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Review

Non-tuberculous mycobacterium skin infections after tattooing in healthy individuals: A systematic review of case reports

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Abstract

In recent years, several case reports and outbreaks reported occurrence of non-tuberculous mycobacteria (NTM) infections within 6 months after receiving a tattoo in healthy individuals. NTM species (e.g., *Chelonae, Fortuitum, Hemophillum, and Abscessus*) are widespread in the environment and it is often suspected that contamination may occur through unsterile instrumentation or unsterile water used for diluting tattoo ink to dilute color. In reported cases, lesions were mainly restricted to a single color 'gray' part of the tattoo. Mycobacterium *Chelonae* was the most common cause of tattoo associated NTM infections. Less than 50% of the case reports tested tattoo ink for acid fast bacilli stains and cultures. Subjects required treatment with either clarithromycin alone or in combination with quinolones for 6 to 9 months. An increase in NTM skin infections in healthy individuals after tattooing indicates the need for sterile standards during tattooing and improved local and regional regulatory oversight.

Keywords: non-tuberculous mycobacteria, NTM, mycobacteria, tattoo, systematic review, case reports, culture.

Introduction

Permanent tattoos are increasingly popular among American adults, with an estimated 21% reported to have received at least one tattoo in 2012 [1].Individuals getting tattoos are at a greater risk of being infected with various pathogens, some of which can be difficult to diagnose and treat. Recently, public health officials reported multiple outbreaks of non-tuberculous mycobacterium (NTM) skin infections in the United States among immunocompetent adults after recent tattooing, which on further investigation was associated with contamination of tattoo ink [2;3]. NTM species (e.g., Chelonae, Fortuitum, Hemophillum, and Abscessus) are thought to be widespread in the environment and it is often suspected that contamination may occur through unsterile instrumentation or unsterile water used for dilution of tattoo ink to obtain a gray color. Rapidly growing and slow-growing NTM species are commonly associated with traumatic wound infections, cosmetic surgery, permanent tattoo make-up, and body piercing.

NTM skin infections around the tattoo site are difficult to diagnose based on symptoms alone and may be mistaken for allergies. These skin lesions can appear as red papules or as a diffuse macular or papular rash at the tattoo site, specifically restricted to a single color region. Confirmatory diagnosis often requires skin biopsy and culture on special media that can take up to 6 weeks for a definitive diagnosis. Rapid and new diagnostic techniques such as radio-immunoassay, enzyme-linked immunosorbent assay, and polymerase chain reaction can also be used in the diagnosis, but these are more technically involved and costly and are not considered a first-line of diagnostic investigations. Misdiagnosis of NTM infections often leads to receiving ineffective treatments, necessitating prolonged periods of treatment before receiving a definitive diagnosis. Furthermore, treatment choices with antibiotics may be limited depending on the susceptibility profile of organisms infecting the tattoo site. The occurrence of NTM infection at the tattoo site has not been systematically documented. To increase awareness of these infections among patients and clinicians, we conducted a systematic review of the published literature on NTM skin infections associated with tattooing.

Methods

We used methods detailed by the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. We searched MEDLINE® and EMBASE for studies of all designs examining permanent tattoo and NTM infection, which were published through November 2013. No language restriction was applied. We combined search terms for “tattoo” or “tattoo ink” with Medical Subject Heading terms for“non-tuberculous mycobacterium”. We also hand searched bibliographies of published reports and reviews. The exposure of interest was history of recent tattooing and the outcome of interest was documentation of NTM skin infection at tattoo site through culture and histopathological examination of skin biopsy.

Data extracted from eligible articles included information on study and participant characteristics, time of onset, clinical presentation of infection, documentation of tattoo ink contamination, microbiological examination, histopathology of skin biopsy, prior treatment, time to diagnosis, culture susceptibility, and treatments. Data was extracted into a structured table in duplicate. No assessment of risk of bias or study quality was conducted because most of the identified studies were case reports. No quantitative synthesis was performed.

