To ASLO or Not to ASLO: Utility of the ASLO Test in Dermatology

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ABSTRACT **Background:** Group A Streptococcus (GAS) causes a wide spectrum of acute infections and immune-related diseases, most of which include a dermatological presentation. However, dermatological findings have a wide range of other possible etiologies. The diagnosis of GAS-related disease requires an indication of preceding GAS infection by direct culture or by measuring antistreptolysin O (ASLO) titer.

Objectives: To explore the correlation between ASLO positivity and dermatological diseases.

Methods: We analyzed clinical data from all cases of patients over 18 years of age who underwent ASLO testing between the years 2016 and 2020 in the Department of Dermatology at Rambam Health Care Campus.

Results: Of 152 adult patients with ASLO tests, 100 had diagnoses that were potentially related to streptococcal infection. Vasculitis and psoriasis were the most suspected diagnoses. Positive ASLO test was found in 44 (29%) patients. The diagnoses showing the highest ratio of positive ASLO were psoriasis (60%), erythema nodosum (46%), skin infections (43%), Sweet syndrome (33%), and vasculitis (15%). Psoriasis types included plaque psoriasis (8 patients), guttate psoriasis (3 patients), and palmoplantar pustulosis and erythroderma (2 patients each).

Conclusions: Although the applicability of ASLO for the spectrum of dermatological diseases remains unclear, our results enhance the practical relevance of the test. We showed a higher prevalence of positive ASLO tests in psoriasis and erythema nodosum cases and a lower prevalence in vasculitis. Notably, ASLO was positive in all psoriasis subtypes, suggesting high utility of the test for psoriasis.

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KEY WORDS: antistreptolysin O (ASLO), erythema nodosum, psoriasis, streptococcal infection, vasculitis

Group A Streptococcus (GAS) is a Gram-positive, β-hemolytic bacterium that can cause a wide variety of diseases. Some of these diseases are caused directly by acute GAS infection, such as tonsillopharyngitis, peritonsillar abscess, otitis media, pneumonia, and cellulitis [1]. Others are immune-mediated, such as rheumatic fever, glomerulonephritis, reactive arthritis, and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS). The immune-mediated diseases usually appear post-infection [1]. Several dermatological conditions are associated with GAS infection, such as psoriasis (and especially guttate psoriasis) [2-4], erythema nodosum [5], vasculitis [6], polyarteritis nodosa [7], Henoch–Schönlein purpura [8], Kawasaki disease [9], and cutaneous leukocytoclastic vasculitis [10].

There are two methods of detecting GAS infection of the throat: throat culture and antibody serology test; however, each method has limitations. Even during acute GAS infection, a throat culture may test negative. Possible reasons for false-negative cultures are previous antibiotic treatment or an inexperienced sampler. However, an asymptomatic carrier might have a positive culture, which is unrelated to the immune phenomena. Therefore, antibody testing has become the preferred method for substantiating a previous GAS infection [1].

The most useful antibody for this test is antistreptolysin O (ASLO), which is secreted by specific B-cells against the antigen streptolysin O, a hemolytic exotoxin secreted by most strains of GAS. The ASLO titer begins to rise within 1 week of infection, peaks at 3–6 weeks of infection, and then declines [1]. We explored the correlation between ASLO positivity and dermatological conditions diagnosed by physicians.

PATIENTS AND METHODS

All patients consecutively tested for ASLO at the Department of Dermatology at Rambam Health Care Campus between the years 2016 and 2020 were included in the study. Files of all patients were reviewed for diagnosis and relevance of the ASLO test. The study was approved by the local institutional review board committee (55-22-RMB-D).

Our laboratory's lower titer limit is 1:200. Therefore, ASLO was considered negative for levels below 1:200 and positive if ASLO was ≥ 1:200. We also checked for the presence of a positive throat culture for GAS and a history suggesting a recent GAS infection (recent sore throat).

RESULTS

We considered ASLO levels of 152 adult patients from 2016 to 2020, 100 had a diagnosis with possible association to streptococcal infection [Figure 1]. Vasculitis was the diagnosis most frequently associated with testing (46 patients), but only 15% of these patients had a positive ASLO test. Psoriasis was the second-most tested diagnosis (25 patients) and had the highest positive result ratio, with 60% patients testing positive for ASLO [Figure 2]. Interestingly, not only guttate psoriasis but also other psoriasis types were connected to streptococcal infection in our cohort [Figure 3]. Similarly, 2 of the 3 palmoplantar pustulosis patients tested positive for ASLO [Figure 3].

