Thyroid autoimmunity in female post-adolescent acne: A case-control study

Thomas Jonathan Stewart, BBioMedSc, MBBSa,c and Carl Bazergy, MBBS, RACGPb

aDarlinghurst Medical Centre, Darlinghurst 2010, Sydney, Australia; bKogarah Railway Medical Centre, Kogarah 2217, Sydney, Australia; cSchool of Medicine, University of New South Wales, Sydney, Australia

Introduction

Acne vulgaris is an incompletely understood disorder of poliosebaceous follicles. A scourge of adolescence, it is increasingly persisting into the mid-forties, especially in females. 45% of women aged 21–30 years, 26% aged 31–40 years, and 12% aged 41–50 years, suffer from clinically-visible acne.1 The reasons for this rising prevalence have been unclear. Polycystic ovarian syndrome (PCOS) has been suggested as a possible contributor, however most acne sufferers have normal serum androgen levels.2,3

There has been increasing suspicion of a key autoinflammatory role in pathogenesis of chronic acne vulgaris. Autoinflammatory syndromes associated with acne have been described as possibly sharing common pathogeneses, involving dysregulated immunity with abnormal interleukin-1 signaling, leading to clinically significant inflammation.4,5 Thyroid autoimmunity has been detected in a number of chronic inflammatory skin conditions including acne vulgaris and chronic idiopathic urticaria.6,7

In 2012, Vergou and colleagues were the first to show female post-adolescent acne sufferers had significantly higher rates of thyroid autoimmunity compared with healthy controls.7 The relationship has not been examined since, despite a sound theoretical grounding. We aimed to confirm this association between thyroid autoimmunity and post-adolescent acne in adult women, as well as qualify its practical value with subsequent endocrinologist referral and intervention.

Results

130 patients and 65 controls satisfied the inclusion criteria and were enrolled in the study. Patients and controls had consulted one of 10 different family physicians. Patients ages ranged from 21 to 36 years with a median age of 26 years. Controls ages ranged from 20 to 37 with a median age of 27 years.

116/130 (89%) patients and 60/65 (92%) controls returned thyroid function tests in the normal range (TSH 0.4–5.0mIU/L, FT4 10–20pmol/L, FT3 2.3–5.7pmol/L. The most prevalent abnormal thyroid function finding was a high TSH in the setting of a normal FT3 and FT4 (See Table 1).

32/130 (24.5%) patients recorded positive (>20IU/ml) anti-thyroglobulin antibodies compared with 7/65 (10%) controls. 24/130 (18%) patients recorded positive (>35IU/ml) anti-TPO antibodies compared with 4/65 (6%) controls. 7/130 (5%) patients recorded both positive anti-thyroglobulin and anti-TPO antibodies compared with 0/65 (0%) controls.

There was a statistically significant difference between the groups for positive anti-TG (p = 0.023) and anti-TPO (p = 0.021) antibodies but not for presence of both (p = 0.098) (Table 2). Differences in TSH, FT3 and FT4 between the groups were not statistically significant. There was no statistically significant association between abnormal thyroid function tests and positive thyroid antibodies.

Patient follow-up after referral

95 patients were referred to one of eight endocrinologists and 89 successfully made contact with the spe-
cialist, for which we were able to source return corre-
spondence for 82.

35/82 (42%) patients indicated some form of thy-
roid intervention which consisted of at least one of the
following: active surveillance, selenium, thyroxine,
antithyroid medication, radioiodine treatment or sur-
gery (Table 3).

Discussion

Acne pathogenesis involves an interplay of follicular
hyperkeratinisation, sebum production, Cutibacte-
rium acnes (C. acnes) and inflammation. It is less clear
in adult acne but smoking, genetics, resistant bacteria,
oral contraceptives, cosmetics and underlying hor-
monal abnormalities have all been implicated.8

McGeown et al.9 found higher sebum excretion rates
in women with post-adolescent acne compared with
non-acne sufferers, and PCOS is the leading theory,
however the majority of patients with adult acne have
normal androgen levels.

Thyroid hormone action on sebaceous glands is
unclear. In hypothyroid states, sebocytes exhibit
reduced rates of secretion (SER),10 and TSH and Thy-
roxine, with co-administration of testosterone, have
both been shown to increase sebum secretion.11

Although SER increases with thyroxine, it still remains
subnormal.12 Studies have failed to show significant
changes in thyroid function parameters in adult
acne.7,13 The exact role of thyroid hormone remains
unclear but it seems unlikely that it is mediated princi-
pally through sebum secretion.