Results

The systematic search yielded 156 abstracts. Full-text screening identified 25published reports [3-28] and a systematic review [29] on the occurrence of NTM infections after tattooing. Eligible reports examined a total of 114 cases that had NTM infections after receiving tattoo (**Table 1**). Clinical symptoms occurred any time after 1 week to 6 months in healthy individuals after receiving a tattoo. Mycobacterium *Chelonae* was the most common cause of NTM infection after tattooing; other less commonly associated mycobacteria were *Immunogenum*, *Abscessus*, Fortuitum, and *Haemophilum*. Skin manifestations appeared mostly in the form of tender erythematous papules, pustules, and nodules, predominantly within the borders of tattoos. Lesions were mainly restricted to a single color, generally the gray part of the tattoo. Definitive diagnosis was arrived in most cases with histopathological examination, culture and sensitivity, and Zeihl-Neelsen staining. In general, studies used polymerase chain reaction when acid-fast bacilli stains and cultures were negative. Ten of the 25 eligible studies reported testing tattoo ink for acid fast bacilli stains and cultures [3;7-11;13;14;17;22].

Table 1. Study Characteristics of Tattoo Site Infection with Non-Tuberculous Mycobacterium

Reference, Country	N, Sex Age	Time of Onset	Tattoo Site Presentation	Tatoo Ink tested for NTM	Non-response to prior treatment	Tattoo Site Culture	Time to diagnosis	Susceptibility to antibiotics determined	Medication (duration)
Bechara 2010, France[4]	1,M 51 yr	10 d	Papulopustules, erythematous plaques	No	Yes	NR	NR	Yes	Clarithromycin (1 mo)
Binic 2011 Serbia[5]	2, M 26, 35 yr	2-3 wk	Pruritic, red papules	No	Yes	M.Chelonae	NR	Yes	NR
Curco 2012, Spain[6]	1,M/1,F 33, 25 yr	1-2wk	Papulopustules	No	Yes	M. Chelonae (1 case)	NR	NR	Clarithromycin (3mo)
Drage2010, USA[7]	5, M/1, F 20-49 yr	1-2 wk	Red papules And pustules	Yes (ink +ve for AFB)	Yes	M.Chelonae (2 cases)	18wk	Yes	Clarithromycin (6 mo)
Falsey 2013, USA[8]	5 cases NR	1-3 wk	Red papules and pustules	Yes (ink +ve for M.Chelonae)	Yes	M.Chelonae (2 cases) M. Abscessus (3 cases)	NR	Yes	Clarithromycin or Ciprofloxacin (3 wk)
Giulieri 2011, Switzerland[9]	12, F 56yr	3 wk	Red papules or pustules or erythematous plaque	Yes (ink +ve for M.Hemophilum)	NR	M. Hemophilum (10 cases)	NR	Yes	Triple-drug combination of clarithromycin, ciprofloxacin,

