Identifying and Managing Keratoacanthoma

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By

Catherine C. Patnode

WASHINGTON STATE UNIVERSITY – SPOKANE, WA

College of Nursing

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KERATOACANTHOMA

To the Faculty of Washington State University:

The members of the Committee appointed to examine the master's project of CATHERINE PATNODE find it satisfactory and recommend that it be accepted.

[Signatures]

Mel Haberman
Chair

Denise Smart

Ann M. Haich
KERATOACANTHOMA
Identifying and Managing Keratoacanthoma

Abstract

By Catherine Patnode, RN
Washington State University
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Chair: Mel Haberman

Keratoacanthomas (KAs) are a cutaneous condition of skin and mucous membrane neoplasms occurring on sun-exposed areas of light-skinned people. The fact that these tumors can be either benign or malignant fosters controversies about KAs to this day. Histopathology resembles squamous cell carcinoma (SCC) but unlike SCC, KAs will usually self-resolve. Keratoacanthomas can be isolated lesions or multiple-lesion syndromes. Depending upon the patient and the lesion(s), the patient can be treated in a variety of ways to reduce cosmetic and/or physical deformity. This paper presents the pathology of KAs, its clinical forms and management of these lesions.

Key Words: Skin cancer, squamous cell carcinoma, keratoacanthoma, keratoacanthoma types, keratoacanthoma classification, keratoacanthoma causes, keratoacanthoma pathophysiology, keratoacanthoma treatments, keratoacanthoma clinic-pathologic controversies, keratoacanthoma nursing implications.
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Identifying and Managing Keratoacanthoma

Keratoacanthomas (KAs) are relatively common epithelial tumors that originate in the pilosebaceous follicles of the skin and mucous membranes. Characterized by rapid (weeks to months) growth, a papule will have a keratin-filled center and then will usually self-resolve within 4 - 6 months. The word usually fuels controversies as to whether these tumors are benign or malignant and thus is the impetus for this review. Squamous cell carcinomas (SCC) and Keratoacanthomas are histopathologically so similar that dermatopathologists diagnose them as Squamous Cell Carcinoma, Keratoacanthoma-Type (Chuang & Brashear, 2010). KA tumors grow rapidly and are possibly aggressive; however, they rarely metastasize and are characterized by a swift and spontaneous self-resolution. Due to the rare invasive progression of KAs, the standard of practice is to remove the lesions surgically.

KAs usually appear on sun-exposed areas of the skin and share similar causative factors with SCC lesions, such as solar radiation, trauma, genetic factors, immunocompromised status and possibly human papilloma virus (though the last has been contradicted by several studies). Keratoacanthomas can be isolated lesions or multiple-lesion syndromes.

Statement of Purpose

The true incidence of keratoacanthoma is difficult to determine because of the diagnostic overlap with squamous cell carcinoma. Due to the nature of KA, each case should be individually evaluated with respect to diagnosis and treatment. Knowing the variety of types and treatments available to the patient, health care providers can impart the knowledge needed to help the patient make an informed decision on the best option that would allow for an excellent prognosis. This article presents a review of keratoacanthomas, the pathology of KAs, its clinical forms and management of these lesions.
Theoretical Framework

The Health Belief Model (HBM) is a health behavior change and psychological model that focuses on patient compliance and preventative health care practices (Polit & Beck, 2008). A person’s perception of the threat posed by a health issue assigns value to actions taken to diminish the threat and thus influences health behavior decisions. The Health Belief Model (HBM) facilitates the exploration of patients’ perceptions of personal susceptibility and, the severity of the condition and personal benefits of treatments and care. Additionally, the HBM includes components of cost, motivation, modifying behaviors and enabling factors. People’s perception of contracting a serious condition is perceived susceptibility and the individual’s evaluation of the seriousness and potential consequences of a condition is perceived severity (Polit & Beck, 2008). “Perceived barriers” discourage an adoption of a particular behavior while the perception of perceived positive consequences are perceived benefits (Polit & Beck, 2008). The complexity, accessibility and duration of treatment are “perceived costs” while the actual desire to comply with a treatment would be considered motivation (Polit & Beck, 2008).

