, M	Neck, Cheek	2	Cutaneous or subcutaneous swellings	NP	Benign

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Nemoto	2002	56	F	Little finger of the right hand	1	Soft tumor with a diameter about 10 mm	NP	Benign
Reis-Filho	2002	29	M	Palmar aspect of hand	1	Slowly enlarging flesh-colored nodule measuring 2 cm in maximum diameter	NP	Benign (Hyaline cell-rich CS)
Miracco	2002	65	M	Scalp	1	Painless nodule in the vertex	NP	Benign (lipomatous mixed tumor)
Yavuzer	2003	23-65	10 M, 6 F	Face and upper extremity	16	NP	NP	Benign
Satter	2003	25	M	Upper lip	1	Slowly enlarging nodule appearing after minor trauma to the area	NP	Benign
Sungur	2003	55	M	Shoulder	1	Clinically malignant mass measuring 10 x 8 x 10 cm	NP	Benign
Arikan	2004	72	M	Upper lip	1	Firm non-tender nodular mass	NP	Benign
Shashikala	2004	32	F	Scalp	1	Mass 5 x 4 cm in size with an irregularly nodular surface and firm-to-hard consistency	NP	Malignant
Gee	2004	40	M	Cheek	1	Firm rubbery subcutaneous nodule with a more superficial protuberant lesion arising within it	NP	Benign
Chao	2004	46	M	Chin	1	Firm painless mass (1.4 x 1.2 x 1.4 cm) with a smooth surface except for the lower portion, which was ulcerative	NP	Benign
Awasthi	2004	43	M	Cheek	1	5 cm in diameter, firm non-tender freely mobile lump	NP	Benign (with extensive ossification and marrow formation)
Takahashi	2004	22	F	Left big toe	1	25-mm dome-shaped ulcerated nodule	NP	Malignant (recurrent and with bone invasion)
Mandeville	2004	22, 34, 36, 45, 52, 54, 58, 65, 73	4 F, 5 M	Periocular	9	Enlarging/recurrent/inflamed nodule	NP	Benign
Radhi	2004	46	M	Scalp	1	Scalp nodular lesions. The tumors were mobile and slowly increasing in size.	NP	Benign (with small tubular lumina)
Kaushik	2005	57	F	External auditory meatus	1	Non-tender smooth firm lesion	NP	Benign
Smiri	2005	NP	M	Face	7	Single painless skin lesion of about 1,5 cm	NP	Benign

Table 3 continues

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Mathiasen	2005	64	M	Infraorbital facial skin	1	6-mm erythematous papule	NP	Malignant (with recurrence)
Ogawa	2006	61	F	Lower eyelid	1	Painless and slowly developing mass (31 x 22 x 19 mm)	NP	Benign
Villalón	2006	67, 77, 58, 60, 71, 44, 46, 63		Lip, Ear, Nose, Mandibula	8	Well-defined bluish nodular lesions with a smooth shiny surface (max diameter: 5-10 mm)	Case 4: Well-defined edges and with a homogeneous whitish-blue color pattern	Benign
Gündüz	2006	46	M	Lower eyelid	1	Solid painless mass (20 x 15 x 15 mm in size)	NP	Benign
Karnwal	2006	40	M	External ear canal	1	Fluid-containing cyst	NP	Benign (cystic structure)
Kuwabara	2006	69	F	External auditory canal	1	Painless mass	NP	Benign
Kerimoglu	2006	53	F	Proximal right pretibial region	1	Nodular subcutaneous painless mobile mass.	NP	Benign
Mebazaa	2006	43	F	Arm	1	Firm painless mobile 2-cm nodule covered by normal skin.	NP	Benign
Sivamani	2006	84	M	Glabella	1	Enlarging bluish painless subcutaneous nodule	NP	Benign
Eccher	2007	27	M	Frontal region	1	Slow-growing nodule localized in the subdermis	NP	Benign (with extensive ossification)
Torres González	2007	29, 50	F, M	Nostril, dorsum of the nose	2	1) Exophytic pedunculated smooth skin-colored firm lesion, 8 mm in diameter and; 2) Well-circumscribed firm hemispherical nodular lesion (5 mm in diameter)	NP	Benign
Kazikdas	2007	26	F	Helix	1	Firm 1 x 1-cm freely mobile superficial mass	NP	Benign
Cýralýk	2007	72	M	Axilla	1	Subcutaneous painless, mobile, and slowly increasing in size (3 cm in diameter)	NP	Benign
Choudhury	2007	45	F	Multiple sites	1	Multiple masses in the flank, chest wall, arm, -thigh and neck	NP	Benign
Varsori	2007	84	M	Lower eyelid	1	Adherent asymptomatic subcutaneous nodule	NP	Benign
Ryu	2007	46	M	Heel	1	Painless and mobile nodular mass	NP	Benign
Markou	2008	60	F	External ear canal	1	Exophytic mass	NP	Benign

