

Bioethics and Psoriasis

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Abstract

We have presented the clinical, epidemiological, microbiological, pathological, immunopathological, serological, and therapeutic studies showing how the streptococcus may be strongly linked to psoriasis. With this as background, we have presented three ethical arguments that are cogent for psoriasis. First, this microbial "pathogen" theory is both ignored and overlooked even with the abundance of evidence supporting it. That being the case, current treatments, consequently, are aimed not at the onset of the disease, but much later in the pathogenic cascade. Last, the continued use of "biologics" or costly immunosuppressives, which are not curative, presents bioethical challenges. We consider psoriasis a sequela of streptococcal infection similar to rheumatic fever, where treatment, at the earliest stages of the disease, has resulted in its disappearance.

Keywords: Pathogen; Biologics; Serological; Streptococcal pharyngitis

Psoriasis-discussion of Microbial Pathogenesis of the Disease

We have recently completed an ethical analysis of Lyme disease and have found the ethics to be challenged in all aspects of that disease from diagnosis through laboratory evaluation to treatment and outcomes [1]. Psoriasis differs from Lyme disease in that many fewer targets for ethical discussion are present. There are still some that are worthy of evaluation from an ethical standpoint.

First and foremost, in the ethics discussion is whether the cause of psoriasis is the streptococcus or not. We have previously presented findings from clinical, microbiological, immunopathological, serological, epidemiological and therapeutic studies that all point to a streptococcal origin for the disease [2]. A brief discussion of each of those aspects follows.

It is well known that guttate psoriasis follows streptococcal pharyngitis. Bacterial cultures and ASO titers may be positive for streptococcus, and the patients routinely benefit from a course of penicillin (or a penicillin derivative) added to their treatment regimen [3]. Plaque psoriasis, however, has no apparent link to streptococcal pharyngitis. Recent observations may illuminate this apparent situation and demonstrate how the bacterium is still present and involved.

Streptococci have been shown to internalize in tonsillar epithelial cells, live inside the cells for up to a year, then externalize and recolonize [4]. When they are inside the cells, their presence is not detectable either by culture or serology. Thus, they can be present in the disease but not visible.

Another way the organism escapes detection is by forming biofilms. These have been shown to be present in tonsillar tissue in psoriasis [5]. The streptococcal organisms spin out a polysaccharide (slime) coating providing a means to evade the immune system as well as a shield of protection. Periodically, "exporter" cells leave the biofilm, recolonize,

and subsequently make new biofilms. Through internalization and biofilm external formation, the streptococcus has the unique capability to "hide in plain sight" despite having a known presence in psoriasis.

Immunopathology provides further insight on the role and impact of biofilms. We have recently found Toll-like receptor 2 (TLR2) in the upper dermal capillaries in biopsies of psoriatic plaques [2]. Located here, in the blood supply of the psoriatic plaques, TLR2 is in a prime location to cause the changes in psoriasis. It is well established that TLR2 activates the MyD88 pathway which has TNF α as its endpoint [2]. TNF α is the "prime" mode by which TLR2 destroys organisms. TLR2 also upregulates IL 17 and IL 12/23 [6,7]. The TNF α , IL 17 and IL 12/23 are all well-known cytokines involved in the pathogenesis of psoriatic lesions. Inhibition of the above cytokines, results in ultimate clearing of the psoriatic lesions [8] TLR2 targets the biofilms via receptor sites within the biofilm itself [9]. We have shown its presence surrounding the biofilms in the eccrine sweat ducts in eczema and associated with the plaques in the brains of Alzheimer's disease patients [10,11]. Interestingly, TLR2 has also been found by Carrasco in circulating monocytes in psoriatic arthritis [12].

The serological findings in plaque psoriasis are indeed compelling: anti-streptococcal IgG has been shown to be markedly elevated in plaque psoriasis [13]. Of note, the presence of IgG is different from ASO titer which is the ordinary serologic marker for streptococcal disease. One might also broadly consider the TLR2 found in the dermal capillaries and the TLR2 on circulating monocytes as part of the serologic response to streptococcus.

The epidemiologic findings strongly point to streptococcus as the etiology of psoriasis. Most noteworthy in this regard is where there is no streptococcus in the environment (northernmost Europe and certain Pacific islands), there is no psoriasis. Further, psoriasis becomes more prevalent as streptococcus increases with decreasing latitude [14].

