

Multiple Endocrine Syndrome Type 2B Associated with Keloids

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Abstract

Keloids are benign fibrous growths that result from an abnormal connective tissue response in certain predisposed individuals. Trauma, foreign-body reactions, infections, and endocrine dysfunction have all been proposed as precipitating factors. The association of multiple endocrine neoplasia (MEN) and keloids has not been described. We report a case of multiple endocrine neoplasia type 2B who presented with multiple keloids.

INTRODUCTION

Keloids are defined as excessive scar tissue formation extending beyond the area of the original skin injury and occurring in predisposed individuals. They are considered to be a result of abnormal wound healing. Evidence supports a relationship between genetic predisposition, race, and gender, and an individual's propensity to form keloid scars. In addition, endocrinologic factors have also been associated with keloid formation. We describe a patient with multiple endocrine neoplasia type 2B who presented with multiple keloids.

CASE REPORT

A 31-year-old white Caucasian with a history of prophylactic total thyroidectomy at the age 8 after her mother was diagnosed in her 30's with multiple endocrine neoplasia (MEN) 2B (metastatic medullary thyroid carcinoma and pheochromocytoma). At the time of her total thyroidectomy, she was found to have medullary thyroid carcinoma. In 1999, the patient began having headaches, diaphoresis, pallor, and palpitations. She was diagnosed with right-sided pheochromocytoma, which was surgically treated with an adrenalectomy. In 2000, she had elevated calcitonin levels, and an exploratory neck surgery failed to reveal evidence of disease. The patient continued to have elevation in calcitonin levels, and in 2004, a bilateral radical neck dissection showed 13 out of 26 lymph nodes positive for medullary thyroid carcinoma. During this time, she again began experiencing headaches, diaphoresis, pallor, and palpitations. She was diagnosed with recurrent pheochromocytoma and then underwent a left cortical

sparing adrenalectomy with implantation of adrenal tissue in the left forearm.

The patient reports developing keloids on her shoulders, back and chest since high school. They are not bothersome, not associated with trauma, and are getting larger. She denies any family history of keloids or hypertrophic scars. Examination revealed flesh colored, firm, irregular shaped nodules with bulbous expansions on the shoulders, back and chest (Figure 1)

Figure 1

Figure 1: Flesh colored, firm, irregular shaped nodules with bulbous expansions on the shoulders consistent with keloids.



Small pink-colored papules consistent with neuromas on the tongue and thickened, protruding lips were also seen (Figure 2)

Figure 2

Figure 2: Multiple neuromas on the anterior aspect of the tongue. Lesional skin biopsy of a shoulder keloid showed thickened collagen bundles on histology.



DISCUSSION

Keloids are the result of an overgrowth of dense fibrous tissue that usually develops after healing of a skin injury.¹ The tissue extends beyond the borders of the original wound, does not regress spontaneously, and tends to recur after excision. In 1806, Alibert used the term *cheloide*, derived from the Greek *chele*, or crab's claw, to describe the lateral projections of tissue into unaffected skin.² As in our patient, keloids are often multiple. The most common location is the sternal region, and keloids can also occur on the neck, ears, trunk, and extremities.³ Epidemiologic data on keloids is limited, but suggests differences among racial groups, with higher rates in African-Americans, Hispanics and Asians.⁴ The risk of developing keloids is approximately 15 times greater in dark-skinned individuals, compared with lighter-skinned persons.⁵ The prevalence has been reported to be higher in young females than in young males, probably reflecting the greater frequency of earlobe piercing among females.⁶ No consistent pattern exists in the mode of genetic transmission, which is reported to occur as both an autosomal dominant and autosomal recessive pattern.⁷ Trauma, foreign-body reactions, infections, and endocrine dysfunction have all been proposed as precipitating factors.^{8,9}

Multiple endocrine neoplasia (MEN) syndromes consist of rare, autosomal dominant mutations in genes regulating cell growth.¹⁰ Type 2B MEN is defined by medullary thyroid tumor and pheochromocytoma, and is associated with mucosal neuromas (lips, tongue, gingival, and conjunctiva), medullated corneal nerve fibers, and marfanoid habitus. MEN is caused by a mutation in the RET proto-oncogene,

and specific codon mutations within RET correlate with disease phenotype and severity.¹⁰

Some children may develop medullary thyroid carcinoma as young as 12 months of age, and prophylactic thyroidectomy with lymph node dissection is recommended in those younger than 5 years who have a RET germline mutation.

Our patient presented with multiple keloids, thickened protruding lips, and multiple neuromas of her tongue. Although the latter two are commonly associated with MEN type 2B syndrome, keloid formation associated with MEN syndrome has not been described. Several reports have been published describing endocrine factors associated with keloids, including the thyroid, parathyroid, ovary, and pituitary gland dysfunction, pregnancy, puberty and acromegaly as a cause for keloids.^{8,11} Our patient had endocrine dysfunction, including increased levels of calcitonin and catecholamines, associated with her diagnosis of MEN type 2B. These hormonal factors could have played a causative factor in her development of her keloids.

Several published case reports have suggested hyperthyroidism as a possible cause for keloids.^{8,12,13} One report of young patients treated with surgical thyroidectomy for Grave's disease had a propensity to form keloids of their surgical wounds.¹³ It has also been reported that keloids regressed in a young woman after unilateral resection of the thyroid gland.¹⁴ Regression of a large keloid has also been demonstrated after parathyroidectomy.⁸ In addition, acromegaly has been associated with keloid formation. This association is attributed to the action of growth hormone and its stimulation of collagen and formation of connective tissue.¹⁵ Keloids also grow more rapidly when there is physiologic hyperactivity of the pituitary gland, especially during pregnancy and puberty.^{8,16}

Whether the association of keloids and endocrine factors, including MEN syndrome type 2B, is causal or simply coincidental is debatable. As more experience and data is gathered, the relationship between keloids and endocrine factors will be clarified.

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