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Ogawa	2009	40	M	Lower lip	1	Skin tumor that was hard, well-demarcated (keloid-like)	NP	Benign
Hafezi-Bakhtiari	2009	71	F	Scalp	1	Slow-growing 2.0 × 2.0 × 1.0 cm nodule scalp	NP	Benign (with predominant myoepithelial component)
Magro	2009	74	F	Breast	1	6-cm firm painless freely mobile pedunculated mass, with a smooth polylobulated external surface covered by normal skin, focally ulcerated	NP	Benign (with lipomatous differentiation)
Brewer	2009	20	M	Left nostril	1	1-cm firm lobular mass with telangiectasias	NP	Benign
Baran	2009	47	M	Eyebrow	1	0.7 cm lesion	NP	Benign
Borman	2009	56	M	Hand	1	Soft and fixed subcutaneous mass	NP	Benign
Siddaraju	2009	43	F	Dorsum of the nose	1	0.8 × 0.8 cm soft-to-firm, tender, and not fixed to the underlying bone swelling	NP	Benign
Kakitsubata	2009	58	M	Arm	1	Large palpable mass in subcutaneous tissue	NP	Benign
Skoro	2010	63	M	Neck	1	Small soft nodule	NP	Benign
Tokyol	2010	57	F	Philtrum	1	Slow-growing lump	NP	Benign
Beals	2010	42	F	Forefoot	1	Non-tender 1.5-cm firm mass on the medial side of the forefoot	NP	Benign
Sirivella	2010	66	F	Right chest	1	Firm non-tender slightly bulging mass (measuring 9 cm × 5 cm) covered by skin with a pinkish-purple hue.	NP	Benign
Kumar	2010	20	M	Dorsum of nose	1	Firm non-tender swelling	NP	Benign
Dubb	2010	32, 18, 23	F, F, M	Scalp, upper lip, scalp	3	1) 2-cm mass involving the skin/soft tissue; 2) 0.5-cm mass; 3) 2-cm mass involving the skin/soft tissue	NP	Benign
Zirbs	2011	81	F	Lower eyelid	1	Skin-colored slow-growing tumor	NP	Benign
Sánchez Herreros	2011	93	F	Nasal ala	1	Reddish 2.5-cm ulcerated firm nodule	NP	Malignant
Watarai	2011	46	M	Sole	1	Solitary dome-shaped skin-colored firm nodule measuring 30 mm x 30 mm,	NP	Malignant (nodal metastasis)

Table 3 continues

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Solanki	2011	16, 21	M, F	Nose, cheek	2	1) Well-defined non-tender mobile nodule of 1.5 cm x 1.5 cm with slight violaceous discoloration in its center; 2) Well-defined nodule of 4 cm x 3 cm, firm-to-hard in consistency, non-tender.	NP	Benign
Sirinoğlu	2011	63	M	Fifth toe	1	Subcutaneous mobile mass with rubber consistency, approximately 3 x 2 x 1 cm in size	NP	Benign
Paik	2011	51	M	Scalp (parietal area)	1	Firm painless mobile, 1 × 1-cm nodule covered by skin and located	NP	Benign
Kazakov	2011	32, 29, 44, 66	M, M, M, F	Nose, Nose, Forehead, Fifth toe	4	1) Solitary nodule (3 x 2 cm); 2) Solitary 1.5 x 0.8 cm; 3) Solitary 1.5 cm nodule (preoperative diagnosis: trichilemmal cyst) 4) Solitary 1.5 cm nodule	NP	Benign (apocrine mixed tumor with intravascular tumor deposits)
Yaakub	2012	60	F	Nasal ala	1	Smooth firm bluish 10-mm nodule	NP	Benign (recurrent CS)
Abil	2012	65	F	Cheek	1	Well-defined rounded nodule of firm consistency, painless, adhering to the skin, measuring 3 cm in long axis, flesh-colored, with an irregular and telangiectatic surface	NP	Benign
Walls	2012	68	F	Eyebrow	1	1-cm firm mobile flesh-colored nodule	NP	Benign (recurrent)
Araújo	2012	31	F	Scalp (occipital area)	1	Hardened ulcerated lesion in the occipital region, with deep plane infiltration and elimination of tenuous purulent secretion	NP	Malignant (local invasion of cranium and occipital lobe)
Su	2012	64	F	Vulva	1	Solitary round-to-oval, non-tender mobile mass (measuring 2.1×1.0×0.8 cm)	NP	Benign
Arango-Duque	2012	27	F	Nose	1	Papular exophytic firm, well-defined lesion, 0.4 cm in diameter with some superficial telangiectasia	NP	Benign
Bahrami	2012	0.5-84	4 M, 6 F	Limbs, Trunk, Head	10	NP	NP	Benign
Jun	2012	55	F	Right malar area	1	Slowly growing subcutaneous mass	NP	Benign (apocrine type with calcification)
Siraj	2012	59	M	Scalp	1	Gradually enlarging non-tender cystic tumor	NP	Benign (with prominent pilomatricomal differentiation)

