Clinical Communications

Eosinophilic occupational asthma caused by padauk wood dust

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Clinical Implications

This report highlights the respiratory sensitizing potential of padauk wood dust and provides further insight into the inflammatory mechanisms involved in the development of wood dust–induced occupational asthma by demonstrating a highly eosinophilic airway response to challenge exposure.

The asthmagenic potential of a number of wood species has been convincingly documented through specific inhalation challenges (SIC) in case reports and a few case series,1 even if the underlying pathophysiological mechanisms remain largely uncertain.[2]

Padauk (or padouk, *Pterocarpus soyauxii*, botanical family of *Fabaceae*) is a hardwood growing in Equatorial Africa. Because of its bright reddish orange coloration and its high durability, padauk wood is widely used for furniture, veneer, and outdoor flooring and cladding.

Herein, we report the clinical and immunological findings in a patient with occupational asthma (OA) induced by padauk wood dust confirmed by a positive SIC and a marked post-challenge increase in sputum eosinophil count.

A 54-year-old man developed work-related asthma and rhinoconjunctivitis symptoms approximately 7 years after starting work as a cabinet maker. He was intermittently exposed to various wood dusts, including padauk, *Afzelia africana* (botanical family of *Fabaceae*) and Eastern white cedar (*Thuja occidentalis,* botanical family of *Cupressaceae*). The subject noticed that his symptoms occurred predominantly when he was exposed to padauk wood dust. Nevertheless, he did not seek medical advice and took no asthma medication. Nine years later, he started working as a wood teacher and was no longer exposed to exotic woods. However, he experienced acute asthma symptoms while he was exposed for several days to padauk wood dust during a home renovation. He consulted a chest physician who established an asthma diagnosis, raised a suspicion of OA due to wood dusts, and referred the subject to our center for further investigation. At that time, he was treated with a combination of inhaled beclometasone dipropionate/formotérol 100 μg/6 μg twice in the morning as well as on demand. He had smoked 1 pack of cigarettes per day for 16 years, but had stopped smoking 20 years prior.

The subject gave informed consent to perform a SIC with the suspected wood dusts according to international recommendations (Figure 1).[3] Baseline spirometry showed a forced expiratory volume in 1 second (FEV_1) of 2.94 L (82% predicted) and a FEV_1/forced vital capacity (FVC) ratio of 70%. As a control challenge, the subject was exposed to pine wood dust for 30 minutes without eliciting significant changes in FEV_1 over the following 6 hours. At the end of this control day, the concentration of histamine causing a 20% decline in FEV_1 (PC_{20}) measured using the tidal breathing method was 0.50 mg/mL, indicative of a moderate degree of nonspecific bronchial hyperresponsiveness. The analysis of a sputum sample induced by inhaling increasing concentrations (3%, 4%, and 5%) of nebulized hypertonic saline revealed a 2% eosinophil count.

On the next day, grinding padauk wood for gradually increasing time periods elicited marked symptoms of rhinoconjunctivitis and an isolated early asthmatic reaction with a maximum fall in FEV_1 of 34% from baseline value after a 16-minute cumulative duration of exposure. Twenty-four hours after the end of the challenge exposure, the histamine PC_{20} was decreased to 0.16 mg/mL, and the analysis of sputum cells showed a significant increase in eosinophil count to 42%. One month later, challenge exposure to afzelia and cedar wood dusts for 60 minutes on separate days failed to induce significant change in FEV_1 and post-challenge histamine PC_{20} values (0.37 mg/mL) (data not illustrated).

Skin prick testing (SPT) elicited a positive response to the house-dust mite, but was negative with padauk, afzelia, and cedar wood dusts extracted in phosphate-buffered saline (10% weight/volume [w/v]) stirred overnight. Subsequently, aqueous and ethanolic extracts of the 3 wood dusts were prepared and specific immunoglobulin E (sIgE) binding was investigated *in vitro* with the subject's serum using ImmunoCAPs (ThermoFisher, Uppsala, Sweden) as described in this article's Online Repository (available at www.jaci-inpractice.org). A slightly increased sIgE concentration against a mix of aqueous and ethanolic padauk extract (0.62 kU_A/L) was detected and sIgE levels against the other wood extracts were less than 0.35 kU_A/L. However, no IgE-binding proteins could be identified in immunoblotting experiments with aqueous and alcoholic extracts of wood dust.

To the best of our knowledge, this is the first account of OA induced by padauk wood dust documented through an SIC. The significant increase in the post-SIC level of nonspecific bronchial hyperresponsiveness and the marked eosinophilic airway response provided evidence supporting an immunologically mediated sensitizing mechanism rather than a nonspecific irritant bronchial reaction, although we were unable to ascertain the underlying immunological mechanism.

The pathophysiological mechanisms involved in wood-induced OA remain poorly understood. Occupational asthma due to Western red cedar has been the most extensively investigated form of OA due to wood dust and is thought to be caused by sensitization to plicatic acid, a low molecular weight organic chemical. However, sIgE antibodies directed against plicatic acid conjugated to human serum albumin have been detected in only 40% of the subjects with red cedar asthma.[1] Conversely, IgE-mediated sensitization to wood dust has been supported by positive SPT and the detection of sIgE against a number of wood species, most consistently in subjects with OA caused by obeche

