

Squamous Cell Carcinoma of the Nail Unit: Review of the Literature

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Squamous cell carcinoma of the nail unit (SCCNU) is often misdiagnosed and improperly treated because it mimics a number of other conditions. This review details current knowledge of anatomy, pathophysiology, clinical presentation, diagnosis, and treatment of SCCNU. A heightened clinical awareness is critical to treating SCCNU and preventing development of advanced disease at which time amputation is needed and metastasis may occur. Physicians should consider SCCNU in each case of a nail abnormality unresponsive to topical treatment. For adequate diagnosis and excision of SCCNU, timely and appropriate specialist referral is necessary. (*J Hand Surg Am.* 2018; ■(■):■–■. Copyright © 2018 by the American Society for Surgery of the Hand. All rights reserved.)

Key words Finger, nail, squamous cell carcinoma, subungual carcinoma.

SQUAMOUS CELL CARCINOMA OF the nail unit (SCCNU) is considered to be very rare.^{1,2} The symptoms of SCCNU are usually nonspecific and SCCNU may mimic a wide variety of other diseases, such as fungal and bacterial infections and verruca vulgaris. This frequently causes misdiagnosis and late presentation.^{3–5} Referral to a specialist is often made only after failure of several protracted treatments by other medical professionals.⁶ The hand surgeon should proceed directly to a biopsy in every nail abnormality not responding to initial treatment.⁷ However, taking a biopsy of the nail unit risks deformity or obtaining an inadequate specimen.⁸ Several types of therapy have been suggested for SCCNU, but excision is the treatment of choice.⁹ It is still controversial whether local excision, Mohs surgery, or amputation is the best choice.

In this review, current knowledge on SCCNU is summarized. A total of 74 international publications regarding invasive SCCNU of the nail complex dating from 1850 to March 2016 are included. These publications were used to derive information on anatomy, pathophysiology, clinical presentation, diagnosing, and treatment of SCCNU. We also combined information from all 304 described cases of confirmed SCCNU in 1 data set (Table 1). Three SCCNU cases that presented to our department were added. Analysis of this data set revealed the best possible evidence on epidemiology, potential predisposing factors, clinical presentation, potential for misdiagnosis, bone involvement, recurrence rate, dissemination, and mortality.

Achieving an understanding of clinical presentation may prevent delays in diagnosis and treatment of SCCNU and thereby prevent SCCNU from becoming an advanced condition in which (partial) amputation of the digit is needed and even metastasis and mortality may occur.

RELEVANT ANATOMY

The nail unit is composed of 4 structures: nail bed, nail plate, nail fold, and hyponychium. The nail bed is a specialized form of epithelium that consists of a proximal zone of germinal matrix and a distal zone of sterile matrix.¹⁰ The germinal matrix is responsible for

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TABLE 1. Included Publications Describing SCCNU