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Franco	2013	68	F	Second left toe	1	Voluminous nodular lesion with smooth erythematous surface, telangiectasias	NP	Benign
Kumar	2013	27	M	Upper eyelid	1	Firm, non-tender, subcutaneous, and not fixed to underlying tissues (1.5 x 1.5 cm)	Erythematous background and telangiectatic vessels	Benign
Requena	2013	82	M	Glabella	1	Subcutaneous area of swelling	NP	Malignant
Hernandez	2013	40	M	Medial calf	1	4.0 cm firm mass	NP	Benign
Palioura	2013	53	F	Upper eyelid	1	Asymptomatic "cystic" lesion	NP	Benign
Kau	2013	71	F	Upper eyelid	1	Firm painless polypoidal mass with superficial telangiectatic vessels and ulcerations (4.0×3.0×2.4 cm)	NP	Benign
Whittle	2013	49	F	Index finger	1	Slowly-enlarging painless focal subcutaneous mass	NP	Benign
Malik	2013	61	F	Scalp	1	Giant ulcero-fungating ulcerated growth	NP	Malignant (invasion of dural meninges)
Tural	2013	34	F	Nasolabial region	1	Slow-growing subcutaneous nodular lesion	NP	Malignant
Boyaci	2014	55	M	Elbow	1	Slow-growing painless mass	NP	Benign
Nangia	2014	24	M	Forehead	1	1 cm in diameter, firm nontender nodule	NP	Benign (extensive osseous differentiation)
Paraskevopoulos	2014	53	M	Left medial canthus	1	1 cm in diameter exophytic nodule	NP	Benign
Wollina	2014	71	M	Flank	1	Subcutaneous firm nodule	NP	Benign
Choi	2015	58	M	Nasal dorsum	1	Movable soft mass with elevation of the normal-appearing skin	NP	Benign
Park	2015	84	F	Nose	1	Soft cylindrically shaped protruding nodule with telangiectatic vessels	Arborizing vessels and white shiny streaks	Benign
Krishnamurthy	2015	41	M	Helix	1	Skin-colored nodular lesion	NP	Malignant (nodal metastasis)
Menéndez	2015	63	F	Epigastrium	1	Subcutaneous nodule	NP	Malignant (spinal cord)
Kelten	2015	78	F	Breast skin	1	Non-tender mobile, palpable lump localized superficially	NP	Benign
Mahindra Nayyar	2015	33	M	Cheek	1	1.8 x 1.3 cm reddish firm deep-seated nodule on the right medial cheek	NP	Malignant

