

## CASE REPORT

# Unusual pneumoconiosis in two patients with heavy print toner, and paper dust exposure

Mrinal Sarwate MD<sup>1</sup> | Adela Vrbenska MD<sup>2</sup> | Kristopher Cummings MD<sup>3</sup> |  
Henry D. Tazelaar MD<sup>1</sup> 

<sup>1</sup>Department of Laboratory Medicine and Pathology, Mayo Clinic, Scottsdale, Arizona

<sup>2</sup>Department of Pathology, National Institute for TB, Lung Diseases and Thoracic Surgery, Vysne Tatry, Slovakia

<sup>3</sup>Department of Radiology, Mayo Clinic, Scottsdale, Arizona

## Correspondence

Henry D. Tazelaar, MD, Department of Laboratory Medicine and Pathology, 13400 East Shea Boulevard, Scottsdale, AZ 85259.  
Email: [tazelaar.henry@mayo.edu](mailto:tazelaar.henry@mayo.edu)

## Abstract

Workers in a print shop are exposed to photocopier toner dust and paper dust over a prolonged period of time. However, there are only rare case reports of toner and paper dust induced lung damage in humans. We reviewed our consultation files for a period of 30 years from 1987 to 2018 to look for cases with a diagnosis of giant cell interstitial pneumonia (GIP), printer toner exposure and paper dust exposure resulting in lung disease. There were two cases which met our inclusion criteria. Slides, clinical histories and imaging were reviewed. Both the patients had worked in print shops, and had no history of exposure to hard metals. Patient 1 presented with shortness of breath and cough over several months, while patient 2 was asymptomatic at presentation. Both the patients underwent surgical lung biopsies. Histopathologic examination from both the cases showed a spectrum of pathology, including features of GIP, desquamative interstitial pneumonia, chronic bronchiolitis with lymphoid hyperplasia, and particulate matter consistent with toner. Energy dispersive spectroscopy was performed on one case, and it revealed no cobalt or tungsten particles. The unusual combination of findings is very suggestive that toner particles with or without paper dust exposure were responsible for the pathologic changes in the lungs of these patients. This possibility should be explored further with additional patients who work in print shops where they are exposed to paper dust and paper toner and have signs or symptoms of diffuse lung disease.

## KEYWORDS

desquamative interstitial pneumonia, giant cell interstitial pneumonia, paper dust, paper toner, pneumoconiosis

## 1 | INTRODUCTION

Printer toners are commonly used for laser printing. The toners are composed of fine powders containing polyester, polypropylene wax, carbon black, silica particles, and additives like titanium. Over the past few years, the effect of toner particles on the lung has been studied in experimental animals and human cell lines.<sup>1-6</sup> However,

there are only rare reports examining the effects of toner on human lungs,<sup>7-9</sup> with some studies showing no short term effects.<sup>10,11</sup> In addition, we are not aware of any reports of paper dust exposure resulting in human lung disease, but exposure to paper dust and toner may be closely related. Herein, we report two patients employed in print shops both of whom had diverse reactions in the lung, associated with deposition of various toner pigments.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *American Journal of Industrial Medicine* published by Wiley Periodicals LLC

## 2 | MATERIALS AND METHODS

Cases were collected from Pulmonary Pathology consultation files of the authors. Consultation files were reviewed for a period of 30 years from 1987 to 2018 (24 311 cases) to look for cases with a diagnosis of giant cell interstitial pneumonia (GIP), printer toner exposure and paper dust exposure. The study was evaluated by the Mayo Clinic Institutional Review Board IRB, who approved waiver of the requirement to obtain informed consent in accordance with 45 CFR 46.116 as justified by the Investigator, and waiver of HIPAA authorization in accordance with applicable HIPAA regulations.

Clinical histories and imaging of the cases were reviewed. Routine formalin-fixed and paraffin-embedded tissue sections were stained with hematoxylin & eosin and with antibodies to the following utilizing the Ventana immunohistochemistry platform: CD68 (Clone KP1), pankeratin (Clones AE1/AE3/PCK21), and thyroid transcription factor 1 (TTF-1, Clone SP141).

