

# Multiple Keratoacanthoma, Ferguson Smith Type

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## Abstract

*Keratoacanthoma (KA) is a common benign epithelial tumor of pilosebaceous origin, which is composed of keratinizing squamous cells. It is characterized by rapid evolution and, most often, by spontaneous resolution. Ferguson Smith multiple KA is one of two familial forms of multiple KA's described (the other being [Muir-Torre syndrome](#)). Multiple KA's of Ferguson Smith type is a very rare disorder that is inherited in an autosomal dominant manner. The responsible gene has been mapped to chromosome 9q22-q31. KA's usually begin in childhood, adolescence, or in early adult life. Several of them appear suddenly, mostly on the head, slowly involute, and periodically reappear for years. The diagnosis is based on history and physical examination and it is confirmed by histological examination. Although KA's usually involute spontaneously, treatment hastens resolution and provides improved cosmetic result. All therapeutic modalities for solitary KA are applicable also for multiple KA's. Systemic approaches such as retinoids, methotrexate, 5-Fluoro-Uracil or interferon alfa-2a have been shown to be effective and promising for the management of multiple KA's.*

## Key words

Familial keratoacanthoma, Multiple self-healing squamous epithelioma, Epithelioma self-healing squamous, multiple keratoacanthomas of Ferguson Smith type, locus 9q22-q31, MSSE gene

## Introduction

Keratoacanthoma (KA) is a common benign epithelial tumor, which originates from the pilosebaceous follicle; it is composed of keratinizing squamous cells. It is characterized by rapid evolution and, most often, by spontaneous resolution. Clinically and histologically, it may be confused with a *de novo* highly malignant squamous cell carcinoma (SCC). However, KA may be viewed as an abortive cancer that only rarely progresses into an aggressive SCC (1)

KA is classified into solitary KA and its variants, and various forms of multiple KAs. Among the latter, two familial forms have been described: multiple self healing squamous epitheliomas and Muir-Torre syndrome.

**Disease name and synonyms**

Multiple keratoacanthomas of Ferguson-Smith type.  
Ferguson-Smith syndrome.  
Familial self-healing squamous epitheliomas,  
Multiple self-healing squamous epithelioma, MSSE,  
Epithelioma Self-Healing Squamous, ESS1

**Definition**

An inherited disorder characterized by several KA's that suddenly appear, slowly involute, and periodically reappear for decades. Ferguson Smith originally described it in 1934 (2).

**Genetics**

Multiple self-healing epitheliomas of Ferguson Smith have been described in two large Scottish kindred. The condition is inherited in an autosomal dominant manner (3). The responsible gene has been mapped to chromosome 9q22-q31 (4). However, there are also sporadic cases.

Richards *et al.* (5) studied the question of whether XPA (Xeroderma Pigmentosum type A) or PTCH (PATCHED), both genes that map to the same region as *MSSE*, is the site of the mutation in this disorder. By analysis of a polymorphism in the 5-prime untranslated region of XPA, they excluded XPA as the site of the mutation. The *PTCH* gene is mutated in [Gorlin syndrome](#); Families with Ferguson-Smith Keratoacanthomas were shown to share a common haplotype at 3 novel intragenic *PTCH* polymorphisms. Although no mutations were detected in these families, *PTCH* had not been excluded as the *MSSE* gene. The authors stated that the most likely location of the *MSSE* gene is between D9S197 and D9S287/D9S1809.

**Epidemiology**

Multiple KA's of Ferguson Smith type are very rare. They usually begin in childhood, adolescence, or in early adult life. This condition affects both sexes with equal severity, but the distribution differs because of differences in sun exposure patterns between males and females (3).

**Etiology**

The distribution of lesions in sun exposed areas dictates a major role for solar radiation. It has been postulated that in genetically predisposed individuals, the sunlight may activate an oncogene or it may inactivate a suppressor gene. Regression of KA's is likely to be mediated by activated CD4+ T lymphocytes, possibly via cytokine secretion (6).

**Clinical description**

Lesions begin to appear singly or in crops during the second decade of life and follow an individualized pattern of development and distribution. They are located on sun-exposed sites, especially around the nose or the ears, as well as on the scalp. They also tend to develop at sites of trauma. The early lesion is a dull red macule that becomes papular and grows rapidly over 2-4 weeks to an ordinary nodular KA, 2-3 cm in diameter, which later may become ulcerated or crusted. The number of lesions varies from a few to a hundred. It remains stable for 1-2 months and then gradually resolves leaving a deep disfiguring scar (7,8).

**Diagnostic methods**

Histologically, the epidermis may be ulcerated, with marked cellular atypia and loss of polarity. At the base of the lesion, invasive tongues of epithelial cells are seen, as well as clumps of epithelial cells, detached from the main tumor mass. Compared with keratoacanthoma, there is no marked "shouldering" and the leucocyte abscesses are absent.

**Diagnosis and differential diagnosis**

The diagnosis is based on history and physical examination and is confirmed by lesional skin biopsy and histological examination.

Multiple KA's of Ferguson Smith type must be differentiated from non familial multiple persistent KA's and generalized eruptive KA's of Grzybowski, as well as from KA in [Muir-Torre syndrome](#) or in [xeroderma pigmentosum](#).

## Treatment

Although KA's usually involute spontaneously, treatment hastens resolution and provides improved cosmetic result. In addition, surgical excision and biopsy helps to establish diagnosis and to rule out SCC. (1) All therapeutic modalities for solitary KA are applicable also for multiple KA's, including surgical excision, curettage and electrodesiccation, radiotherapy, cryotherapy and laser surgery. Intralesional and topical 5-fluorouracil (5-FU) and intralesional bleomycin have been tried with encouraging results. Treatment choice depends on the number and location of the lesions, as well as on the available methods and experience. Systemic approaches such as retinoids (isotretinoin, acitretin, etretinate), methotrexate, intravenous 5-fluoracil, or interferon alfa-2a have been shown to be effective and promising for the management of multiple KA's (9).

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The image shows a banner for Orphanet, a portal for rare diseases and orphan drugs. The banner features the Orphanet logo at the top, which consists of the word "orphanet" in a blue, lowercase, sans-serif font with a stylized blue and white graphic element resembling a globe or a network. Below the logo, the website address "www.orpha.net" is displayed in a large, black, sans-serif font. Underneath the website address, there is a paragraph of text in a smaller, black, sans-serif font: "The portal of rare diseases and orphan drugs for the European rare disease community: patients and their carers, healthcare professionals, researchers, industry and regulators." Below this paragraph, there is another paragraph of text, also in a smaller, black, sans-serif font: "Aimed at contributing to the improvement of the diagnosis, care and treatment of patients with rare diseases." At the bottom of the banner, there is a final paragraph of text in a smaller, black, sans-serif font: "Includes the rare diseases encyclopedia and a directory of services (information on specialised outpatient clinics, clinical laboratories, research activities and support groups)."