This framework simplifies health-related processes in a broad manner and may neglect specificity and social factors. However, its common-sense constructs are easy for non-psychologists to incorporate into everyday practice in the hopes of modifying and addressing a patient’s perceptions to encourage behavior that is health-beneficial. It also provides the clinician with a framework to point out those large threats might be offset by perceived costs and that small threats, when dealt with, might have large benefits.

For example, if a patient is diagnosed with keratoacanthoma and recognizes his/her susceptibility to this skin cancer because of a past desire to sun bathe, future actions after diagnoses will depend on how severe he/she perceives the cancer to be. Given the knowledge
and education of the care provider, the patient will decide the best manner to remove the Keratoacanthoma based on the outcome, costs and personal benefits of each type of treatment and may even modify his/her future lifestyle by applying sunscreen when appropriate. The HBM predicts the likelihood that the patient will follow the recommended preventative or curative health actions.

**Literature Review**

**Methods**

A variety of databases were searched including CINAHL, PubMed, Dermatology Abstracts, E-medicine, Epocrates, www.cancer.org, and Google for articles from 1990 to 2010. Older articles illustrate the foundational knowledge research has built upon and emphasizes the difficulty, even these days, to diagnose and manage this type of skin cancer. Keywords used were skin cancer, squamous cell carcinoma, keratoacanthoma, keratoacanthoma types, keratoacanthoma classification, keratoacanthoma causes, keratoacanthoma Pathophysiology, keratoacanthoma treatments, keratoacanthoma clinic-pathologic controversies, keratoacanthoma nursing implications. Of more than 40 articles and abstracts reviewed, 34 were chosen based on clarity, relevance and thoroughness about this topic.

The literature is organized into 14 topics: Keratoacanthomas Defined, Types of Keratoacanthoma, Epidemiology, Causative and Risk factors, Controversies, Clinical Presentation, Pathophysiology, Differential Diagnosis, Diagnosis, five subtopics under Treatment and another five subtopics under Chemotherapy followed by Follow-up and Nursing Implications.

**Keratoacanthoma**

Keratoacanthoma is a fast-growing, cutaneous neoplasm of the skin produced by
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pilosebacious follicles (Karaa & Khachemoune, 2007; Paterno, Campione, Diluvio, Orlandi, & Sergio, 2008) with a central keratinous core that develops in a crater often with involution and scarring (Schwartz, 1994). KAs usually occur on sun-exposed areas on light-skinned people (Karaa & Khachemoune, 2007) and may spontaneously regress (Karaa & Khachemoune, 2007; Paterno et al., 2008; Schwartz, 1994) depending upon the patient’s immune response (Paterno et al., 2008). These growths are considered unpredictable since some can grow and metastasize to the fatty tissues just beneath the skin and, rarely, to the lymphnodes or to distant parts of the body (American Cancer Society, 2011). The histological pattern is well-differentiated squamous epithelium and rarely progresses to squamous cell carcinoma (Vargo, 2006). The frequent self-resolution is what differentiates KA from SCC (Sarabi, Selim, & Khachemoune, 2007; Vargo, 2006). Additionally, tumor markers, p53 enzyme marker or telomerase have been used to find molecular differences for identification purposes (Putti, Teh, & Lee, 2004). They can form dome-shaped, colorful horns or flat, dried-out ulcers with elevated borders and measure up to a few centimeters (Schwartz, 1994).

Types of Keratoacanthoma

Cutaneous conditions of larger than 20 – 30mm have been described as “Giant Keratoacanthoma” (Pickrell, Villereal-Rios, & Neale, 1979; Schaller, Korting, Wolff, Schirren, & Burgdorf 1996; Schwartz, 2004; Wolff & Johnson, 2009). Multiple keratoacanthomas is a cutaneous condition distinguished by multiple, sometimes hundreds, of keratoacanthoma lesions (Odom, James, & Berger, 2000). Multiple tumors growing in a localized area is known as Keratoacanthoma Centrifugum Marginatum (Odom et al., 2000; Schaller et al., 1996). Hundreds to thousands of minute follicular keratotic papules over the entire body is called Generalized Eruptive or Grzybowski Keratoacanthoma (Schaller et al., 1996). However, in clinical practice,
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KA will usually present as a single lesion (J. Berreman, personal communication, February 15, 2011.)