Energy dispersive spectroscopy (EDS) was performed on an FEI Tecnai 12 transmission electron microscope at 80 KeV using an Oxford AZtecEnergy Energy Dispersive Microanalysis System. The tissue sample was deparaffinized and subsequently back-processed for electron microscopy elemental analysis. EDS was also performed on areas just adjacent to the particles for a control spectrum.

## 3 | RESULTS

There were two cases which met our inclusion criteria (see Table 1). Among 61 cases of giant cell interstitial pneumonia in the files, only two had documented printer toner or paper dust exposure. The

majority (although not all) of the patients with GIP had tungsten carbide exposure.

Patient 1 was a 53-year-old male who presented with complaints of shortness of breath and cough over several months. He worked 5 to 6 years in a shop that printed flyers for government offices. Paper arrived in 1000 pound rolls and one of his jobs was to cut the paper to size on a machine which would frequently jam. A vacuum would be used to clear the jam, but this would also clog. When this happened, the vacuum flow would be reversed and fill the air with paper dust. The dust was vacuumed and workers would continue to cut paper. For printing, powder toner was used. It was prepared by shaking the bottle and then loading the dispenser several times a day during which toner dust was also generated. He was usually completely covered in both paper and toner dust by the end of the day. The print shop was poorly ventilated. He also had coworkers who complained of similar symptoms. Two ventilation machines were eventually installed, but they were insufficient to clear the air where he worked in the building. He only started using respiratory protection after he developed symptoms. From the age of 25 to 33 years, the patient worked with pesticides, but he had never worked with hard metals, cobalt or tungsten. He was a lifelong nonsmoker and denied substance abuse. He had a history of gastro-esophageal reflux disease, but no history of cardiac disease, exposure to lung toxic medications, birds or molds. His connective tissue disease work-up was negative. High resolution computed tomography of the chest showed predominantly peripheral subpleural ground glass opacities; mild reticulation in the upper lobes with traction bronchiolectasis and early minimal honeycombing (Figure 1).

Patient 2 was a 59-year-old female with a 5-year history of bronchial asthma on treatment with inhaled steroids. She was asymptomatic at presentation. During routine follow up radiology for

**TABLE 1** Clinical history and work-up of the two cases

	Patient 1	Patient 2
Age	53-y-old	59-y-old
Sex	Male	Female
Chief complaint	Shortness of breath and cough	None
Smoking history	Nonsmoker	Nonsmoker
Occupation	Works in print shop	Worked in print shop
Past medical history	History of GERD	Bronchial asthma on treatment, thyroid disease, allergies and vasomotor rhinitis
Medications	None	Inhaled steroids, NSAIDS, desloratadine, enoxaparin
Radiology	Prominent upper and lower lobe peripheral ground glass opacities, traction bronchiolectasis and early honeycomb	Peripheral ground glass opacities
PFT	Restrictive lung defect	Unknown
Connective tissue work-up	Negative	CRP normal
Current status	In good health after leaving his print shop work	Unknown

Abbreviations: CRP, C-reactive protein; GERD, gastro-esophageal reflux disease; NSAIDS, nonsteroidal anti-inflammatory drugs; PFT, pulmonary function test.



**FIGURE 1** Patient 1—High resolution computed tomography scan of chest showing the presence of peripheral subpleural ground glass opacities with traction bronchiolectasis and early minimal honeycombing

her asthma, she was suspected to have an interstitial lung disease. Although she had retired 4 years ago, she formerly worked as a cleaner in a factory producing electronics. Later, for 9 years she worked in a print shop where she refilled toner cartridges. The print shop was poorly ventilated. The patient had no coworkers who performed this task and she used no respiratory protection. She had no exposure to hard metals, cobalt or tungsten. The patient was a nonsmoker. She had a history of thyroid disease, vasomotor rhinitis and allergies. She had no history of significant cardiac disease, exposure to lung toxic medications, birds, or molds. The patient was receiving nonsteroidal anti-inflammatory drugs, desloratadine and enoxaparin. A high-resolution computed tomography her chest raised suspicion for interstitial lung disease.