Table 3 continues

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Sereflican	2015	64	M	Breast	1	12 x 9.8 cm non-tender firm polylobulated nodule covered by normal skin	NP	Benign
Phelps	2015	63	F	Eyelid	1	Slow-growing mass	NP	Benign (apocrine differentiation)
Limaiem	2015	26, 45, 50, 38	F, F, F, M	Lower eyelid, Nasogenien groove, Nose, and Chin	4	Slow-growing painless firm subcutaneous nodule	NP	Benign
Aoun	2015	NP	5 M, 5 F	Limbs, Face	10	NP	NP	Benign
Shobhanaa	2016	57	F	Scalp (occipital region)	1	Firm-to-hard, fixed to the underlying structures, and measuring 3 × 3 cm in their maximum dimension with a few tiny satellite nodules of 2–3 mm diameter.	NP	Malignant
Odhav	2016	19	M	Preauricular region	1	Firm fixed non-tender subcutaneous nodule	NP	Benign
Ka	2016	53	M	Axillary region	1	Invasive 10 cm mass	NP	Malignant
Charles	2016	77	M	Eyebrow	1	Subtly elevated nontender faintly erythematous subcutaneous mass with eyebrow madarosis	NP	Benign
Madi	2016	47	F	Plantar aspect of left foot	1	Tender mobile subcutaneous mass with overlying intact skin	NP	Benign
Peria	2016	47	M	Tip of the nose	1	Firm mobile nodule measuring 2 × 2 cm, covered by skin	NP	Benign
Ismail	2016	74	F	Nasal alar	1	Exophytic cystic mass with occasional superficial telangiectasia and a violaceous hue	NP	Benign
Matsuyama	2016	26-85	6 F, 10 M	Face, Nose, Scalp, Back	16	NP	NP	Benign
Rogers	2016	67	F	Axilla	1	Solitary well-demarcated extremely firm freely mobile non-tender subcutaneous nodule	NP	Benign (cytology)
Azari-Yam	2016	68	F	Upper eyelid	1	0.7 cm firm freely moving non-tender nodule	NP	Benign (apocrine differentiation)
Shalini	2017	45	M	Thigh	1	Firm non-tender lesion	NP	Benign (cytology)
Alfonso Fernández	2017	49	F	Finger (thumb)	1	1-cm diameter painful nodule	NP	Benign (invading the distal phalanx of the thumb)
Laxmisha	2017	68	M	Ear lobe	1	Solitary firm asymptomatic 2 × 2-cm skin-colored nodule	NP	Benign

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Prieto-Granada	2017	42	F	Upper back	1	NP	NP	Benign (with tyrosine-rich crystalloids)
Turhan-Haktanir	2017	11	M	Ala of the nose	1	Hard fixed 13 × 10 mm mass	NP	Benign
Khotiya	2017	51	F	Thigh	1	NP	NP	Malignant (with lung metastasis)
Hudson	2017	41	M	Lower Eyelid	1	Non-tender multilobulated firm freely movable mass	NP	Benign
Sundling	2017	43	M	Foot	1	Firm nodule/mass	NP	Benign
Park	2017	46	F	Cheek	1	Slow-growing nodular protruding mass	NP	Benign
Fernandez-Flores	2017	81	M	Scalp (above the hairline)	1	Subcutaneous mobile 1.2 cm nodule, which was apparently cystic,	NP	Malignant
Nguyen	2017	52	F	Thumb	1	Slow-growing nodular lesion associated with mild pain	NP	Malignant (local recurrence after 20 years)
Jain	2018	70	F	Lower eyelid	1	0.5 cm × 0.5 cm nodular non-tender swelling (preoperative diagnosis: sebaceous cyst)	NP	Benign (with cystic change and syringometaplasia)
Nakanishi	2018	44	M	Fingertip	1	Subcutaneous painless swelling (1 cm in diameter)	NP	Malignant
An	2018	41	M	Nose	1	Painless well-defined subcutaneous or intradermal nodule	NP	Benign
Masamatti	2018	65	F	Finger	1	Well-circumscribed mass measuring around 3 cm in diameter	NP	Benign
Rogalski	2018	24	M	Nose	1	Firm non-tender 7-mm skin-colored papule with telangiectasias	NP	Benign
Lal	2018	86	M	Left scapula	1	Pink indurated plaque	NP	Malignant
Chauvel-Picard	2018	32	F	Right eyebrow	1	Palpably mobile subcutaneous nodule	NP	Malignant
Agrawal	2018	32	M	Forehead	1	Firm painless mobile 5 mm x 5 mm nodule	NP	Benign
Lu	2018	72	M	Third toe of his right foot	1	Firm mass (2.3 × 1.5 × 1.2 cm)	NP	Benign
Russel-Goldman	2019	32-88	15 M, 10 F	Head and neck, Trunk, Limbs	25	NP	NP	Benign: 16 Apocrine, 9 Eccrine
Nel	2019	78, 72	M, F	Scalp, Thigh	2	1) Fungating mass with central ulceration (4.0 × 3.6 × 1.2 cm); 2) Hard mobile mass with protruding component (maximal diameter of 8 cm)	NP	Malignant