**Epidemiology**

Schwartz (2004) asserts that keratoacanthoma is a relatively common skin neoplasm that often occurs during the summer months. However, in clinical practice they appear all year long (J. Berreman, Personal Communication, February 15, 2011). KA frequents men twice as often as women on hairy, sun-exposed, actinically damaged skin—although it may also be present on mucosal membranes such as the hard palate, lips, nasal mucosa and genetalia (Vargo, 2006; Sarabi, et al., 2007).

**Causative Factors**

Causative factors are uncertain (Vargo, 2006) but are known to be derived from hair follicles in keratin studies (Bart, Popkin, Kopf, & Gumport, 1975; Garcia-Zuazaga, Malcolm, & Lee, 2009) and include sun damage (Bart et al., 1975; Garcia-Zuazaga et al., 2009; Sarabi et al., 2007; Schwartz, 1994; Schwartz, 2004; Shulstad & Proper, 2010;) The human papillomavirus has often been blamed (Bart et al., 1975; Garcia-Zuazaga et al., 2009; Schwartz, 1994; Schwartz, 2004). However, there is no evidence to link KAs with HPV (Vandergriff, 2010) and the assertion is debatable (Sarabi et al., 2007; Shulstad & Proper, 2010). Also mentioned as possible causative risk factors are trauma (Sarabi et al., 2007; Shulstad & Proper, 2010), immunodeficiency (Paterno et al., 2007; Sarabi et al., 2007), and genetic aberrations although there is discrepancy about the ambiguous process of KAs progression into an SCC variant (Sarabi et al., 2007). Occupational exposure to chemical agents has been implicated (Bart et al., 1975; Garcia-Zuazaga et al., 2009; Pickrell et al., 1979; Schwartz, 1994) including carcinogens and/or teratogens (Sarabi et al., 2007).
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Risk Factors

Risk factors include fair complexion, age above 50 years and gender since KA occurs in males by a 2:1 ratio compared to females (Wolff & Johnson, 2009). The amount of sun exposure (a causative factor) is included here as a risk factor, though no study detailed the necessary amount of sun required for KA’s to develop. Still, KA’s usually appear on sun-exposed skin as evidenced by solar elastosis, atrophy, dyspigmentation and actinic keratosis (Vandergriff, Nakamura, & High, 2008; Sarabi et al., 2007) on areas such as the face, forearms and hands (Schwartz, 2004).

Challenges/Controversies

True KA incidence is problematic due to the diagnostic overlap with SCC (Vandergriff, 2010). No immunohistochemical stains or molecular analysis can distinguish between KA and SCC because they look so similar to one another (Bart et al., 1975; Garcia-Zuazaga et al., 2009; Schwartz, 2004; Vandergriff, 2010; Wolff & Johnson, 2009). For this reason, most dermatologists refer to them as Squamous Cell Carcinoma, Keratoacanthoma-type as the diagnostic verbiage (Vandergriff, 2010; Paterno et al., 2008).

Keratoacanthomas can be unpredictable and aggressive or self-resolving. However, the mechanism for regression is not well explained. It may be related to the immune response of the patient (Paterno et al., 2008). For this reason, dermatologists usually treat KAs empirically as SCC rather than waiting for spontaneous resolution (Paterno et al., 2008; Vargo, 2006; Wolff & Johnson, 2009). However, one wonders how the changing United States (U.S.) politics and healthcare reform may affect this practice in the future.

The causes of keratoacanthomas are multifactorial. Keratoacanthomas exhibit aggressive growth containing cytological atypia, SCC-type margins, an expression of mutated tumor
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suppressor genes and aneuploidy which, together, favor the malignant theory (Chuang & Brashear, 2010; Sarabi et al., 2007). However, regression favors the opposite benign theory and KA’s may actually be SCC in situ since it does not contain Syndecan-1 adhesion molecule which decreases tumor invasiveness (Huang, Chiquet-Ehrismann, Moyano, Garcia-Pardo, & Orend, 2001).

