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Letter to Editor

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Dermal Titanium Dioxide Deposits in Frontal Fibrosing Alopecia – A Pilot Study

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Abbreviations:

FFA: Frontal Fibrosing Alopecia; SEM-EDS: Scanning Electron Microscopy and Energy Dispersive X-Ray Spectroscopy; TiO_2: Titanium Dioxide

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1. To the Editor

Frontal Fibrosing Alopecia (FFA) was initially described in 6 patients in 1994 as a "frontal variant of lichen planopilaris [1]. Considered a primary lymphocytic chronic cicatricial alopecia [2,3], it was a relatively uncommon diagnosis following its reporting, however in the past 15 years it has begun to be seen with increasing frequency [4]. Exposure to sunscreen has been postulated as a potential culprit in FFA with the presence of Titanium Dioxide (TiO_2) on the hair shaft of an affected patient raising the possibility that this inorganic product may be playing a role [5].

Twelve women and 3 men with the clinical and histologic features of FFA were selected for study. Biopsy tissue was subjected to Scanning Electron Microscopy and Energy Dispersive X-Ray Spectroscopy (SEM-EDS) with attention paid to the dermis adjacent to hair follicles.

Seven patients (5 women and 2 men) demonstrated the presence of TiO_2 within the dermis adjacent to hair follicle epithelium (Figure 1).

Patients with FFA experience frontotemporal hairline recession and more than half have loss of eyebrow hair [2,6]. Postmenopausal women are the most commonly afflicted although it affects men and patients in all age groups. Loss of eyelashes, facial papules and body hair involvement may also occur particularly in patients with more severe disease [6]. Perifollicular hyperkeratosis and erythema are typically appreciated although signs of inflammation may be lacking [2]. Histologically, dermal fibrosis around affected follicles is noted with lymphocytic interface inflammation involving the infundibulum and isthmus [1,2]. The inflammatory focal point has been hypothesized to reside in the bulge area of the follicle [2].

The etiology has been postulated to be due to genetic predisposition, hormone imbalance and immune dysfunction [5]. Disease in first degree relatives has been reported [2].

Studies on the association between sunscreen exposure and FFA have involved the use of questionnaires. In 2016 Aldoori et al [4]. queried 105 women with FFA and 100 age and sex matched controls regarding their skin and hair care practices. A statistically significant association with sunscreen use was noted in patients with FFA compared to controls. The authors postulated that sunscreen accumulates in hair follicles and that lower sebum production during aging allows a greater retention of sunscreen at this site. The largest study to date involved querying 308 men and women with FFA and 347 controls searching for associated environmental and hormonal factors [3]. In women, a statistically significant relationship with pregnancy, hormone replacement therapy and facial sunscreen use was noted. For men, application of sunscreen and anti-aging cream was significantly associated. A recent study from Australia with 130 women with FFA and 130 female controls found a statistically significant greater number of patients reported regular and more frequent application of sunscreen and cosmetics [2]. In none of these studies was the composition of the sunscreen mentioned.

In 2019 16 women with FFA and 3 with no disease had hair shafts evaluated with SEM-EDS for the presence of TiO_2 [7]. All showed the presence of the metal on the hair shafts as well as one unaffected male who denied using facial moisturizer or sunscreen. The authors speculated that TiO_2 might penetrate at the isthmus and incite a lichenoid inflammatory reaction. A case report with similar findings suggested that FFA may result from sensitization akin to oral lichen planus developing from metal containing implants [5].

This is the first demonstration of TiO_2 in the dermis adjacent to intact hair follicle epithelium. Limitations of this study include the small number of patients, that this study emanates from a single medical center and a lack of information regarding what patients were applying to their skin/scalp. Control specimens were also not evaluated although tissue subjected to SEM-EDS in at least one study failed demonstrate the presence of titanium suggesting it is not normally found in skin tissue [8].

Roughly half of patients with FFA exhibit the presence of TiO_2 in the dermis adjacent to affected hair follicles and hypothetically may play a role in its pathogenesis. It's possible the failure to detect TiO_2 might have resulted from tissue sampling error or that the finding of TiO_2 in these cases may be a random finding unrelated to the disease process'. As this is a pilot study, evaluation of larger numbers of biopsies with appropriately age and sex matched controls is being undertaken.

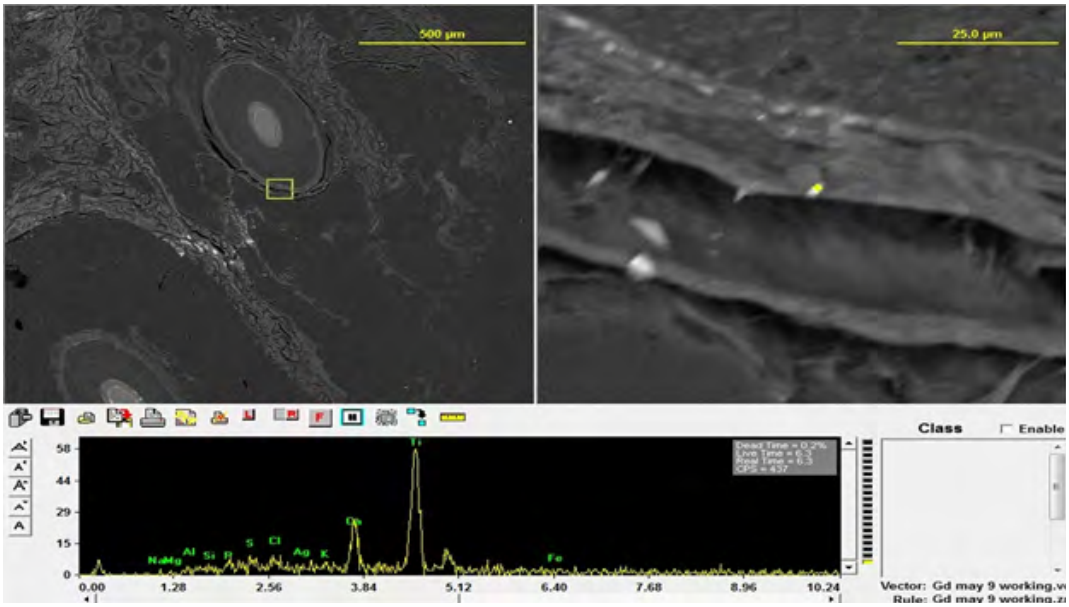

Figure 1: Scanning electron microscopy of a biopsy of frontal fibrosing alopecia demonstrating a focus of TiO_2 adjacent to hair follicle epithelium and energy dispersive x-ray spectroscopy confirming the deposit as containing titanium.

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