Velpau, 1850 (n = 1)	Moy and Eliezri, 1989 (n = 10)	Conolly et al, 2008 (n = 5)
Ellis, 1948 (n = 2)	Eliezri and Silverstein, 1990 (n = 2)	DePond et al, 2009 (n = 1)
Falk, 1954 (n = 1)	Lombardi et al, 1990 (n = 1)	Turowski et al, 2009 (n = 2)
Ashby, 1956 (n = 2)	Guitart et al, 1990 (n = 12)	Wessendorf et al, 2009 (n = 1)
John, 1956 (n = 1)	Rapini and Magee, 1991 (n = 3)	Sbai et al, 2009 (n = 1)
Gelmann, 1963 (n = 1)	Echt et al, 1991 (n = 1)	Tanese et al, 2009 (n = 1)
Canipe et al, 1964 (n = 4)	Ashinoff et al, 1991 (n = 1)	Rosen et al, 2010 (n = 3)
Eichenholtz and Deangelis, 1965 (n = 3)	Connil et al, 1993 (n = 1)	Meesiri, 2010 (n = 1)
Campbell and Klokarn, 1966 (n = 1)	Tosti at al, 1994 (n = 1)	Goméz et al, 2010 (n = 2)
Shapiro and Baraf, 1970 (n = 7)	McHugh et al, 1996 (n = 1)	Ruiz Santiago and Morales-Burgos, 2011 (n = 1)
Eibel, 1971 (n = 2)	Lai et al, 1996 (n = 1)	Abner et al, 2011 (n = 1)
Mauro et al, 1972 (n = 1)	De Berker et al, 1996 (n = 7)	Choughri et al, 2011 (n = 1)
Caroll, 1976 (n=27)	Downs et al, 1997 (n = 1)	Patel et al, 2011 (n = 1)
Kaminsky et al, 1978 (n = 1)	Hale and Dawber, 1998 (n = 2)	Dika et al, 2012 (n = 11)
Attiyeh et al, 1979 (n = 12)	Chang et al, 1999 (n = 1)	Lecerf et al, 2013 (n = 20)
Tomsick and Menn, 1981 (n = 8)	Obiamiwe and Gaze, 2001 (n = 1)	Potter and Griffin, 2013 (n = 1)
Hazelrigg and Renne, 1982 (n = 2)	Zabawski et al, 2001 (n = 5)	Ishida et al, 2014 (n = 1)
Kouskoukis et al, 1982 (n = 1)	Dobson et al, 2002 (n = 1)	Batalla et al, 2014 (n = 4)
Lumpkin et al, 1984 (n = 1)	Alam et al, 2003 (n = 2)	Wong et al, 2015 (n = 1)
Mikhail, 1984 (n = 24)	High et al, 2003 (n = 1)	Ormerod and de Berker, 2015 (n = 17)
Tomsick and Menn, 1984 (n = 9)	Peterson et al, 2004 (n = 3)	Dika et al, 2015 (n = 39)
Fleckman et al, 1985 (n = 1)	Wong et al, 2004 (n = 3)	Nicholls et al, 2015 (n = 1)
Shelley and Shelly, 1986 (n = 1)	Lazar et al, 2005 (n = 3)	Lobato et al, 2015 (n = 1)
Goldberg and Robins, 1986 (n = 1)	Figus et al, 2006 (n = 6)	Feily, 2015 (n = 1)
Schwartz, 1988 (n = 1)	Kurokawa et al, 2006 (n = 1)	

n, number of cases included from publication.

90% of the production of the nail plate.¹¹ The sterile matrix is the secondary site of nail production, and its surface allows adherence of the nail plate.^{10,11} The nail plate covers the nail bed and is composed of hard, keratinized, squamous cells.¹¹ It provides stability to the fingertip during grip and acts as a stabilizer for the pulp.^{12,13} The nail plate is bordered on either side by the lateral nail folds (paronychia) and emerges from the proximal nail fold.¹¹ The end of the proximal nail fold (eponychium) produces the nail cuticle, a layer of stratum corneum that adheres to the nail plate and protects the nail unit from infection and external irritants.^{11,12} The hyponychium is situated at the junction between the distal end of the nail and the pulp and provides an important barrier against infections.¹¹

PATHOPHYSIOLOGY

Squamous cell carcinoma is a common skin tumor that usually develops on sun-exposed areas of the skin. It is the most common tumor of the hand and nail unit, causing 90% of all hand malignancies.¹⁴ Nonetheless,

SCCNU is rare, with an estimated incidence ranging from 3 cases in 250,000 hospital admissions to 14 cases in 50,000 dermatological consultations.^{1,2} These numbers, however, could be an underestimation of the actual incidence because SCCNU is often misdiagnosed and therefore underreported.

The etiology of SCCNU remains uncertain. A strong correlation with human papillomavirus has been demonstrated⁹ and many potential etiologic factors have been suggested (Table 2). In addition, SCCNU may arise *de novo* or from premalignant skin conditions.¹ Progression from carcinoma *in situ* to invasive SCCNU is thought to occur in up to 15% of the cases.³

Although SCCNU is considered a low-grade malignancy, it has a tendency to invade the distal phalanx.¹⁵ Analysis of the cases surveyed revealed bone involvement in 50% of the cases. Five cases (1.6%) had dissemination to distant sites, including lymph nodes and lungs, of which SCCNU was fatal in 40%. Also, SCCNU may in itself be a distant metastasis from a primary malignancy of the lung, esophagus, or foot.^{16,17}

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