Clinical Presentation

Most keratoacanthomas are isolated lesions that are dome-shaped or nodular with a central closure filled with keratin that are commonly found on sun-exposed areas of skin (Sarabi et al., 2007; Shulstad & Proper, 2010). Size ranges from a few millimeters to several centimeters (Sarabi et al., 2007; Shulstad & Proper, 2010). However, there are various subtypes associated with syndromes (Wolff & Johnson, 2009).

In the Grzybowski subtype, the sheer number of lesions challenge successful treatment (Vandergriff et al., 2008). There are hundreds to thousands of multiple tiny lesions that develop suddenly, rapidly and involve mucosal surfaces in older adults which can be a source of morbidity (Vandergriff et al., 2008). In a younger-aged populations, multiple larger KAs that occur and spontaneously resolve are part of an autosomal dominant inherited condition known as Ferguson-Smith syndrome (Vandergriff et al., 2008). Sebaceous tumors, internal malignancies and eruptive KAs may indicate a subtype of hereditary nonpolyposis colorectal cancer called Muir-Torre syndrome which has MLH1 and MSH2 mutations leading to DNA microsatellite instability (Vandergriff et al., 2008). Any patient with sebaceous neoplasms other than sebaceous hyperplasia should be screened for colon cancer (Vandergriff, 2010).

Pathophysiology
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Keratoacanthomas originate in squamous epithelial cells and extend upward and around a keratin-filled crater and then downward into the dermis to form a dome-like lesion. Eosinophilic cytoplasm produce keratin in the large atypical, well-differentiated epithelial cells (Shulstad & Proper, 2010). The ability to change shape or form (pleomorphism) is minimal, and then once the keratinization occurs, an invasion of elastic and collagen fibers within the dermis of the skin ensues (Chuang & Brashear, 2010). Within the dermis of the skin, KA demonstrates elastic tissue trapping, eosinophilic infiltration and the presence of microabcesses (Chuang & Brashear, 2010; Shulstad & Proper, 2010). Following that, pseudocarcinomatous infiltration usually exhibits a well-demarcated, smooth and regular front that does not extend beyond the level of the sweat glands. (Sarabi et al., 2007; Schwartz, 2004; Shulstad & Proper, 2010).

Paterno’s “Regression Theory” (2008) hypothesizes an individual’s immune response elevates the number of T-cells in regressing KAs which then express granzyme B as compared to SCC lesions. It is the higher number of CD8 T-cells which can kill tumor cells and lead to the regression of the neoplasm (Paterno et al., 2008). In fact, one of the reasons that Imiquimod works is because the drug enhances granzyme B in local tissues and causes the recruitment of CD8 and augments the cytotoxic effect of the T-cell population (Paterno et al., 2008).

Differential Diagnosis

The most important clinical differential diagnosis is Squamous Cell Cancer. After biopsy, rapid growth and large portions of the tumor rolling inward may indicate KA while the formation of ulcers and atypical cells may point toward SCC (Sarabi et al., 2007; Shulstad & Proper, 2010; Vandergriff, 2010).

Actinic Keratosis (AKs) should also be considered (Chuang & Brashear, 2010; Vandergriff, 2010). However, AKs usually progress gradually. They begin as a small papule or
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plaque on sun-exposed areas of fair skin in patients older than 30 (Chuang & Brashear, 2010; J. Berreman, personal communication, February 15, 2011; Vandergriff, 2010). Histologic analysis may find parakeratosis, dyskeratosis, cellular atypia and mutated keratinocytes with mitotic figures (Chuang & Brashear, 2010; Sarabi et al., 2007; Vandergriff, 2010).

Another consideration is verruca vulgaris lesions. Verrucous lesions will present as wart-like growths in areas of chronic irritation and inflammation (Vandergriff et al., 2008). These lesions are slow-growing and penetrate from the skin to the bone (Vandergriff et al., 2008). Intracytoplasmic glycogen stores are what differentiate these from keratoacanthomas. (Sarabi et al., 2007; Shulstad & Proper, 2010).