Figure 1. Main dermatological conditions with possible association to GAS infection
GAS = Group A streptococcus, PPP = palmoplantar pustulosis

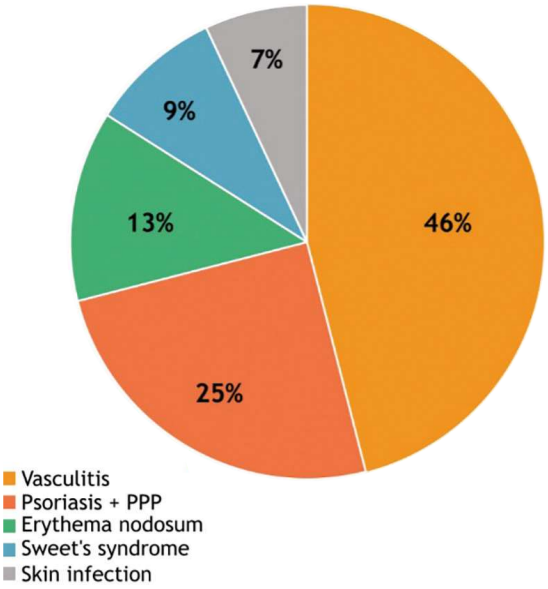
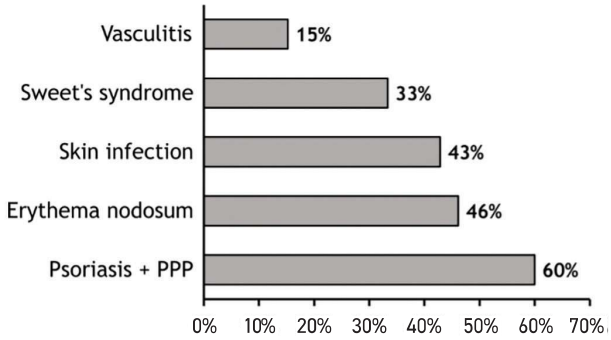


Figure 2. Diagram showing the rate of positive ASLO tests for the presented diagnoses
ASLO = antistreptolysin O, PPP = palmoplantar pustulosis



Erythema nodosum was also frequently studied by ASLO test with 46% positive results (6/13). Less frequently tested diagnoses were Sweet's syndrome, with 3 of 9 patients testing positive for ASLO, and skin infections, with 3 of 7 patients testing positive. Other less common diagnoses were erythema multiforme and pityriasis rubra pilaris (PRP) [Figure 4]. Last, there were diagnoses that were not associated with streptococcal infection and for which the ASLO test was negative [Figure 4].

DISCUSSION

To date, there have been few studies discussing the relevance of ASLO in the clinical spectrum of skin diseases. In dermatology, the ASLO test is mainly used in the context of searching for the etiology of streptococcus-related immune phenomena such as vasculitis and erythema nodosum. Latha and colleagues [11] studied the relevance of the ASLO test in vasculitis. They showed a positive ASLO titer in 52.1% of the examined patients (82 of 156) with cutaneous vasculitis [11]. The prevalence of positive ASLO was higher than in our cohort, which showed 15% positive results (7 of 46 patients).

Kim et al. [12] examined ASLO titers in a group of 30 adult patients with psoriasis. They found titers to be elevated in 33% (10 patients) [12]. The most common clinical type of psoriasis was plaque psoriasis (6 patients). Less frequent were guttate psoriasis (3 patients) and pustular psoriasis, with only one case [12]. In our cohort, we found 25 patients diagnosed with either psoriasis or palmoplantar pustulosis, and 15 showed a positive ASLO titer. This finding suggests higher rates than reported

by Kim et al. [12] (a total of 60% positive). Similarly, the most common clinical type of psoriasis with positive ASLO titer was plaque psoriasis, demonstrated in 32% of our cases (8 patients). Less frequent was guttate psoriasis with 12% (3 patients). Palmoplantar pustulosis and erythroderma secondary to psoriasis were ASLO-positive in 8% of the patients (2 patients each).

We also studied the data from erythema nodosum and Sweet's syndrome patients. Cribier and co-authors [13] checked 129 patients who were diagnosed with erythema nodosum; 22% (29 patients) tested positive for ASLO [13]. Our research demonstrated positive ASLO titers in 46% of the patients with erythema nodosum (6 of 13 patients). Kemmett and colleagues [14] checked 29 patients who were diagnosed with Sweet's syndrome, 21% (6 patients) tested positive for ASLO [14]. We found a similar ratio of positive ASLO titers in 33% of patients with Sweet's syndrome (3 of 9 patients). These results suggest a possible correlation to GAS infection in a substantial percentage of patients with erythema nodosum and Sweet's syndrome.

This study provides important insights into the relevance of the ASLO test in dermatology. However, some limitations affect the applicability of the results. First, the sample size might limit the inferences that could be drawn regarding each of the studied dermatological conditions. Second, we looked at the different diseases that were positive for ASLO. Thus, our cohort only included patients for whom the test was conducted, and we may have overlooked some of the patients, although presenting with a GAS-related dermatological condition.

