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ERYSIPELAS AND SECONDARY ACUTE INFLAMMATION (SAI) IN LYMPHOEDEMA

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A common complication in lymphoedema is attacks of fever combined with an erythematous rash of the lymphoedematous extremity. This condition has been called secondary acute inflammation (SAI)(1).

The cause of this condition is not known and the aim of this study is to highlight the role of streptococci by serologic means.

SAI is clinically indistinguishable from erysipelas and cellulitis, diseases mostly caused by group A streptococci. This bacteria has never been demonstrated as a cause of SAI, neither directly nor in culture.

It is difficult to obtain satisfying material for microbiological examination from the dry skin, and any penetration of the inflamed, lymphoedematous epidermis for better samples is contraindicated (2).

In streptococcal infection of the skin the amount of antistreptolysin O (ASO) and anti-deoxyribonuclease (ADN-ase B) are elevated in 50 and 78 per cent respectively (3). Antibodies of ADN-aseB are probably specific for group A streptococci and are regarded as a sensitive indicator of streptococcal skin affection (4,5).

If streptococci are responsible of SAI, elevated titers, particularly of ADN-aseB, would be expected in this disease.

Material

The study included 43 lymphoedematous patients consecutively drawn from hospital files who, within a period of 12 months to 14 days prior to blood-sample, had sustained one or more attacks of SAI (SAI+ group), and 50 patients with lymphoedema who never had attacks of SAI (SAI- group).

SAI is defined as a sudden (within hours) onset of fever with an erythematous rash (> 24 hours duration) in the lymphoedematous area.

Patients with primary and secondary lymphoedema were included. Patients with suspected other probable streptococcal infections in the period (eg. tonsillitis), and patients with a broken skin barrier were excluded.

Nearly all patients in the SAI+ group had been treated with penicillin, reliable information on doses and treatment duration was not obtainable. The number of SAI attacks in the period, inflammation due to other reasons, age and sex were registrated.

There were 7 males (16%) in the SAI+ group, but none in the SAI- group. Secondary lymphoedema was present in 87% in the SAI+ group and in 70% in the SAI- group (Table 1). Blood samples were analyzed for C reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood cell count (WBC), and gamma glutamyl-transpeptidase (GT).

The sera were stored at -20C and analyzed en bloc for ASO and ADNase-B according to standard procedures (5). ASO > = 250 and ADNase-B > = 800 were regarded as elevated values (6).

Different subgroups were statistically compared with the two tailed chi-square test with Yates correction for continuity, 95% confidence interval.

Results

One patient in the SAI+ group and none of the SAI- group had an elevated ADN-aseB titer. The patient with the high ADN-aseB value also had a raised ASO titer.

The findings of ASO are presented in Table 2. There is a statistically significant higher number of elevated ASO in the SAI+ group.

When comparing only female patients there was still a difference between the groups, but not significant (Table 3). Six of the 7 men in the SAI+ group had an elevated ASO. Lymphoedema of the upper extremity were all caused by mastectomy and radiation, this subgroup did not show any difference in the frequency of high ASO (Table 4). Patients with lymphoedema of the lower extremity is a heterogenous group: Primary lymphoedema, secondary lymphoedema after malignancy and skin inflammation years previously. Table 5 shows a tendency toward higher frequency of elevated ASO for the SAI+ group compared to the SAI- group.

When comparing the elevated ASO to other subgroups like frequency and time of SAI- attack, other infections, laboratory results (CRP, ESR, WBC and GT) no significant differences were found.

Discussion

The very low number of patients with elevated ADN-ase B titer contrasts the findings of elevated ADN-ase in streptococcal skin infections reported by other authors (2,3,4,7). Elevated ADN-ase B titer following streptococcal infections usually persists several weeks to months. Thus our findings seem to rule out SAI as a skin disease caused by streptococci, group A. However, a possible influence by penicillin, given to all patients may have altered the serological response (2). An altered immune response in lymphoedema might be another explanation. There is a local susceptibility of infection in lymphoedema, and a multiinfectious etiology of SAI has been brought forward (8,9). This might include different groups of streptococci. SAI might be an ordinary reaction to several different infections or noxious traumas in lymphoedema patients who have a defective immunologic system.

The elevated ASO in 49% of the patients of the SAI+ group compared to 22% of the SAI- group together with clinical signs of skin infection may indicate streptococcal involvement. The normal titer of ADN-aseB could indicate involvement of other groups of streptolysin O producing streptococci (10). Infection in various organs and tissues give different serologic response (3,11). SAI might be a result of a "non-epidermal" streptococcal infection, for instance in deep subcutaneous layers which more readily raise the ASO than ADN-ase B (11). Also non-streptococcal infections associate with elevated ASO titers and even non-infectious disorders (10).

The SAI+ and SAI- groups are not comparable regarding sex and diagnoses. Elevated ASO in 6 of 7 men in the SAI+ group and the lack of men in the SAI- might indicate a higher vulnerability of SAI and/or higher incidence of infection in the male. The low number of patients with elevated ASO in SAI- group of lower extremity coincides with high frequency of primary lymphoedema, a diagnosis more seldom connected with SAI.

Conclusion:

This study disproves SAI as an infection of the epidermis caused by streptococci group A. A high ASO titer in many of the patients who had sustained SAI attacks may be related to infection in non-epidermal layers of the skin, by other groups of streptococci, by other microorganism or by non-infectious disorder.

	SAI +	SAI -
	43	50
AGE		
mean	57	59
st.d.	13,2	12,8
SEX		
male	7	0
female	36	50
DIAGNOSIS		
mastectomy	16	31
sec.lo., leg	21	4
prim.lo.,leg	6	15

Tabel 1.
Distribution of age, sex and diagnosis of the material.

	SAI +	SAI -	TOT
ASO≥250	21	11	32
ASO<250	22	39	61
	43	50	93

X^2 = 6,234 $p < 0.05$

Tabel 2
Frequency of ASO > 250
in the SAI+ and SAI- groups.

	SAI +	SAI -	TOT
ASO≥250	15	11	26
ASO<250	21	39	60
	36	50	86

X^2 = 2,96 $0,05 < p < 0,1$

Tabel 3
Frequency of ASO > 250 in the SAI+
and SAI- groups, women only.

	SAI +	SAI -	TOT
ASO≥250	7	7	14
ASO<250	9	24	33
	16	31	47

$X^2 = 1{,}362 \quad 0{,}1 < p$

Tabel 4
Frequency of ASO > 250 in the SAI+ and SAI- groups, upper extremity.

	SAI+	SAI-	TOT
ASO≥250	14	4	18
ASO<250	13	15	28
	27	19	46

$X^2 = 3{,}24 \quad 0{,}05 < p < 0{,}1$

Tabel 5
Frequency of ASO > 250 in the SAI+ and SAI- groups, lower extremity.

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