Finally, benign epithelial neoplasms such as irritated seborrheic keratosis known as prurigo nodules should be ruled out (J. Berreman, personal communication, February 15, 2011). These nodules will sometimes itch and often appear on the arms or legs. These are also known as Picker's Nodules since they result from excoriation to an irritated area and then develop as the patient continues to scratch and pick at the bump that develops (J. Berreman, personal communication, February 15, 2011).

Diagnosis

Diagnosis is based on history, clinical exam, and histology report. A punch biopsy will often reveal a well-differentiated, mildly atypical, squamous cell suggestive of actinic keratosis or squamous cell carcinoma (Wolff & Johnson, 2009). Schwartz (2004) asserts the pathologist needs an entire lesion to make a correct diagnosis. A shave biopsy is impractical and will only reveal keratin fragments (Schwartz, 2004). However, in clinical daily practice, it has been demonstrated that a shave biopsy is not only practical, complete and useful for diagnosis, it is also a clean and immediate procedure that can be done in the clinical setting that leaves minimal
scarring (J. Berreman, personal communication, February, 15, 2011). Because the impression exists that KA’s are benign and do not require surgery, there is a need to expressly dictate

*Squamous Cell Carcinoma-Keratoacanthoma variant* so that it is given the respect and treatment it deserves (Schwartz, 2004). The specificity of the diagnosis indicates the higher risk and morbidity of an SCC than the more relatively benign basal cell carcinoma (Schwartz, 2004). Though treatment is elective (J. Berreman, personal communication, February 15, 2011; Paterno et al., 2008) the standard of care is to remove the lesion because of its potential for sizable growth and scarring if it spontaneously resolves and because of the risk that it may be invasive (Paterno et al., 2008; Vandergriff, 2010). In fact, non-treatment should only be considered when the diagnosis of KA is certain and requires the clear communication between the experienced dermatopathologist and the practitioner (Vandergriff, 2010).

**Nursing Measures**

The perspective of the patient must be taken into consideration (Beilan, 2003). Some patients may hesitate to initiate treatment because of fear of shortened life span or that it is simply too much to deal with at the time. This hesitation makes matters worse. However, it is important to inform the patient that the lesion can become larger and painful and that there is a risk of secondary infection if they ulcerate and bleed. In one case, the nurse practitioner covered the lesion with a piece of plastic wrap and dated it (Beilan, 2003). The patient promised to return immediately to have the lesion excised if it changed, grew or ulcerated or wait two months if the lesion remained unchanged (Beilan, 2003). Educating medical staff members and patients about the different types of keratoacanthomas may lead to early identification, heighten the awareness of the importance of self-skin examinations and boost the importance of annual follow-up.
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appointments with a dermatologist or doctor (Beilan, 2003; J. Berreman, personal communication, February 15, 2011).

Treatment/Management

Treatment is based on patient history, the presentation of the lesion and the diagnostic evaluation. Unique diagnosis and approach to treatment of each case should be individually evaluated (Garcia-Zuazaga et al., 2009). Excision of the entire lesion is needed to confirm clinical diagnosis (Schwartz, 2004). If it is on the trunk, arms, or legs, electrodiesiccation and/or curettage often suffice (Garcia-Zuazaga et al., 2009; Sabari et al., 2007; Schwartz, 1994). Recurrence after electrodiesiccation and curettage is often the case and can be identified and treated promptly with further curettage or surgical excision (Wolff & Johnson, 2009). Another option is cryosurgery which will resolve the lesion 95% of the time (J. Berreman, personal communication, February 15, 2011). Mohs surgery, a more intensive type of cryosurgery, allows for good margin control and minimal tissue removal if the lesion is on the face or head, though insurance companies demand the correct diagnosis before agreeing to cover the procedure (J. Berreman, personal communication, February 15, 2011). Mohs surgery has a 98% successful outcome but may seem more menacing because of the risks associated with surgery (Beilan, 2003; J. Berreman, personal communication, February 15, 2011).

Grzybowski subtype (multiple occurring KAs) that develop suddenly and rapidly and involve mucosal surfaces can be a source of morbidity. The sheer number of lesions make treatment problematic. However, treatment with oral retinoids has been successful for this type of KA (Vandergriff, 2010).