Table 3 continues

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Owen	2019	19, 41	F, M	Upper eyelid, preauricolar cheek	2	1) 5.5 x 4.5 cm firm painless freely mobile tumor; 2) 14 x 9.9 cm pedunculated firm painless freely mobile keloid-like lesion	NP	Atypical CS, Benign giant CS
Panagopoulos	2019	61	M	Delto-pectoral fold	1	Tender growing lump	NP	Malignant
Linares González	2020	48	M	Nasogenian sulcus	1	Nodular lesion (1 cm in diameter) with a smooth pearly surface	Mimicking basocellular carcinoma: irregular telangiectatic vessels associated with cotton-white structures on an erythematous-white bed	Benign
Favareto	2020	60	F	Knee	1	2 cm painful nodular mass	NP	Malignant (nodal metastasis)
Mittal	2020	19	F	Cheek	1	Multinodular mass of about 4 cm × 3 cm size with a subcutaneous swelling	NP	Atypical CS
Wernham	2020	53	M	Posterior heel	1	4 cm ulcerated exophytic nodule	NP	Benign
Zia	2020	84	M	Arm near axilla	1	9 × 7 cm subcutaneous nodule	NP	Malignant
Rosell-Díaz	2020	74	M	Scalp	1	Well-circumscribed polylobed nodule	NP	Benign
Panagopoulos	2020	59, 60	M, M	Thigh, Ankle	2	NP	NP	Benign
Ki	2020	54	F	Axilla	1	1 cm-sized oval hypoechoic mass	NP	Benign
Okay	2021	53	M	Right middle finger	1	a 3.5 -3 cm well-circumscribed firm lesion	NP	Benign
Purkayastha	2021	7	M	Left cheek	1	Firm lesion with blue discoloration and a surrounding area of hypervascularity	NP	Benign
Vázquez Hernández	2021	65	M	Upper lip	1	Chronic indolent subcutaneous tumor	NP	Benign
Agarwal	2021	52, 71, 47	F, M, F	Nose, postauricular region, nose	3	Progressively growing swelling	NP	Benign
He	2021	47	M	Lateral canthus	1	Well-demarcated asymptomatic dermal-based 0.9 cm nodule	NP	Benign (with pilomatrical differentiation)

Table 3. List of Publications Included in This Systematic Review. *(continued)*

Author	Year	Age	Sex	Site	Cases	Clinical Morphology	Dermoscopy	Histology
Palit	2021	42	M	Upper lip	1	Solitary 1 × 1 cm firm non-tender skin-colored-to-erythematous nodule	Structureless area, milia-like cyst, irregular brown blotches, erythematous rim at the periphery and linear curved vessels	Benign
Petrovic	2022	88	F	Right gluteal region	1	Subcutaneous mass	NP	Atypical CS (with diffuse nuclear expression of the p16 stain)
Gotoh	2022	56	M	Lower lip	1	Non-tender slightly hard mobile mass measuring ~11 x 11 x 7 mm	NP	Benign
O'Rourke	2022	42, 58, 72	M, M, M,	Eye canthus	3	Soft mobile nodules	NP	Benign
Bal	2022	26	M	Upper lip	1	Smooth-surfaced firm pedunculated nodule measuring approximately 1.1 cm in diameter	Pleomorphic globules and irregularly enlarged branching telangiectasias conferring a marbled appearance	Benign (with focal areas of ossification)
Ungureanu	2023	73	F	Fifth finger	1	Two contiguous nodules with a solid whitish appearance	NP	Benign
Prajapati	2023	58	M	Upper eyelid	1	Recurrent CS after surgery	NP	Benign
Miranda	2023	77	M	Right cheek	1	Subcutaneous nodule, color of the skin, with multiple telangiectasias, multilobulated, firm.	NP	Malignant (with cerebral metastasis)
Kisova	2023	58	F	Upper lip	1	Firm mass on the upper lip measuring 10/8/7 mm	NP	Benign
Ferragina	2023	76, 53	F, M	Orbital cavity, lip filter	2	1) non-tender multilobulated firm slightly painful mass2) non-tender well-defined mobile nodule of about 10 mm	NP	Benign
Di Guardo	2023	28	F	Philtrum	1	Firm non-tender mobile nodule, which was 1.2 cm in diameter	Crown of dilated vessels, white structures ("cotton area"), erythematous background, and milia-like cyst	Benign