Reference, Country	N, Sex Age	Time of Onset	Tattoo Site Presentation	Tatoo Ink tested for NTM	Non-response to prior treatment	Tattoo Site Culture	Time to diagnosis	Susceptibility to antibiotics determined	Medication (duration)
			(Permanent makeup)						and rifampin (7 mo)^
Goldman 2010,France[10]	30 cases NR	3-35 d	Papules and pustules	Yes (ink +ve for M.Chelonae)	NR	M. Chelonae (43% cases)	2 mo (mean)	NR	Clarithromycin in 41 patients + tobramycin (10 patients)**
Hamsch 2010, Germany[11]	7, F Age NR	2wk	Granulomatous, purulent skin reactions, swelling of the loco-regional lymph nodes (Permanent makeup)	Yes (ink +ve for M.Lentiflavum)	NR	M. Haemophilu m (2 of 7)	NR	NR	Systemic tuberculostatic therapy ethambutol, clarithromycin, and rifampicin (3 patients)**
Kappel2011, USA[12]	1,M 41 yr	6 wk	Tender erythematous Plaques and pustules	NR	Yes	M.Chelonae	2 wk	NR	Clarithromycin (6 mo)
Kay2009, USA[13]	2,M 35, 44 yr	1-8 wk	Pustulo-nodular skin infection	Yes (ink -ve for NTM)	Yes	M. Haemophilu m (1 case)	NR	Yes	Rifampin, ciprofloxacin, and clarithromycin (6 mo)
Kennedy 2012, USA[3]	13, M/6 F 35 yr	3wk	Erythematous rash	Yes (ink +ve for M.Chelonae)	NR	M. Chelonae	NR	Yes	NR
Kluger 2008, France[14]	6,M/2, F 23 yr	10-21 d	Papules, pustule	Yes (ink +ve for AFB)	Yes	None* Culture results were negative	2-5 mo	NR	Minocycline hcl, (1 mo)
Mitchell 2011, USA[15]	1,F 18 yr	Several mo	Erythematous painful papules, nodules	NR	NR	M. Immunogenu m (16s rRNA gene sequencing)	NR	Yes	Clarithromycin (9 to 12 mo)
Peterson 2011, USA[16]	1,F 56 yr	6 mo	Erythematous plaques	No	Yes	None	2 mo	NR	Clarithromycin (4mo)
Preda 2009,Australia[17]	1,M 32 yr	3 wk	Erythema, edema and painful nodules	Yes (ink +ve for M.Chelonae)	Yes	M.Chelonae	2 mo	Yes	Clarithromycin and Moxifloxacin(4 mo)
Ricciardo 2010,Australia[18]	1,M 23 yr	1wk	Tender, erythematous, non- pruritic papules	NR	Yes	M. Abscessus	NR	Yes	Clarithromycin (5mo)
Rodríguez- Blanco 2010, Spain[19]	3,M/2,F 21 yr	3-30 d	Red papules,superficial hyperkeratosis	No	Yes	Culture positive (3 patients), molecular methods positive (2 cases)	NR	Yes	Clarithromycin (3-5 mo), topical gentamicin 2xd (3 patients)!
Schwartzman 2012, USA[20]	NR	4 wk	Erythema, tenderness, and nodular rash.	No	Yes	M. Chelonae	NR	NR	Clarithromycin (9 mo)
Scott-Lang 2012, UK[21]	1, M 42yr	NR	Rash	NR	NR	M. Chelonae	NR	NR	Clarithromycin (NR)
Sergeant2012, UK[22]	3, M/1, F 21-35 yr	2wk	Erythematous papules, with overlying scales, and small pustules	Yes (ink +ve for M.Chelonae)	Yes	M. Chelonae	NR	Yes	Clarithromycin (6mo)
Shinohara 2012, USA[23]	1,F 35 yr	3 wk	Erythematosus papule	NR	NR	M. Chelonae	2 wk	Yes	Clarithromycin (4 mo)
Suvanasuthi 2012, Thailand[24]	1, M 25 yr	NR	Erythematous papules	NR	Yes	M. fortuitum	2 wk	Yes	Clarithromycin and ciprofloxacin (10 mo)
Winthrop 2012, USA[25]	1,F 29 yr	2 wk	Papules	NR	NR	M. Chelonae	19 d	Yes	Linezolid 600 mg (2 mo)

Reference, Country	N, Sex Age	Time of Onset	Tattoo Site Presentation	Tatoo Ink tested for NTM	Non-response to prior treatment	Tattoo Site Culture	Time to diagnosis	Susceptibility to antibiotics determined	Medication (duration)
									azithromycin 250 mg (3 mo), and vitamin B6 100 mg (2 mo)
Wolf 2003, Israel [26]	1,F 27yr	3 mo	Erythematous nodules	No	NR	No 65-kd antigen gene was positive.	NR	NR	Patient refused systemic antibiotic therapy
Wollina2011, Germany[27]	1,F 46 yr	8 wk	Erythematous nodules (Permanent makeup)	No	Yes	M. Haemophilum	NR	Yes	Clarithromycin and ciprofloxacin (3 mo) Rifampin (6 mo)

* Acid-fast bacilli staining of a sample from the bottle of tattoo ink used for all the patients proved positive

^ 10 pts who did not respond after 2 mo of therapy underwent partial parotidectomy, local eyebrow excision and selective neck dissection

! 2 of 5 patients were lost to follow-up

Spontaneous healing in 1 patient (Hamsch 2010) and 6 patients (Goldman 2010)

d = days; M = mycobacterium; mo = month, NR = not reported; wk = week; yr = year.

Patients were initially treated with topical antibiotics such as fusidic acid, bacitracin, neomycin, topical steroids, or oral antibiotics without much benefit. Subsequent histopathological examination showed lymphocytic infiltration and granulomatous reaction with central necrosis; in most cases cultures grew Mycobacterium *Chelonae*, which was sensitive to clarithromycin. Treatment regimens varied considerably across reports; a majority of the studies reported using clarithromycin either alone or in combination with quinolones for 6 to 9 months [12]. Despite the slow response and prolonged treatment period, studies in general reported improved outcomes. Two studies reported spontaneous resolution of infection in some patients [12;22].

