



## Case report

## Titanium exposure and yellow nail syndrome

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## ABSTRACT

Yellow nail syndrome is a rare disease of unclear etiology. We describe a patient who develops yellow nail syndrome, with primary nail and sinus manifestations, shortly after amalgam dental implants. A study of the patient's nail shedding showed elevated nail titanium levels. The patient had her dental implants removed and had complete resolution of her sinus symptoms with no change in her nail findings. Since the patient's nail findings did not resolve we do not believe titanium exposure is a cause of her yellow nail syndrome but perhaps a possible relationship exists between titanium exposure and yellow nail syndrome that requires further studies.

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## To the Editor,

Yellow nail syndrome (YNS) is a rare disorder characterized by a triad of yellow nails, lymphedema, and respiratory manifestations including chronic sinusitis, bronchiectasis, or pleural effusions [1]. The pathogenesis of the disease has not been elucidated, however, there have been reports suggesting an association between titanium exposure and YNS.

We observed a 56-year-old Caucasian female who presented with a two-year history of chronic sinusitis and cough that had been resistant to standard medical therapy. During these two years, the patient had an extensive work-up that was unrevealing for an inciting cause, including normal chest computed tomography scans with no evidence of bronchiectasis or pleural effusions. However, the patient's clinical examination revealed thick yellow nails (Fig. 1). The culmination of chronic sinusitis and yellow nails led to the diagnosis of YNS. Further inquiry revealed that her symptoms and nail changes started within a year of receiving amalgam dental implants.

Amalgam implants and fillings used in dental work contain a

combination of metal alloys, including titanium (Ti), that are susceptible to galvanic chemical corrosion. This complex phenomenon occurs when two different metals, at the same or distant location, interact through a potential difference. The titanium dioxide (TiO<sub>2</sub>) is oxidized into titanium ions (Ti<sup>2+</sup>), which is absorbed and distributed throughout the circulation into various tissue beds, including the liver, spleen, lung, and peritoneal tissue, with the exception of the heart and kidneys [2].

Titanium dioxide is also a common excipient used as a coating agent, whitener and opacifier in many medications including capsules, suspensions, tablets, and topical preparations [2]. It is unlikely that a standardized amount is used in the formulation of capsules or tablets since it is a ubiquitous substance. Despite the widespread use in the food and pharmaceutical industry, there is very limited information on the absorption, distribution, and toxicity of titanium in humans.

Recent papers evaluated the possibility of titanium exposure, via implants or medications, as a cause of yellow nail syndrome through an analysis of nail clippings in patients who have received dental amalgams and knee titanium implants [3–5].

Upon recognizing the patient's amalgam dental implants as a potential etiology for her YNS, a complete nail shedding was sent for analysis. Inductively coupled plasma sector field mass spectrometry and inductively coupled plasma atomic emission spectrophotometry were used to analyze the composition of the nail

Abbreviations: Yellow nail syndrome, (YNS).

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**Fig. 1.** Findings of thick, discolored yellow nails on examination.

specimen. A positive nail titanium level was present at 28 mcg/g (normal value 0 mcg/g). Given this finding the patient had her implants removed and within a year was observed to have complete resolution of her sinusitis symptoms but without change in her nail findings.

While the presence of titanium in the nails alone does not establish a cause and effect relationship with YNS, we believe that further studies in this field are warranted. It is possible that specific patients may have an underlying genetic or immunological disposition to develop YNS when exposed to titanium. Further studies are needed in this field. Although, the rarity of YNS and the difficulty of obtaining nail titanium levels are limiting factors. We recommend a thorough evaluation of potential titanium exposures, including implants and medications, in this population and removing the patient's source, if feasible, to determine a casual relationship.

It remains unclear to the authors why the patient's sinus symptoms improved but not her nail findings. One potential theory is that the patient has not shed her nails that already contain the titanium. Normal nails grow at a rate of 3 mm per month, taking an average of 3–6 months to regrow completely. In YNS nail growth is halted or slowed to a rate of less than 0.25 mm per week. We will continue to follow up with the patient to determine if this theory holds true.

#### Authors contributions

AA, KK, JC, and HA were all involved in the drafting and revision of the manuscript.

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