Series Editor: Camila K. Janniger, MD

Thyroid Abnormalities in Pediatric Patients With Vitiligo in New York City

Odelya E. Pagovich, MD; Jonathan I. Silverberg, PhD; Elie Freilich; Nanette B. Silverberg, MD

The link between vitiligo and thyroid disease has been well-established. However, the types of patients at risk for thyroid disease and the strength of this connection in childhood are debatable. We retrospectively reviewed 67 charts of pediatric dermatology patients with vitiligo vulgaris (53 with nonsegmental vitiligo) who were tested for thyroid disease. In our cohort of 28 patients with available thyroid test results, we identified 7 patients (25%) with active thyroid disease. None of the 7 patients with thyroid disease had segmental vitiligo. If we had included the broader number of patients (N=67), the rate may have been as low as 10.4% overall (7/67), which is still a substantial rate of thyroid disease. These results are comparable to the European literature and highlight the need for thyroid screening in children with vitiligo vulgaris of a generalized nonsegmental type.

Cutis. 2008;81:463-466.

akourou et al¹ reported on a cohort of children and adolescents with vitiligo who had a high incidence of thyroid disease. They concluded that Hashimoto thyroiditis occurs 2.5 times more frequently among children and adolescents with vitiligo compared to healthy children and adolescents. Iacovelli et al² also reported a high incidence of

Accepted for publication July 26, 2007.

Dr. Pagovich is from Sackler University, Tel Aviv, Israel.
Dr. J.I. Silverberg is from the State University of New York Downstate Medical Center, Brooklyn. Mr. Freilich is from Yeshiva University, New York, New York. Dr. N.B. Silverberg is from the Department of Dermatology, St. Luke's-Roosevelt Hospital Center, New York.
The authors report no conflict of interest.

Correspondence: Nanette B. Silverberg, MD, Pediatric Dermatology, St. Luke's-Roosevelt Hospital Center, 1090 Amsterdam Ave, Suite 11D, New York, NY 10025 (nsilverberg@chpnet.org).

thyroid disease in children with vitiligo. In their cohort, they found nonsegmental vitiligo to be linked to thyroid disease, as opposed to segmental vitiligo, which was not linked. Of 121 children with vitiligo studied, 13 (10.7%) were found to have thyroid abnormalities, all affected by the nonsegmental type of vitiligo.² Our treatment center sees many patients with vitiligo vulgaris and we initiated a chart review to explore the association with thyroid disease.

Methods

An institutional review board—approved chart review of patients treated for vitiligo in the dermatology offices of St. Luke's-Roosevelt Hospital Center, New York, New York, from 2003 to 2005 was conducted. Patient charts were reviewed for characterization of vitiligo, age at onset, type, duration, distribution, personal and family history of thyroid disease and/or autoimmune disease, and thyroid studies. As part of a broad screening protocol, we ordered thyroid function testing for thyroxine, triiodothyronine resin uptake, triiodothyronine, thyrotropin, and anti–thyroid peroxidase antibodies in children and adolescents with vitiligo. Patients had the option to have thyroid function tests performed by a primary care physician or deferred to a later date.

Results

We reviewed the charts of 67 pediatric patients with vitiligo, 53 with the nonsegmental type. Of these 67 patients, thyroid test results were only available for 28 patients. In a review of charts of pediatric patients with available thyroid test results, we found thyroid abnormalities in 28.6% (8/28) of patients. Six patients were hyperthyroid or hypothyroid; 1 patient had anti-thyroid peroxidase antibodies as a marker of autoimmune thyroid disease but no