CS =chondroid syringoma; F = female; M = male; NP = not published

46%), with the foot and sole being the most frequent site (20/50). The head and neck region accounted for 38% of cases (19/50), with 15 cases were reported on the scalp. Additionally, eight cases were noted on the trunk skin (16%), and two cases were found on multiple sites (4%). The median maximum diameter of MCS lesions was 4.0 cm, with a size range of 0.7 to 19 cm. The most common clinical subtype observed was a deep subcutaneous mass with intact overlying skin (19/47; 40.43%), followed by firm superficial nodules (15/47; 31.91%) and protruding or fungated masses (8/47; 19.15%). Five records presented with evident infiltrative lesions (10.64%). Ulceration was reported in eight cases (17.02%), while giant masses (≥8 cm) were observed in 14 cases (29.79%). No dermoscopic descriptions were reported. Regarding metastatic spreading, nine cases of distant metastasis were reported at the time of diagnosis (19.15%). The most common sites of organ metastasis were the lung and pleura (6/9), followed by the brain (4/9), bones (3/9), and liver (2/9). Other locations included the spinal cord (1/9), kidney (1/9), and thyroid (1/9). Nodal metastasis at the time of diagnosis was found in 14 cases (29.79%). Out of the 47 listed cases, 27 patients presented with no metastasis at the time of diagnosis (57.45%). Regarding records of local recurrence, it was found in nine cases (19.15%), while MCS with obvious features of local invasion were reported in five cases (10.64%).

Discussion

Chondroid syringoma (CS) stands as an exceptionally rare mixed tumor originating from sweat glands within the skin, characterized by histopathological features reminiscent of both glandular and cartilaginous tissues. Despite its infrequency, it garners attention due to its unique nature, accounting for less than 0.2% of all diagnosed skin tumors. Predominantly, CS manifests as a solitary painless firm-to-hard nodule predominantly localized in the head and neck region, notably on the nose, cheek, and upper lip. Nevertheless, occurrences have been documented across various anatomical sites, including the trunk, genital area, and extremities.

Contributing to the expanding literature on CS, a recent case involves a 28-year-old woman with no significant medical history presenting with a gradually enlarging lump on her left nasolabial fold, consistent with the clinical profile of CS. Dermoscopic examination revealed unique features such as the "signet ring" pattern. Subsequent histopathological analysis confirmed the lesion as a benign chondroid syringoma, with negative surgical margins.

A systematic review of the existing literature identified 347 unique cases of CS, with the majority classified as benign (83.6%). The clinical characteristics observed in these cases were consistent with previous descriptions, with a predilection for the head and neck region and a median age of diagnosis around the fifth decade of life. Interestingly, the review highlighted variations in clinical morphology, with a spectrum ranging from superficial nodules to deep subcutaneous masses. Dermoscopic descriptions, albeit sparse, disclosed patterns like the "white-cotton" area and telangiectatic vessels. While benign CS predominates, malignant cases constitute a notable subset (14.4%), underlining the significance of accurate diagnosis and management. MCSs may exhibit distinct clinical features, including larger size, more frequent occurrence on the limbs, and a considerable propensity for metastasis, notably to the lung, pleura, and brain. Distant metastasis was observed in a significant proportion of cases at diagnosis (19.15% of cases), highlighting the aggressive nature of this variant.