Surgery. Cryosurgery for early and small lesions (Vandergriff, 2010; Vargo, 2006) on the extremities (Sabari et al., 2007) is recommended. Surgical excision is the most common
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treatment (Vandergriff, 2010; Garcia-Zuazaga et al., 2009; Pagini, Lorenzi, & Lorusso, 1986; Paterno et al., 2008; Vargo, 2006) and the treatment of choice (Goldenhersh & Olsen, 1984; Sabari et al., 2007). MOHS surgery involves careful excision in conjunction with liquid nitrogen freezing and should be considered for aggressive tumors, tumors larger than 2 centimeters or those on cosmetically or critically important areas (Pagani, et al., 1986; Shriner, McCoy, Goldberg, & Wagner, 1998; Vandergriff, 2010). There is a 3 - 5% chance of recurrence after surgery (Bart et al., 1975; Garcia-Zuazaga et al., 2009; J. Berreman, personal communication, February 15, 2011; Schwartz, 1994; Schwartz, 2004; Pickrell et al., 1979). All of the pertaining literature agrees that while there is a risk of loss of function or cosmetic damage depending upon the anatomical site, the advantages of this treatment are rapid removal and success, histopathological examination opportunity, minimization of scarring and prevention of invasion.

Electrodessication and curettage (ED&C). Electrodessication and curettage is acceptable for lesions on the extremities (Garcia-Zuazaga et al., 2009; Sabari et al., 2007; Schwartz, 1994) or for large lesions (J. Berreman, personal communication, February 15, 2011) and have the advantage of being a rapid, and 95% effective treatment, with minimal invasion (J. Berreman, personal communication, February 15, 2011). However this type of treatment can leave a significant amount of scarring (J. Berreman, personal communication, February 15, 2011).

Laser therapy. Laser therapy has successfully managed benign and malignant non-melanocytic tumors (Garcia-Zuazaga et al., 2009; Theile, Ziemer, Fuchs, & Elsner, 2004; Vargo, 2006). Giant KA lesions can be treated with pulse energies of 1000-2000 mJ at 8Hz (spot size of 5 mm) in four consecutive sessions at seven day intervals (Garcia-Zuazaga et al., 2009). In these cases, 5-FU was topically applied to the treated area. There was no recurrence six months after
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laser treatment (Garcia-Zuazaga et al., 2009). Er:Yag laser enhances the transdermal distribution of lipophilic and hydrophilic drugs and it has been postulated that pretreatment of the target area would improve the delivery of 5-FU by disrupting the stratum corneum (Garcia-Zuazaga et al., 2009, Theile et al., 2004).

Radiation therapy. Radiation therapy is rarely the first line treatment (Bart et al., 1975; Garcia-Zuazaga et al., 2009; Schwartz, 1994; Schwartz, 2004; Vandergriff, 2010; Vargo, 2006). This treatment is reserved for recurrence or for use of tumors that are in inoperable areas or where scarring would cause too much of a deformity, or for adjuvant therapy after giant KA surgery or where other therapies or surgery are contraindicated (Garcia-Zuazaga et al., 2009; Goldschmidt & Sherwin, 1993). Radiation therapy for KAs do not have clear guidelines, but full cancercidal doses of 40 – 60Gy for giant KA is recommended (Donahue, Cooper, & Rush, 1990; Garcia-Zuazaga et al., 2009; Goldschmidt & Sherwin, 1993). A study of 55 patients treated from 1976 to 1986 using this therapy found that this radiation therapy obtained complete regression within one month after the termination of the radiotherapy with satisfactory cosmetic results (Caccialanza & Sopelana, 1989) although the Goldschmidt & Sherwin (1993) study found that recurrence occurred in 14 tumors of the 16 patients that were treated.

Chemotherapy. Topical creams or oral chemotherapy treatments should be considered if there are many lesions (Sabari et al., 2007). Options in this discussion include Imiquimod, Methotrexate (MTX), 5-Flourouracil (5-FU), Interferon (FN α-2a) and Systemic Retiniods.