Psoriasis Treatment-comparing Current and Alternative (antimicrobial) Therapies

Treatment strongly implicates streptococcus as the etiology of psoriasis. Antibiotics that will eradicate the microbe when given over a long interval will eradicate psoriasis as well [15]. The same is true for tonsillectomy in psoriasis; the results are nearly as dramatic as those given injectable penicillin over a considerable period of time [16]. The reason the antibiotics need to be administered for a lengthy time is very likely related to the internalization and biofilm formation. The constant presence of the antibiotic is necessary to kill the organisms as they “externalize” and/or become “exporter” cells exiting the biofilm.

The addition of a biofilm-dispersing agent to the regimen may also be necessary [3].

All of this, especially the treatment considerations, has led us to believe that psoriasis is a sequela of streptococcus similar to rheumatic fever and glomerulonephritis [5]. Moreover, with penicillin, it may be possible to decrease the impact of the psoriasis in similar fashion to rheumatic fever and glomerulonephritis.

All the foregoing gives rise to the following paradigm regarding the pathogenesis of psoriasis. In a genetically “primed” patient, streptococcus is planktonic or internalizes or forms biofilms:

Planktonic	Internalized	Biofilms
Acute tonsillitis	Anti strep IgG	TLR2
ASO	TNF α , IL 17, IL 12/23	TNF α , other cytokines
Cytokines	Psoriasis lesion	Psoriasis lesion
Psoriasis		

Table 1: Psoriasis arising from planktonic, internalized, or biofilm-encased *streptococci*.

Ethical Challenges

This raises the ethical challenge of ignoring the microbial “pathogen” theory of this disease. By overlooking or disregarding the evidence as presented above, a vital part of controlling psoriasis is lost. For example, one can administer the (effective) antibiotics simultaneously with one or another of the “biologic” medications and achieve the (usual) excellent response noted with the “biologic”. After 8 or 9 months, the biologic can be discontinued while the antibiotic is continued. All that is necessary for consideration of this treatment is epistemic humility. This is an instance where “Evidence Based Medicine” (EBM) carries a “stipulative definition” as there is not a sound argument to justify restricting the evidence for use of antibiotics while giving heavier weight to what has been deemed mainstream research that focuses on symptomatic therapeutic options and not causative therapies. The word ‘evidence’ reveals its ambiguous nature in the context of research and the precarious position patients may be placed in when used to justify this approach to clinical practice [17,18].

Why not treat at the beginning of the cycle rather than at the end? It seems apparent that streptococcus has the leading role in the production of psoriasis; why not eradicate it? This has been shown to be possible with antibiotics, such as penicillin, and with tonsillectomy [15,16]. Where psoriasis has been linked with metabolic syndrome, arthritis, and other maladies (much the same as rheumatic fever), it seems that eradicating the microbe would very likely eradicate these secondary diseases in like fashion [5].

The other ethical challenge is the actual use of “biologics” in treatment without considering adjuvant therapies or therapeutic alternatives while recognizing costs to patients and society, as well as risks of long term therapy [19]. The costs have been staggering to the healthcare system. According to a report by the Pew Charitable Trusts, in 2015 alone, 1 to 2% of Americans are treated with specialty drugs while these same drugs account for 38% of total drug expenditures. (Specialty Drugs and Health Care Costs: Fact Sheet, the Pew Charitable Trusts.) They do achieve excellent results, but they do not treat the primary source of the disease. Thus, a permanent remission cannot be

achieved; consequently, to continue the remission, the medication must be taken on an ongoing basis. The continued remission in the process comes at great financial cost to both the patient and society (\$20,000 or more per year). The average cost to bring one of these new drugs to market is 2.6 billion dollars. Follow this with promotion and production costs, and one can see why the costs of the final product are so high. Moreover, in addition to financial costs, a portion of the patient’s immune system is disabled and is not responsive in certain situations. The package inserts of these medications attests to that and is replete with warnings.

Continuation of this therapy results in a sort of “rational inconsistency” which overlooks the problems because of the results. Inherent in this is the trust in the physician and respect for the patient that may be subtly undermined by the continuance of this practice. It begs the question of the arrogance of focusing solely on “evidence based medicine” without consideration to what in fact defines “evidence”. It is incumbent upon physicians in clinical practice to reconcile many sources of evidence from a research perspective and consider the implications in the setting of patient care.

Treatment in the other diseases in which biologics are employed may be shown (in the future) to have similar ethical challenges. This would be true if those other diseases also had microbial pathogens as their source. One such disease where monoclonal antibody trials are being undertaken is Alzheimer’s disease where the source is a microbe [20] limiting the body’s reaction to that microbe, without treating the offending agent, not only seems unethical but irrational.

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