Dermoscopy has become a valuable diagnostic adjunct for many skin cancers, although dermoscopic patterns in CS remain poorly documented. Recurrent features, such as whitish structureless areas and telangiectasias, are frequently observed. Additional features like milia-like cysts, erythematous homogeneous areas, and bluish homogeneous areas are also noted. Unique presentations, including a "marble-like" appearance, pigmented blotches, and a "signet ring" of vessels, further complicate specific dermoscopic pattern identification. Understanding these dermoscopic presentations aids in diagnosing mixed tumors of the skin. It is not possible to define pathognomonic dermoscopic patterns for chondroid syringoma due to the paucity of case reports. However, recurrent features can be found. Whitish structureless areas and telangiectasias are observed in almost all cases described in the literature [9,10,11,12]. In addition, milia-like cysts, erythematous homogeneous areas, and bluish homogeneous areas are also recurrent features [11,1]. However, unique dermoscopic presentations such as marble-like appearance, pigmented blotches, and crown of dilated vessels must be considered [10,11]. These rare presentations make it more challenging to identify specific dermoscopic patterns that are useful for diagnostic purposes. In the case of mixed tumor of the skin, dermoscopy also predicts the histological composition [11]. The white structureless area corresponds to the fibrous stroma, the erythema to the increased vascularity, and the blue color represents a dominant chondroid stroma. The dermoscopic feature of milia-like cyst, which corresponds to the dermal keratocyst, points to the follicular-sebaceous-apocrine origin of the tumor. The main dermoscopic differential diagnoses included basal cell carcinoma, nodular hidradenoma, trichoepithelioma, pilomatricoma, and sebaceoma. On dermoscopy, nodular hidradenoma appears as a homogeneous area with varying colors, including white, along with other variable structures. The color of homogenous areas varies from pinkish, bluish, and bluish-pink to brown. The associated vascular structures are arborizing

telangiectasias, polymorphous atypical vessels, and linear irregular vessels [13]. The most recurrent dermoscopic features of pilomatricoma are red-blue background with yellow structureless areas, and ulceration with linear irregular or tortuous or polymorphous vessels [14]. The dermoscopic picture of a trichoepithelioma demonstrates shiny white areas/background and milia-like cysts along with small thin in-focus arborizing vessels [13]. The most common dermoscopic features of sebaceoma are yellow structures (homogenous structureless areas and/or yellowish roundish) with peripheral and thin arborizing or polymorphous vessels [14]. Occasionally, central whitish areas and pigmented structures can be found.

Despite the potential of dermoscopy, histopathological examination remains the gold standard for CS diagnosis. Given its frequent occurrence in cosmetically sensitive areas, such as the face, identifying clinical features and dermoscopic patterns to differentiate benign CS from malignant counterparts holds clinical significance, potentially facilitating preoperative diagnosis. In cases of malignant CS, wide local excision stands as the most effective initial treatment, likely due to the presence of microscopic satellite nodules [15, 16]. Standard excisions without wide margins are associated with higher rates of local tumor recurrence and metastasis. Given the infiltrative nature of the tumor and the presence of satellite nodules, Mohs micrographic surgery is likely a promising treatment option and should be considered [17].

Lastly, this review aimed to augment our understanding of the clinical spectrum of CS, emphasizing the necessity for comprehensive diagnostic approaches and tailored management strategies. Given the rarity of CS, collaborative efforts between clinicians, pathologists, and dermatologists are imperative for optimal patient care.

Limitations

This review is subject to some limitations. Firstly, the rarity of CS precludes the existence of prospective studies analyzing these tumors. Consequently, the analysis in this review is predominantly based on case reports and case series, which inherently limits the generalizability of findings. Variability in the detail and completeness of the available information across publications posed challenges in data interpretation. Additionally, the lack of uniformity in reporting standards hampered a thorough analysis and underscores the necessity for larger-scale studies to enhance our comprehension of this rare skin neoplasm.

Conclusion

In conclusion, cutaneous chondroid syringoma (CS) remains a rare yet clinically significant entity within the spectrum of skin tumors. Despite its infrequency, understanding its clinical presentation, histopathological features, and potential for malignant transformation is paramount for accurate diagnosis and management. Dermoscopy emerges as a valuable adjunct in diagnosing CS, although further research is needed to establish definitive dermoscopic patterns. Treatment primarily revolves around wide local excision, with Mohs micrographic surgery offering promising outcomes, especially in cases of malignant transformation. Collaboration between clinicians, pathologists, and dermatologists is essential for optimal patient care. While this review provides valuable insights into CS, future studies encompassing larger cohorts are warranted to address existing knowledge gaps and to enhance our understanding of this rare skin neoplasm.