Imiquimod. Topical imiquimod stimulates both innate and acquired immune responses with antiviral and anti-tumor effects that provoke cell-mediated cytolytic activity (Paterno et al., 2008). It is a good option for transplant patients that have epithelial skin cancer (Paterno et al., 2008). No adverse effects were observed in Paterno’s (2008) case study: Two weeks of therapy
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resulted in total regression after six weeks, no activation of the patient’s systemic immune response and no cosmetic disfiguring. Additionally, repeated lab work remained within normal ranges with no relapse after three years.

Imiquimod should be administered before going to bed at least two times per week for 16 weeks (Sabari et al., 2007). It should be applied to dry skin and left on for approximately 8 hours and then the area should be washed with mild soap and water. Sun exposure should be avoided and the use of a sun screen of SPF 30 or higher is recommended (Sabari et al., 2007). It should not be applied to the lips, eyes or nostrils. Common adverse side effects include erythema, edema, vesicles, erosion or ulceration, weeping, exudates, scaling, dryness, and crusting (Sabari et al., 2007).

**Methotrexate (MTX).** Methotrexate, formerly known as amethopterin is good for large facial lesions, especially on the eyes, lips or with multiple KAs (Garcia-Zuazaga, et al., 2009; Pickrell et al., 1979). MTX can be given orally or intra-lesionally every 2 weeks for up to 6 weeks with variable results (Garcia-Zuazaga et al., 2009; Schwartz, 1994; Vandergriff, T., 2010; Vargo, 2006.) Lesions usually clear in four to six weeks (Sabari et al., 2007). If the lesion does not decrease in size, surgery is recommended (Garcia-Zuazaga et al., 2009). MTX can also be used as added support to surgery or radiation for aggressive keratoacanthoma (Garcia-Zuazaga, et al., 2009).

**5-Fluorouracil (5-FU).** 5-Fluorouracil (also known as Adrucil, Carac, Efudex, and Fluoroplex) can be applied either topically or intra-lesionally. 5-FU is beneficial for large KAs in difficult-to-treat areas such as the ear concha or the nasal wall) but not as good for KAs that are not aggressive (Schwartz, 2004; Parker & Hanke, 1986). It should be applied twice a day for three to six weeks (Sabari et al., 2007; Garcia-Zuazaga et al., 2009; Gray & Medland, 2000). It
is important to let the patient know that lesions may become erythematous, to avoid excessive sunlight and to use a sunscreen SPF 30 or more (Sabari et al., 2007). With regard to sunscreen, correct application is important. Unless the sunscreen claims to be effective for eight or more hours, it will have to be applied every three to four hours while outside (J. Berreman, personal communication, February 15, 2011). Lesions can be disfiguring with ulceration and some crust formation during treatment (Sabari et al., 2007). 5-FU can be repeated on several occasions.

**Interferon (IFN α-2a).** Interferons are substances produced in the immune response to infection and are classified based on their chemical structure, thus its alpha, beta or gamma forms (Geisse, et al., 2002). The FDA has approved IFNα-20 to treat melanomas in stage IIb (a 4mm + primary tumor) or stage III (has invaded the lymphnodes) when used with surgery or another form of therapy. IFNα-20 increases the likelihood that all cancer will be eliminated and decreases the chance of recurrence (Greisse et al., 2004). After a month of intravenous infusion of the drug, IFNα-20 is given intramuscularly three times per week for up to one year (Garcia-Zuazaga et al., 2009). Side effects include injection site pain and possibly a transient fever after the first two injections (Garcia-Zuazaga et al., 2009). In five of six cases, lesions resolved within five weeks with no recurrences at three years. Cosmetic results were excellent.