Side-effects related to prolonged administration of systemic antibiotics were reported in one study that included gastrointestinal symptoms, including loose stools and abdominal pain. Two patients experienced vaginal candidiasis and one patient developed tineacorporis [8].

Discussion

Our review results indicate that a number of case reports published recently documented the occurrence of NTM infections associated with tattooing among healthy individuals. Mycobacterium *Chelonae* is the most common cause of NTM infections after tattooing; other less commonly associated Mycobacterium include *Immunogenum*, *Abscessus*, Fortuitum, and *Haemophilum*. Reported cases of skin manifestations were mainly restricted to the gray parts of the tattoo, suggesting infection may have occurred through unsterile water used for dilution of tattoo ink to obtain a gray color. According to these reports, patients were initially treated with topical antibiotics without much benefit. The diagnosis was established by histopathological examination and microbiological cultures. Polymerase chain reaction can be useful in detecting a common antigen to all mycobacterium species, especially when acid-fast bacilli stains and cultures are negative.

Although case studies and out-breaks of NTM skin infections have been reported, incidence rates of NTM infections secondary to tattooing still remains unknown. The first case of tattoo-related skin infection related to unclassified species of NTM was identified by polymerase chain reaction analysis in 2003 [26]. According to the recent Harris poll in 2012, approximately one in five US adults (21%) receive at least one tattoo, which is up from the 16% and 14% in 2003 and 2008, respectively [30]. Owing to the growing popularity of tattooing, NTM-related tattoo infections are gaining importance as a public health issue. Recently, CDC disseminated a public health alert to inform the public about NTM skin infections in healthy individuals following reports of *Mycobacterium Chelonae* skin infections after tattooing in fourteen New York residents in January 2012 [2]. Most often patients consult their primary care physicians. An increased awareness among clinicians is needed to better diagnose and treat cases of tattoo-related NTM infections.

Infections with NTM, such as Mycobacterium *Chelonae*, *Abscessus*, *Haemophilum*, which are ubiquitous, and rapidly-growing acid-fast bacilli have been described as the most common causes of infections complicating dermatological procedures. These infections typically occur 4 to 6 weeks following tattooing [31]. It is important to recognize that infections associated with tattooing may occur with rapidly-growing or slow-growing NTM. Tap water is considered to be the major reservoir for human

NTM pathogens [32]. Some case studies have attempted to establish the source of infection through AFB staining and culture of tattoo ink from tattoo parlors. Tattoo inks are a mixture of pigments and diluents. The majority of pigments are considered biologically inert. Different shades and colors are obtained by combining different pigments or diluting with water. The Federal Drug Administration considers tattoo inks to be cosmetics and traditionally has not exercised its regulatory authority [33]. In the US, the practice of tattooing is regulated by state and local jurisdictions.

The limitations of this review reflect – to a large extent – limitations of the data available in primary studies. This is a review of case reports. Therefore, it could not establish incidence rates. Although skin manifestations appeared within weeks in majority of the cases, causes for delayed presentation up to six months are not discernible. Although cultures grew NTM sensitive to clarithromycin in some cases, specific guidelines on the length of treatment for tattoo-related NTM infections are lacking. Though many patients responded to both macrolide and quinolone, efficacy of one over the other in the treatment of tattoo-related NTM infections remain to be established.

In the future, careful documentation of tattoo-related infections will be needed to establish incidence rates and rapid accurate diagnostic methods. When assessing a patient with a tattoo reaction, a very high degree of suspicion is needed for diagnosing tattoo-related NTM infections because of the variability in clinical presentation. Additional studies are needed in this population to assess the efficacy of various treatment modalities and to establish the optimal duration of treatment options for NTM skin infections. Efforts should be made to reach out to the public, tattoo artists, ink and pigment manufacturers, and health care professionals to warn them of the potential for NTM infection after tattooing. Sterile standards during tattooing and improved local and regional regulatory oversight are needed to promote better tattooing practices and to prevent occurrence of tattoo associated NTM infections.

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