Spontaneous Keloids: A Literature Review

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Keywords

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Abstract

Background: Keloids are benign fibroproliferative tumors that extend beyond the original wound. Spontaneous keloids are those that result without a significant history of trauma. There are multiple reported cases in the literature.

Objective: This article provides a summary and review of the cases that have been reported with spontaneous keloids and organizes them according to their associated medical conditions. **Methods:** A literature review was conducted using PubMed and MEDLINE that included all English published cases and case series from May 1955 to February 2018. **Results:** Spontaneous keloids have been reported mainly in association with syndromes such as Rubinstein-Taybi syndrome, Dubowitz syndrome, Noonan syndrome, Goeminne syndrome, Bethlem myopathy, conjunctivocorneal dystrophy, X-linked recessive polyfibromatosis and a novel X-linked syndrome with flamin A mutation. Furthermore, spontaneous keloids were reported in atopic patients and a couple of patients who are medically healthy. **Conclusion:**

Spontaneous keloids are diagnosed clinically based on the patient's history, and it is challenging to confirm since they might be triggered by minimal injury or inflammation especially if it is a single lesion. Reported syndromes indicate a genetic possibility in the pathogenesis of spontaneous keloids.

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Introduction

Keloids are benign fibroproliferative tumors that occur as a response to any kind of injury to the skin of susceptible individuals. Keloid tissue extends beyond the margins of the wound, which distinguishes it from hypertrophic scars [1]. Keloids tend to grow symptomless, but still can often cause pain or itching. They have a functional, aesthetic, or psychosocial impact on patients, as highlighted by quality-of-life studies [2]. Individuals of African, Hispanic, or Asian descent appear to be at an increased risk for the development of keloids [3]. Spontaneous keloids, that is, those keloidal lesions that develop without any history of trauma or surgery, are very rare. It is generally believed that they are triggered by microtrau-

Table 1. Spontaneous keloids and associated genetic disorder

Condition	Age, years	Race	Gender	Site	Ref. No.
Bethlem myopathy	45	White	M	Sternal area, upper back, and lateral side of right arm	4
	32	White	F	Bilateral shoulder	5
	50	White	M	Bilateral shoulder	5
Rubinstein-Taybi syndrome	15	White	M	Back, parasternal area, and arms	6
	25	White	F	Bilateral shoulder	7
	45	Indian	F	Shoulder, back, and extremities	8
Dubowitz syndrome and atopic dermatitis	7	White	M	Right neck, right temporal and right infraclavicular areas	9
Noonan syndrome	6	White	M	Right foot	10
Goeminne syndrome	33	White	M	Chest, back, and arms	11
Conjunctivocorneal dystrophy	57	Norwegian	F	Hands and fingers	12
	22		M	Right index finger	12
	15		M	3 ulnar fingers	12
X-linked recessive polyfibromatosis	40	White	M	Trunk and extremities	13
Novel X-linked syndrome with flamin A (FLNA) mutation	36	White and Native American	M	Thigh, hip, and back	14

ma or minimal cutaneous inflammation in genetically susceptible patients. Their exact etiology is still unknown, although they have been described in multiple conditions discussed below.

Genetic Association

Spontaneous keloids have been reported in association with certain genetic abnormalities in multiple reports in the literature (Table 1). In Echeverría et al. [4], a 45-year-old man with Bethlem myopathy was reported to have multiple keloids in the sternal area, on the upper back, and lateral side of his right arm. Furthermore, he had the tendency to develop keloids over the surgical site that had been done for torticollis release [4]. Another report exists of 32 female and 50 male Bethlem myopathy cases who developed spontaneous keloids on both sides of the shoulder [5]. In Rubinstein-Taybi syndrome, a boy was diagnosed at the age of 8 years and at the age of 15 years developed spontaneous eruption of keloids without any trauma on the back, in the presternal area, and over the upper arms [6]. A 25-year-old woman with Rubinstein-Taybi syndrome presented with bilateral spontaneous keloids of the shoulders present for several years [7]. There is another report of 45 Indian females with Rubinstein-Taybi syndrome who at the age of 43 years developed an