**Systemic retinoids.** Systemic retinoids such as *Etretinate* are good for Keratoacanthoma Centrigugum Marginatum but have several potential adverse effects (Ogasawara, Kinoshita, Ishida, Hamamoto, Fugiyama, & Muto, 2003; Sabari et al., 2007; Schwartz, 1994; Schwartz, 2004). Sun exposure should be avoided until tolerance is achieved (Sabari et al., 2007). This drug may decrease night vision (Sabari et al., 2007). Other adverse effects include hyperlipidemia, hepatitis, pseudotumor cerebri, myalgias, dermatologic changes and hyperostosis (Sabari et al., 2007). Pregnancy is not possible after one takes *Etretinate* and the patient will
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have to wait for three years to donate blood (J. Berreman, personal communication, February 15, 2011; Sabari et al., 2007). Inflammatory bowel disease may occur (Sabari et al., 2007). Diabetic patients may experience blood sugar control issues (Sabari et al., 2007). Treatment should be discontinued if there is any rectal bleeding, abdominal pain or severe diarrhea (Sabari et al., 2007). Additionally, if one is prone to depression, this drug may also cause mood swings or trigger an episode (Sabari et al., 2007).

Photodynamic therapy. Though there is a lack of large studies (Garcia-Zuazaga et al., 2009), there is a report of complete resolutions after two treatments of 20% alpha-linolenic acid (ALA) emulsion under occlusion for more than 20 hours followed by 250W Osram halogen lamp and red filter (580 – 680 nm) in four patients (Radakovic-Fijan, Honismann, & Tanew, 1999). Salicylic acid pretreatment of the lesion(s) facilitated ALA penetration (Radakovic-Fijan et al., 1999). Another study observed that application of ALA induces selective porphyrin accumulation in skin neoplasms that make photodynamic therapy a suitable alternative (Fritsch et al., 1997).

For recurrence or Muir-Torre Syndrome. In the case of recurrence or of Muir-Torre Syndrome, Isotretinoin and interferon α-2a and/or radiation therapy should be considered (Ponti & Leon, 2005; Sabari et al., 2007). In any case of keratoacanthoma, each diagnosis and approach to management of each case should be individually evaluated (Garcia-Zuazaga et al., 2009).

Follow-up. Patients with Muir-Torre syndrome or who have sebaceous neoplasms need close monitoring (Sabari et al., 2007). Annual dermatology exams are recommended for patients who have had KAs and prognosis is usually excellent for single, isolated KAs (J. Berreman, personal communication, February 15, 2011; Ponti & Leon, 2005; Sabari et al., 2007).
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Education about sunscreen application and use of a sunscreen with SPF 30 or more as well as self-skin exams are the standard of practice (J. Berreman, personal communication, February 15, 2011).

Nursing Implications

Nurses and Advanced Registered Nurse Practitioners specializing in dermatology must recognize and understand all of the nuances of skin cancers that present in everyday practice. Understanding the variants of keratoacanthoma, and knowing the etiology, pathogenesis and variety of treatment options enables the care provider to rapidly diagnose and inform and educate the patient. The patient, empowered by this knowledge, can better decide on treatment options. This potentially improves patient outcomes and ongoing patient care.

The HBM assists nurses to help the patient explore his/her perception of personal susceptibility, the severity of the condition and the personal benefits of treatment and care. By using the HBM framework common-sense constructs, the nurse can address a patient’s perceptions to encourage behavior that is healthy. In turn, the patient gains knowledge that they can understand and use to make the next best decision based on his/her understanding. This understanding would then allow the patient practical ways to incorporate modifying their behavior in his/her everyday life.

Summary

Keratoacanthomas are a fast growing cutaneous neoplasm that can either show spontaneous regression or can be invasive and destructive and for this reason, is deserving of further investigation. KAs usually present as reddish-brown, dome-shaped papules or nodules with a central keratin-filled plug that range in size. KAs stem from follicles and pilosebacious units and enlarge with the proliferation of squamous epithelial cells that extend upward and
around the keratin-filled crater and then downward into the dermis. The most important
differential diagnosis of keratoacanthoma is squamous cell carcinoma of which KA is considered
a type. Surgical excision is the treatment of choice although Mohs surgery is appropriate for
giant KAs or where cosmetic results are important or where skin is in limited supply (such as the
top of the ear). KAs are also often treated with cryosurgery or electrodessication and curettage
with success. Other treatments include systemic or topical chemotherapy (retinoids, ethotrexate,
5-fluorouracil, interferon), radiation therapy, and photodynamic therapy. Each case should be
evaluated individually with respect to diagnosis and approach to treatment.
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