References

1. Villalón G, Monteagudo C, Martín JM, Ramón D, Alonso V, Jordá E. Siringoma condroide: revisión clínica e histológica de ocho casos [Chondroid syringoma: a clinical and histological review of eight cases]. *Actas Dermosifiliogr*. 2006 Nov;97(9): 573-7. Spanish. DOI: 10.1016/s0001-7310(06)73468-8. PMID: 17173760.
2. Stout AP, Gorman JG. Mixed tumors of the skin of the salivary gland type. *Cancer*. 1959 May-Jun;12(3):537-43. DOI: 10.1002 /1097-0142(195905/06)12:3<537::aid-cncr2820120313>3.0 .co;2-n. PMID: 13652101.
3. Yavuzer R, Başterzi Y, Sari A, Bir F, Sezer C. Chondroid syringoma: a diagnosis more frequent than expected. *Dermatol Surg*. 2003 Feb;29(2):179-81. DOI: 10.1046/j.1524-4725.2003.29045.x. PMID: 12562350.
4. Bates AW, Baithun SI. Atypical mixed tumor of the skin: histologic, immunohistochemical, and ultrastructural features in three cases and a review of the criteria for malignancy. *Am J Dermatopathol*. 1998 Feb;20(1):35-40. DOI: 10.1097/00000372-199802000 -00007. PMID: 9504667.
5. Min KH, Byun JH, Lim JS, Lee HK, Lee WM, Joo JE. Chondroid Syringoma on Face. *Arch Craniofac Surg*. 2016 Sep;17(3): 173-175. DOI: 10.7181/acfs.2016.17.3.173. Epub 2016 Sep 23. PMID: 28913278; PMCID: PMC5556809.
6. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000 Apr 19;283(15):2008-12. DOI: 10.1001/jama.283.15.2008. PMID: 10789670.
7. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009 Oct;62(10):1006-12. doi: 10.1016/j.jclinepi.2009.06.005. Epub 2009 Jul 23. PMID: 19631508.
8. RStudio Team. RStudio: integrated development environment for R. RStudio, Inc.; 2019. http://www.rstudio.com/
9. Linares González L, Aguayo Carreras P, Rueda Villafranca B, Navarro-Triviño FJ. Chondroid Syringoma Mimicking Basal Cell Carcinoma. *Actas Dermosifiliogr* (Engl Ed). 2020 May;111(4): 341-343. English, Spanish. DOI: 10.1016/j.ad.2018.10.023. Epub 2019 May 25. PMID: 31138414.

10. Bal A, Dazé R, Brahs A, Miller R. Chondroid syringoma with osteoma cutis. *JAAD Case Rep*. 2022 Jan 31;22:2-4. DOI: 10.1016/j.jdcr.2022.01.023. PMID: 35242977; PMCID: PMC8886313.
11. Palit A, Sethy M, Nayak AK, Ayyanar P, Behera B. Dermoscopic features in a case of chondroid syringoma. *Indian J Dermatol Venereol Leprol*. 2021 Jan-Feb;87(1):89-92. DOI: 10.4103/ijdvl.IJDVL_167_20. PMID: 32969355.
12. Park SM, Ko HC, Kim BS, Kim MB, Mun JH. Large protruding telangiectatic nodule on the nose. *Clin Exp Dermatol*. 2015 Jun;40(4):460-2. DOI: 10.1111/ced.12511. Epub 2014 Dec 5. PMID: 25476592.
13. Zaballos P, Gómez-Martín I, Martin JM, Bañuls J. Dermoscopy of Adnexal Tumors. *Dermatol Clin*. 2018 Oct;36(4):397-412. DOI: 10.1016/j.det.2018.05.007. Epub 2018 Aug 16. PMID: 30201149.
14. Lai M, Muscianese M, Piana S, Chester J, Borsari S, Paolino G, Pellacani G, Longo C, Pampena R. Dermoscopy of cutaneous adnexal tumours: a systematic review of the literature. *J Eur Acad Dermatol Venereol*. 2022 Sep;36(9):1524-1540. DOI: 10.1111/jdv.18210. Epub 2022 May 25. PMID: 35536546; PMCID: PMC9545415.
15. Zufall AG, Mark EJ, Gru AA. Malignant chondroid syringoma: A systematic review. *Skin Health Dis*. 2022 Jul 10;3(2):e144. DOI: 10.1002/ski2.144. PMID: 37013126; PMCID: PMC10066760.
16. Clark P. Malignant chondroid syringoma. *Conn Med*. 1987 Sep;51(9):569-72. PMID: 2822351.
17. Devine P, Sarno RC, Ucci AA. Malignant cutaneous mixed tumor. *Arch Dermatol*. 1984 May;120(5):576-7. DOI: 10.1001/archderm.120.5.576b. PMID: 6326689.