measurable abnormality of thyroid activity; and 1 patient had an isolated minimal alteration of triiodothyronine resin uptake, which was deemed within reference range by a pediatric endocrinologist. In total, 25% (7/28) had remarkable thyroid abnormalities (Table). None of the patients reported changes in activity, palpitations, heat or cold intolerance, or hyperhidrosis. Goiter and exophthalmos were not notable in any of the patients. Neck examination by a pediatric endocrinologist revealed 2 patients with somewhat enlarged homogeneous thyroids. Of the 28 patients with available thyroid test results, the mean age at the time of diagnosis of vitiligo was 9.0 years (age range, 1–18 years). If the patients without available laboratory test results were all assumed to have had normal thyroid levels, then the rate of active thyroid disease may have been only 10.4% (7/67) of patients with vitiligo vulgaris or 13.2% (7/53) of all nonsegmental cases. All of the patients with diagnosed thyroid disease were referred to a pediatric endocrinologist for confirmation of diagnosis, with 4 patients diagnosed with hyperthyroidism or Graves disease; 2 with hypothyroidism or Hashimoto thyroiditis; and 1 with evidence of thyroid immunity, found to be euthyroid at the time of examination.

Of the patients with available test results, 21 were euthyroid, with a mean age at the time of laboratory evaluation of 9.4 years. Of these patients, there were 12 females and 9 males. In these patients, vitiligo was most frequently found on the face (ie, eyelids, bilateral cheeks, and forehead) and neck (85.7%; 18/21). Eleven patients (52.4%) presented with the generalized type of vitiligo, 3 (14.3%) with generalized disease limited to acrofacial involvement, 2 (9.5%) with the localized nonsegmental type, and 5 (23.8%) with the segmental type of vitiligo. Average body surface area involvement based on the rule of nines was 9%.

Thyroid Function Test Results in Pediatric Patients With Vitiligo

	n	Comments
Patient Charts Available (N=67)		
Segmental disease	14	
Nonsegmental disease	53	
Patients With Available Thyroid Test Results ^a (n=28	3)	
Female	17	
Male	11	
Patients With Abnormal Thyroid Test Results ^b (n=8	3)	
	7	
Hyperthyroid	4	3 with high anti-TPO
Hyporthyroid Hypothyroid		3 with high anti-TPO Elevated TSH in both; one with high anti-TPO
	4	Elevated TSH in both; one with

Abbreviations: anti-TPO, anti-thyroid peroxidase; TSH, thyrotropin; T3RU, triiodothyronine resin uptake.

^aAged 1-18 y at time of test results.

bAged 1-14.5 y at time of test results.

For the 7 patients with confirmed thyroid disease, average body surface area involvement was 4% and was not statistically different from the patients without thyroid abnormalities. Six of 7 patients had generalized vitiligo and 1 had localized nonsegmental disease. None of the 7 patients reported any symptoms of thyroid disease such as fatigue, heat or cold intolerance, or recent weight shifts. Age trends revealed younger patients with abnormal thyroid parameters. The mean age at the time of abnormal laboratory testing was 7.7 years (age range, 1–14.5 years). However, this mean age was not statistically different from the 21 patients with normal thyroid test results. Five patients were female (71%) and 2 male (29%). Although there was a trend of more females being affected by thyroid disease than males, it was not statistically different from the healthy population and may reflect the greater overall number of females in our study.

There was a trend of a stronger family history in patients with abnormal thyroid parameters but no statistical significance. Fifty-seven percent (4/7) of patients with thyroid disease had a family history of autoimmune disease (ie, thyroid disease, vitiligo, pernicious anemia, type 1 diabetes mellitus, or rheumatoid arthritis) or leukotrichia versus 43% (9/21) of euthyroid patients. Similarly, body site did not statistically vary from euthyroid patients, as 71% (15/21) had facial involvement. The only clear trend was that all the patients with segmental vitiligo had normal thyroid test results.