Both the patients underwent surgical lung biopsies. Patient 1 underwent multiple wedge biopsies of the right lower lobe, while Patient 2 underwent biopsy of left lower lobe. The findings are tabulated in Table 2.

Histopathologic examination of the biopsy from Patient 1 showed many areas with airway centered changes (Figure 2). On higher power, there was diffuse filling of airways by pigmented macrophages in a desquamative interstitial pneumonia (DIP) pattern (Figure 3). In many areas prominent multinucleated giant cells were also present in both alveoli, and lining alveoli. A few giant cells showed emperipolesis (Figure 4). Emperipolesis is the cannibalism of one cell by another, resulting in a cell within cell appearance, in this case giant cells cannibalizing macrophages and lymphocytes. Fine brown black pigment was seen in giant cells, while more coarse brown to black pigment was located extracellularly. The giant cells displayed both epithelial and macrophage differentiation as evidenced by immunohistochemical staining for TTF-1, pankeratin, and CD 68 (Figure 5). Polarization did not reveal any birefringent particles. Mild lymphoid hyperplasia was also present, but it was not a prominent feature.

The auto identify software of the EDS system predominantly detected the particles to contain carbon, and a very small amount of aluminum when compared with the background spectra. The

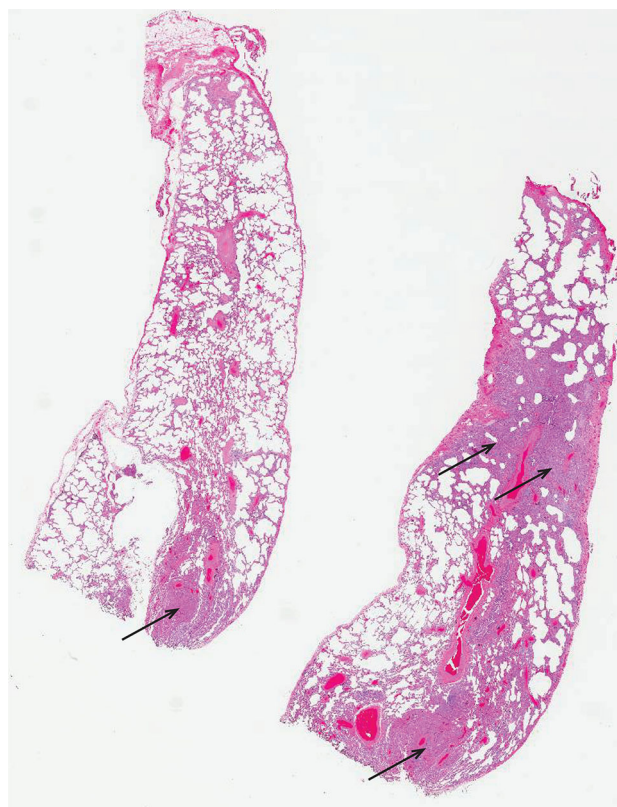
**TABLE 2** Summary of histopathology findings of the two cases

	Patient 1	Patient 2
DIP like changes	+	...
TTF-1 positive multinucleated giant cells	+	...
CD68 positive multinucleated giant cells	+	+
Pigment colors	Brown to black	Cyan, yellow, magenta, black
Interstitial lymphoid infiltrate/lymphoid hyperplasia	Mild	Mild to moderate
Interstitial fibrosis	+	Minimal
Centriacinar emphysema	...	+
Polarizable material	...	...