extensive eruption of keloids on the shoulders, arms, legs, and back [8]. In an analysis of 574 patients with Rubinstein-Taybi syndrome, keloids were observed in 28 individuals: 16 were males and 12 were females; all were white, and ages ranged from 3 to 27 years; 6 of them had spontaneous keloids on the shoulders, upper trunk, and arms while the remaining 22 developed keloids after trauma [9]. Spontaneous keloids have been reported in association with Dubowitz syndrome. A 7-year-old boy with Dubowitz syndrome and atopic dermatitis at the age of 4 experienced a sudden onset of keloids without a preceding trauma on the right temple, right neck and right deltoid, and in the right infraclavicular region [10]. A 6-year-old with Noonan syndrome was found to have a tendency to develop recurrent keloids over his right foot rather than having an eruptive presentation like the cases with the previously mentioned syndrome [11]. Goeminne syndrome has been named in 1967 after Luc Goeminne who reported a novel X-linked syndrome in 3 males of the same family. One 33-year-old male who shared the characteristic of the syndrome of congenital muscular torticollis and cryptorchidism was found to have extensive spontaneous multiple keloids on the chest, back, and arms [12]. A Norwegian family of 3 members – a mother and her 2 sons – with conjunctivocorneal dystrophy reported to have keloidal lesions of the hands and fingers but a history of minimal trauma was stated in the case of

the mother [13]. There is also a report of a 40-year-old Australian male with X-linked recessive polyfibromatosis who developed a sudden eruption of keloids on the trunk and the extremities by the age of 20 years. There was a positive personal history of keloids before the eruption and a family history as well [14]. There is a report of a 36-year-old Caucasian and Native American male with a novel X-linked syndrome that is associated with mutation in flamin A (FLNA) and includes cardiac valvular disease with reduction in joint mobility. At the age of 6 years he had a keloid eruption on the thighs, hips, and back. Later in life, he developed a keloid over the surgical insertion site of a pacemaker [15]. We also reported that a syndromic 27-year-old female who has mental retardation along with orbital hypertelorism, a broad nasal bridge, high arched palate, and repaired cleft lip developed sudden widespread extensive keloids over multiple sites of her body [16].

Medical Conditions

Spontaneous keloids have been reported in atopic patients. A 24-year-old white female known to have asthma, pollen allergy, and contact allergy to nickel developed 4 eruptive keloidal lesions on the back without a history of trauma [17]. Another report describes a 34-year-old woman with severe asthma and chronic idiopathic angioedema who developed 2 keloidal lesions on the back 10 years prior to her presentation that grew in size over time without a trauma [18].

Spontaneous Keloids without Medical Conditions

Spontaneous keloid has been reported in patients who are medically healthy. A report describes an 81-year-old male who is medically healthy but developed a single right postauricular spontaneous keloid [19]. There are another report of a 39-year-old man without a medical history who developed a sudden eruption of multiple keloids on the chest [20] and a report of a 21-year-old female who was otherwise healthy with spontaneous keloids on the chest and back [21]. There is also a report of a 63-year-old man after renal transplantation who shortly after the transplantation developed eruptive keloids that continued to increase in size and number and stabilized after a year. A punch biopsy result was consistent with keloids. Additionally, the lesions stained positive for CD68 and factor XIIIa, both of which are correlated with the lesions

of nephrogenic systemic fibrosis. However, the patient did not present with the classic clinical presentation of nephrogenic systemic fibrosis, had no history of exposure to gadolinium, and staining for CD34 was negative [22]. In one analysis of 259 Syrian patients with keloids, spontaneous keloids were found in 13.4% mostly on the shoulders and in the presternal region, and there was a significant statistical association between blood group A and spontaneous keloids [23]. Another analysis of 88 Iraqi patients with an incidence of spontaneous keloids in 30 patients (34%) showed that these were mostly single keloid lesions on the upper part of the body [24]. Further reports describe single spontaneous keloids over the nipple of a 56-year-old male and a 79-year-old female [25] as well as 2 sisters aged 21 and 19 years who developed insidious numerous keloids mostly on the chest, back, and arms [26].

Medication

The aromatase inhibitor letrozol has been reported to be associated with the development of spontaneous keloid eruption. In Meade et al. [27], the patient had a personal history of keloids, and after 2 months of initiating letrozol she started having new keloidal lesions and aggravation of her existing ones. A discontinuation of letrozol resulted in a stop of getting new keloids [27]. Isotretinoin has also been reported to induce extensive multiple keloidal lesions on the back of a 16-year-old man with nodulocystic acne. The spontaneous eruption began 4 weeks after starting isotretinoin therapy [28]. Another report describes a 27-year-old man with Behçet disease who developed spontaneous multiple keloids on the back around 8 weeks from starting isotretinoin for nodulocystic acne [29].

Conclusion

Spontaneous keloid remains a rare entity and challenging to diagnose. Most of the reported cases were associated with certain syndromes which may raise the question of a genetic link between spontaneous keloids and certain mutations. In addition, it has also been reported in atopic persons and after the use of letrozol and isotretinoin therapy; however, a few reports denied any medical condition which put these cases in a doubtful situation, as there may have been a minor trauma that the patient was unaware of, especially if it was only a single keloid.

Key Message

Spontaneous keloids are associated with genetic disorders and seen in medical conditions or with medications.

Disclosure Statement

The authors have no conflicts of interest that are relevant to the content of this review.

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