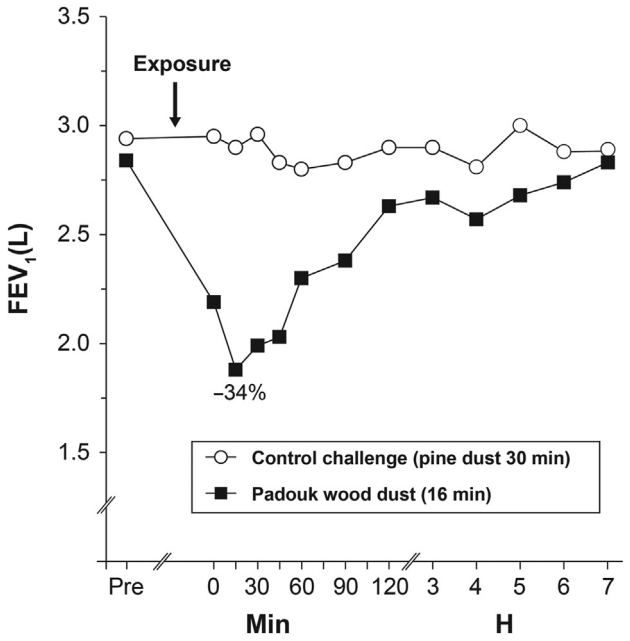

FIGURE 1. Results of specific inhalation challenges illustrate the changes in FEV_1 after a control agent (pine dust) for 30 minutes (white circles) and challenges with padauk wood dust for 16 minutes (black squares). *Pre,* Pre-exposure.

wood *(Triplochiton scleroxylon)*.[2] In addition, IgE-binding proteins have been formally identified through immunoblotting techniques in extracts of some wood species.[2,4] In our patient, we found serological sIgE-mediated sensitization to padauk wood dust but not to afzelia or cedar. However, identification of sIgE-binding proteins in padauk extracts by IgE-immunoblot was not successful.

There is currently scarce information on the airway inflammatory pattern in OA caused by wood dusts. Obata et al[5] reported a significant increase in sputum eosinophils after inhalation challenge with plicatic acid in 9 subjects with red cedar asthma who had developed predominantly late asthmatic reactions. Otherwise, the change in sputum cell profile has been investigated in only 5 published case reports,[6-9] of which 4 demonstrated a significant (≥3%) increase in post-challenge sputum eosinophil count in subjects challenged with obeche,[9] bethabara,[7] and tali wood dusts.[6]

This report highlights the respiratory sensitizing potential of padauk wood dust and the need for further prospective investigation of inflammatory markers and immunological mechanisms involved in wood-induced OA.

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Protein Extraction From Wood Dust Samples

Three samples of padauk, cedar, and afzelia wood dust from the patient's workplace were extracted according to formerly verified extraction protocols. Briefly, wood dust was mixed 1:10 (weight/volume [w/v]) with extraction buffer (phosphate buffered saline [PBS] pH 7.4, 0.1 mM Pefabloc, 2% polyvinylpolypyrrolidones [insoluble]), stirred for 6 hours, 4°C, centrifuged at 12,000 g, 4°C, 45 minutes; supernatant contained soluble wood proteins. Remaining wood dust pellets were resolubilized with 50% ethanol (half of the volume of the first extraction) in extraction buffer 1:10 (w/v), stirred again for 16 hours, 4°C, centrifuged at 12,000 g to obtain a supernatant containing ethanolic wood proteins. All wood dust extracts were dialyzed against *Aqua Bidest* and lyophilized. The quality of extracted proteins was analyzed by SDS-silver-PAGE. For padauk wood extracts in both aqueous and ethanolic fractions, protein bands have been detected in the molecular weight range of 5 to 30 kDa. Extracts of cedar and afzelia wood revealed protein bands only in ethanolic fraction, for cedar proteins in the molecular weight range between 5 and 30 kDa and for afzelia proteins in the range of 5 and 65 kDa (data not shown).

BIOTINYLATION AND COUPLING OF WOOD PROTEINS TO STREPTAVIDIN-IMMUNOCAPS

For biotinylation of padauk wood proteins, aqueous and ethanolic extracts were pooled with same amounts of lyophilisats, respectively. For cedar and afzelia wood proteins, only ethanolic fraction was used. Because the protein concentration of lyophilized extracts could not be determined by Bradford assay because of strong-colored wood samples, a maximum of lyophilized extracts was used for protein biotinylation. For the 3 wood extracts, 60 mg/mL of lyophilized protein material was used. The average molecular weight of the protein extracts was determined according to SDS-silver-PAGE protein pattern as 15 kDa for pooled padauk proteins, 25 kDa for ethanolic cedar proteins, and 50 kDa for ethanolic afzelia proteins. Subsequently, the wood proteins were biotinylated for 2 hours with a 5-fold molar excess (calculated as 1 mg protein/60 mg lyophilized wood extract) of D-biotinoyl-ε-aminocaproic acid N-hydroxysuccinimide ester (NHS-LC-Biotin, ThermoFisher Scientific) in 10 mM carbonate buffer (pH 8.5). Unbound biotin was separated from the biotinylated wood extracts by gel filtration (PD10-columns, Pharmacia). Biotinylated wood proteins (50 µl) were loaded on prewashed Streptavidin ImmunoCAPs (o221, ThermoFisher Scientific, Uppsala, Sweden), incubated for 30 minutes, washed, and used for serological specific immunoglobulin E (IgE) measurement.

SERUM SAMPLES

The subject's serum specificity of IgE-binding to newly prepared padauk, cedar, and afzelia wood proteins was validated using serum from a nonexposed subject that was matched according to the total IgE value of the patient's serum (total IgE 1,335 kU/L). The control serum of the nonexposed subject had a total IgE value of 1,306 kU/L, and the sIgE to all 3 wood extracts was below 0.10 kU_A/L.