Comment

Because vitiligo is often observed in the setting of coexisting autoimmune disorders, there has been recent interest in the association of the two, particularly a link between vitiligo and thyroid disease.^{3,4} Studies have shown that the increased prevalence of Hashimoto thyroiditis in patients with vitiligo seems to be genetically determined. Recently, the NACHT leucine-rich-repeat protein 1 gene, NALP1, has been described to be a gene associated with susceptibility to vitiligo in association with other autoimmune diseases.⁵ One percent of the worldwide population is affected by vitiligo. Of this 1%, approximately 25% are children.⁶ In the United States in 1996, 205,159 children were affected with thyroiditis, thus thyroiditis is not uncommon in the American pediatric population.⁷ In the United States in 1990, the population of individuals younger than 18 years was 63.6 million and increased to 72.1 million in 2000. Therefore, thyroiditis would be expected in less than 1% of the US population.8 Unfortunately, no data on

subclinical pediatric thyroid disease have been published in the United States.

Iacovelli et al² showed that 10.7% (13/121) of pediatric patients with vitiligo, particularly 16% (13/81) of patients with nonsegmental vitiligo, had thyroid abnormalities; all patients with the segmental subtype had normal thyroid test results in the same cohort. Our data showed that thyroid dysfunction seemed to correlate with the type of vitiligo, namely 6 of 7 patients with thyroid abnormalities presented with generalized vitiligo and 1 presented with localized nonsegmental disease. Our patients demonstrated results similar to Kakourou et al1 who reported that 13 of 54 children (24.1%) had laboratory evidence of thyroiditis. However, we note that because of the lack of available thyroid test results for 39 patients in our chart review, there is a possibility that the rate of active thyroid disease in our patients may have been as low as 10.4% (7/67) or 13.2% (7/53) in patients with nonsegmental vitiligo, or possibly greater than 25% if more thyroid test results were available for the entire nonsegmental vitiligo population and followed the same trend as our results (eg, 7/28). The former numbers more closely approximate data derived from the Iacovelli et al² cohort of pediatric patients with vitiligo in Italy.

Conclusion

Although the Kakourou group¹ examined patients in Greece, we find that thyroid abnormalities are similarly detectable in pediatric patients with vitiligo in the United States. It has not been found that specific disease features or family history highlight presence of thyroid disease. Only patients with pediatric segmental vitiligo seemed spared from thyroid abnormalities in our chart review, which supports routine thyroid screening for children with nonsegmental vitiligo in the United States. We ask our patients with nonsegmental vitiligo to receive annual thyroid testing with annual blood testing for screening purposes to aid in early detection.

REFERENCES

- Kakourou T, Kanaka-Gantenbein C, Papadopoulou A, et al. Increased prevalence of chronic autoimmune (Hashimoto's) thyroiditis in children and adolescents with vitiligo. J Am Acad Dermatol. 2005;53:220-223.
- 2. Iacovelli P, Sinagra JL, Vidolin AP, et al. Relevance of thyroiditis and of other autoimmune diseases in children with vitiligo. *Dermatology*. 2005;210:26-30.
- Kurtev A, Dourmishev AL. Thyroid function and autoimmunity in children and adolescents with vitiligo. J Eur Acad Dermatol Venereol. 2004;18:109-111.

Pediatric Dermatology

- 4. Kemp EH, Waterman EA, Weetman AP. Autoimmune aspects of vitiligo. *Autoimmunity*. 2001;34:65-77.
- 5. Jin Y, Mailloux CM, Gowan K, et al. *NALP1* in vitiligo-associated multiple autoimmune disease. *N Engl J Med.* 2007;356:1216-1225.
- 6. Halder RM, Grimes PE, Cowen CA, et al. Childhood vitiligo. J Am Acad Dermatol. 1987;16(5, pt 1):948-954.
- Weetman AP. Autoimmune thyroid disease. In: Rose NR, Mackay IR, eds. The Autoimmune Diseases. 3rd ed. San Diego, CA: Academic Press; 1998:405-430.
- Lugaila T, Overturf J. Children and the households they live in: 2000; Census 2000 special reports, CENSR-14. US Census Bureau Web site. http://www.census.gov/prod/2004pubs/censr-14.pdf. Issued March 2004. Accessed March 24, 2007.