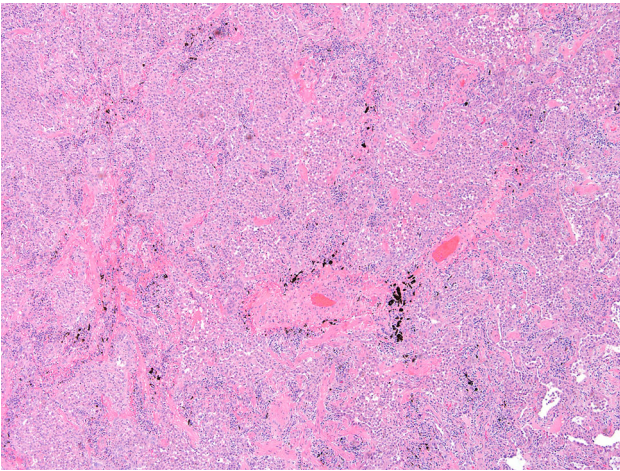
Abbreviations: CD68, a macrophage marker; DIP, desquamative interstitial pneumonia; TTF-1, thyroid transcription factor 1.

aluminum peak was a small peak on the overall spectra and there was very little difference between the particle and the adjacent cell and, therefore, this was not considered a cause of the patient's disease.

Histopathologic examination of the biopsy from Patient 2 showed perivascular and peribronchiolar pigment macules accompanied by centriacinar emphysema and lymphoid hyperplasia (Figure 6).

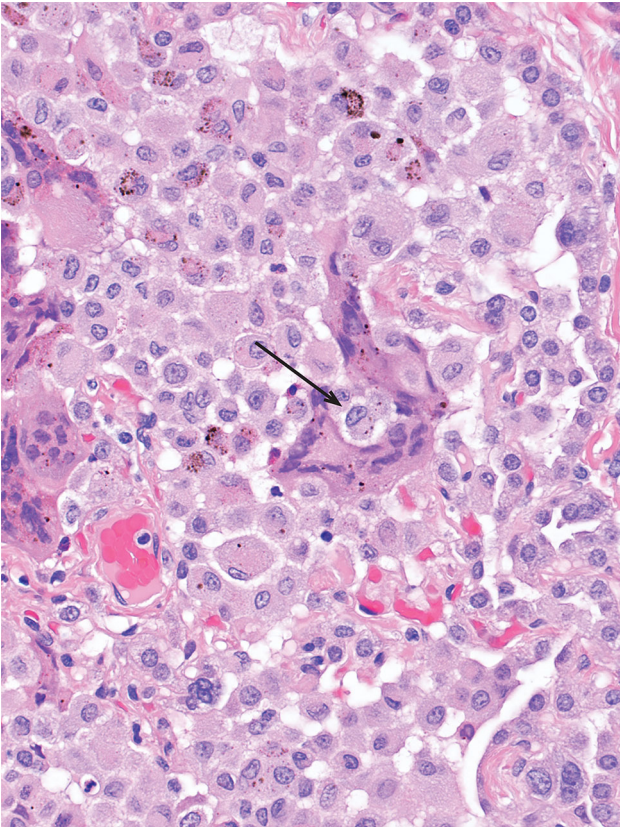


**FIGURE 2** Patient 1. Low power of several sections highlighting the airway centered nature of the process (arrows)

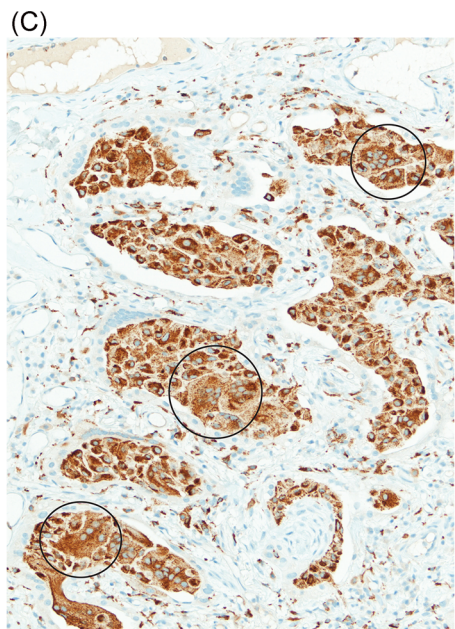
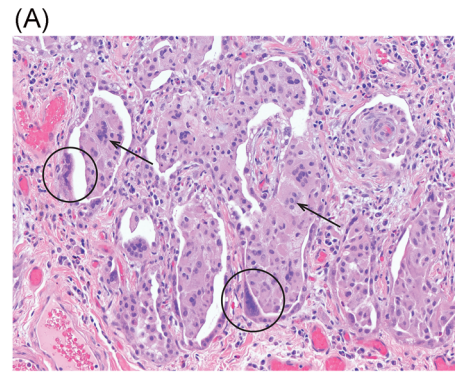