Figure 3. Types of psoriasis and relative rates of positive ASLO tests
ASLO = antistreptolysin O, PPP = palmoplantar pustulosis

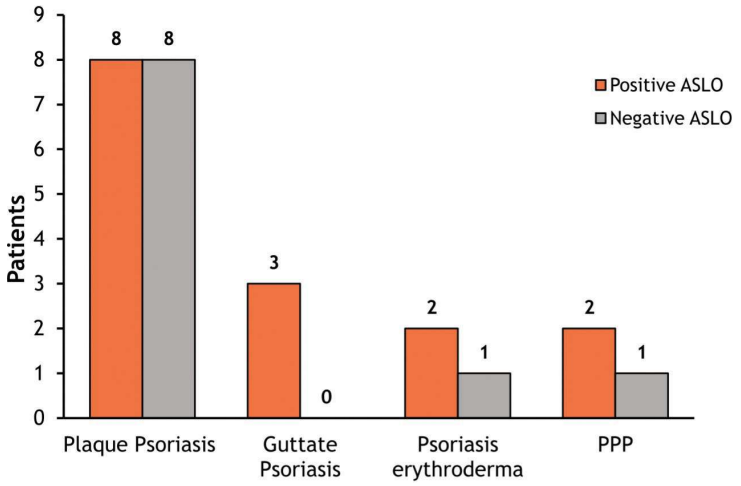
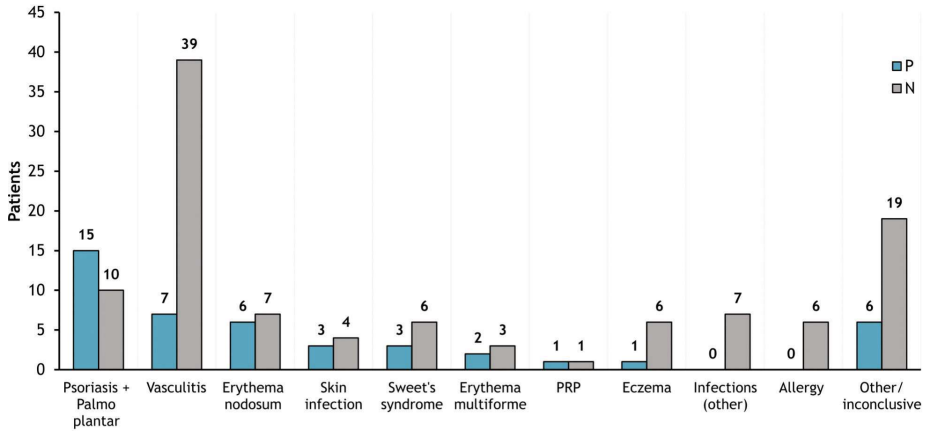


Figure 4. Diagram showing positive and negative ASLO results for all patients divided according to diagnosis (N = negative, P = positive, ASLO ≥ 200)
ASLO = antistreptolysin O, PPP = palmoplantar pustulosis, PRP = pityriasis rubra pilaris



In summary, 44/152 patients (29%) tested positive for ASLO in our study. Of these, 34 had a diagnosis that might be correlated to streptococcal infection. Psoriasis was the most frequent diagnosis testing positive for ASLO. Therefore, we suggest that in cases of psoriasis in which a positive ASLO titer is detected, high clinical relevance should be suspected, even with no evidence of a recent GAS infection. The ASLO test is also indicated in vasculitis, erythema nodosum, and Sweet's syndrome with a somewhat high yield. Our results provide further evidence for the relevance of GAS infection and ASLO testing in different dermatological conditions, specifically in cases of psoriasis. Future studies should focus on prospectively and separately investigating ASLO-positive ratios in each dermatological condition, such as psoriasis and vasculitis. The results should be correlated with concurrent culture results. This type of study may enable estimating the true percentage of patients with positive ASLO for each disease.

CONCLUSIONS

Although the applicability of ASLO in the spectrum of dermatological diseases remains unclear, we believe that our results enhance the practical relevance of the test. We show a higher prevalence of positive ASLO tests in psoriasis and erythema nodosum cases and a lower prevalence in vasculitis. Notably, ASLO was positive in all psoriasis subtypes, suggesting high utility of the test for psoriasis.

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Capsule

Toward personalized therapy for multiple sclerosis

The autoimmune disease multiple sclerosis (MS) is a highly heterogeneous disease with many different treatment options. However, it is not clear whether certain features of MS are associated with distinct immune signatures or if they would benefit from particular therapies. **Gross** and colleagues used peripheral blood mononuclear cells and serum collected from two independent cohorts of patients with MS to identify three endophenotypes of the disease. These peripheral blood immune signatures distinguished patients with distinct clinical disease trajectories and were correlated with efficacy of interferon-b treatment. Peripheral blood analysis could thus be used to guide personalized treatment regimens for patients with MS.

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