Table 1. Results of serum thyroid function testing (TSH, FT4, FT3).

| Patients (n = 130) | Controls (n = 65) |
|-------------------|------------------|
| All normal        | 116              | 60               |
| High TSH alone    | 8                | 2                |
| Low TSH alone     | 1                | 1                |
| High TSH, Low FT4 | 2                | 2                |
| Low TSH, High FT4 | 2                | 0                |
| High TSH, Low FT3 | 1                | 0                |
| Low TSH, High FT3 | 0                | 0                |

Susceptibility to autoimmune thyroid diseases
(AITD) depends on a complex interaction between
environmental and genetic factors. 79% of autoim-
mune thyroid disease may be attributed to genetics.14

Cytokines are crucial in the regulation of immune and
inflammatory responses and are the probable candidate
genes for autoimmune thyroid disease. Immuno-
modulatory genes coding for pro-inflammatory
cytokines such as interleukin-1 and interferon-γ have
thus far been implicated in pathogenesis.15

In autoimmunity, thyroid follicular cells are
induced to express Fas ligand by cytokine stimulation
and antigen-presenting and Th1 cells (e.g. interleukin-
1), leading to apoptosis. IN Hashimoto’s disease, apo-
ptosis occurs in thyroid cells expressing Fas, or normal
thyroid cells in which Fas was induced by IL-1ß. So,
any event in a primed individual may lead to local
production of IL-1ß initiating thyroid-cell induced
apoptosis. TG and TPO antibodies develop secondar-
ily to this thyroid damage inflicted by T
lymphocytes.16,17

There is a more than four-fold risk of acne vulgaris
in individuals with affected first-degree family mem-
bers.18 As well as in autoimmune thyroid disease, IL-
1ß may also play an important role in the develop-
ment of inflammation in acne. IL-1ß has been shown
to propagate inflammation initiated by C. acnes in
human sebocytes.19,20 We suspect this complex inter-
action between genetics, thyroid and sebaceous glan-
dular tissue may help produce the inflammatory
changes of post-adolescent acne observed in thyroid
autoimmune states.

Our results suggest thyroid antibody testing is
indeed warranted in female adult acne as subsequent
referral of positive results leads to intervention in a
high proportion (42.5%) of patients. Prophylaxis for
euthyroid autoimmune thyroiditis remains controver-
sial but has shown benefit.21,22 Additionally, as TG
and TPO antibodies are often positive in other auto-
immune conditions, prudent testing in this cohort

Table 2. Differences in thyroid function and antibody testing
between groups.

|          | Patients | Controls | P-value | Odds ratio (95% CI) |
|----------|----------|----------|---------|---------------------|
| Anti-TG  | 32       | 7        | 0.023   | 2.7                 |
| Anti-TPO | 24       | 2        | 0.021   | 3.45                |
| Both     | 7        | 0        | 0.098   | n/a                 |

Table 3. Outcomes of endocrinological referral.

| Endocrinological intervention | n = 35 |
|-------------------------------|--------|
| Active surveillance           | 9      |
| Selenium                      | 8      |
| Thyroxine                     | 16     |
| Antithyroid medication        | 3      |
| Radioiodine treatment         | 2      |
| Surgery                       | 3      |

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may also alert the clinician to screen for important comorbidities including diabetes mellitus and systemic lupus erythematosus.23,24

The study was limited by its retrospectivity and small sample size. Inclusion of consults from 10 family physicians and 8 endocrinologists may have introduced some heterogeneity in our assessments. Another criticism may be that acne vulgaris diagnoses were not confirmed by a skin specialist, however research has shown that diagnostic agreement between family practitioners and dermatologists for acne is very high,25 likely due in no small part to its significant presence in primary care.

Based on our findings we suggest thyroid autoantibody testing should be routine in women with post-adolescent acne, as positive results may signify a joint presentation qualifying endocrinological input. Even minor derangements should meet a low threshold for referral and importantly, antibody testing retains its value in the setting of a normal screening TSH. Future work should confirm this association in larger cohorts and explore the possible shared genetics between these two conditions.

Patients and methods

We retrospectively screened the electronic records from 2010–2016 at a private family medicine clinic in Sydney for women who had consulted one of the clinic doctors for post-adolescent acne (persisting >21 years of age). Included patients had only been given a categorical diagnosis of acne vulgaris and severity of acne was not quantified.

Subjects were required to have had thyroid-stimulating hormone (TSH), free T3 (FT3), free T4 (FT4), anti-thyroglobulin (anti-TG) and anti-tissue peroxidase (anti-TPO) antibody testing within 12 months of their acne presentation. Thyroid function results were categorised as high, normal or low and antibody tests as either positive or negative.

Subjects with known thyroid disease, PCOS or taking oral contraceptives or antiandrogens were excluded. Records were adjunctively screened for referral to, and correspondence from an endocrinologist.

We randomly selected age- (+/− 12 months) and sex-matched healthy controls from the same population who had presented for reasons not related to acne or any hormonal conditions with skin manifestations. Controls were required to have had the same thyroid function and antibody testing as patients during the study period. Controls with known thyroid disease or taking oral contraceptives or antiandrogens were excluded.

Ethics approval was not sought for this study as all data had been collected as part of the patients routine care at a private institution and is owned in its entirety by the second author. Study procedures were carried out in accordance with the Helsinki Declaration of 1975.

Statistics

Pearson Chi-square and Fisher’s exact test were used to compare categorical variables. Stata’s tables for epidemiologists was used to calculate odds ratios. A p-value of <0.05 was considered significant. Analysis was carried out using STATA14 software.

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