**FIGURE 3** Patient 1. Desquamative interstitial pneumonia (DIP) features. Macrophages and occasional giant cells fill airspaces, characteristic of DIP. Note the dark brown black pigment, which could also be seen within giant cells

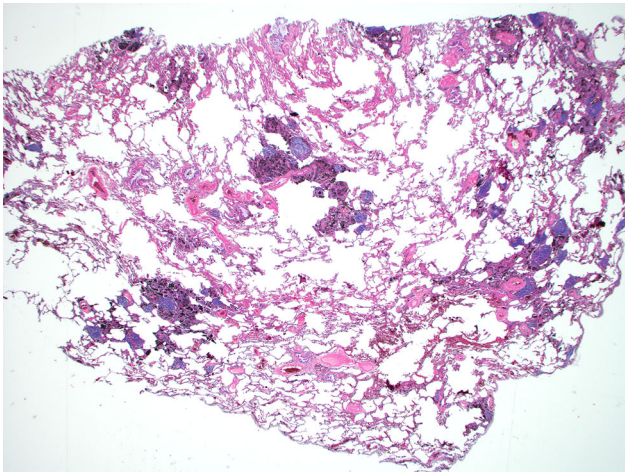
There was mild to moderate interstitial inflammation consisting mostly of plasma cells, lymphocytes and scattered lymphoid aggregates. There was also some mild interstitial fibrosis. Multinucleated giant cells were seen containing the particles in a few foci (Figure 7). The giant cells



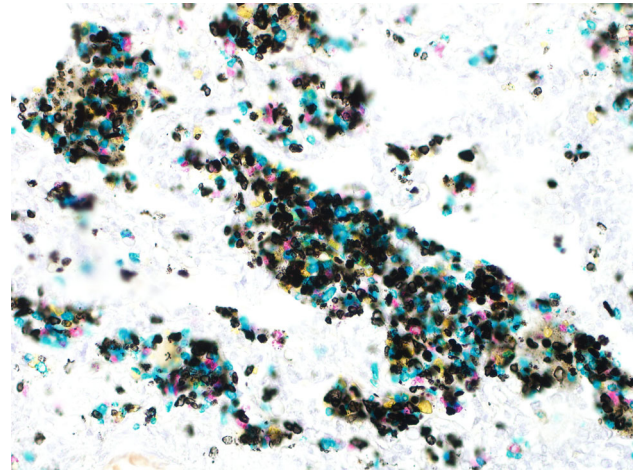
**FIGURE 4** Patient 1. Giant cell with emperipolesis (macrophage engulfed in the cytoplasm of the giant cells, arrow)



**FIGURE 5** Patient 1. The giant cells were of two types - pneumocytic differentiation, lining alveolar spaces (A, circles), with reactivity with antibodies to pankeratin (B, circles); and macrophagic features in airspaces expressing CD68 (A, arrows; C, circles)



**FIGURE 6** Patient 2. Low power showing peribronchiolar pigment associated with centriacinar emphysema and lymphoid hyperplasia



**FIGURE 8** Patient 2. Figure highlights the magenta colored toner particles along with black, cyan and yellow particles. (Light hematoxylin and no eosin stain to improve contrast)

and surrounding lung contained colored (cyan, yellow, black, and magenta) particles (Figure 8). By immunohistochemical staining, the macrophages were of macrophage lineage, expressing CD68 and not TTF-1. Polarization did not reveal any birefringent particles. Particles were also seen within the pleura.

#### 4 | DISCUSSION

In the modern world, use of paper, paper printers and colored cartridges is ubiquitous. Hence, the exposure to toner dust has increased significantly. However, the toxic effects of the toner cartridges are yet not fully elucidated. In this report we highlight an

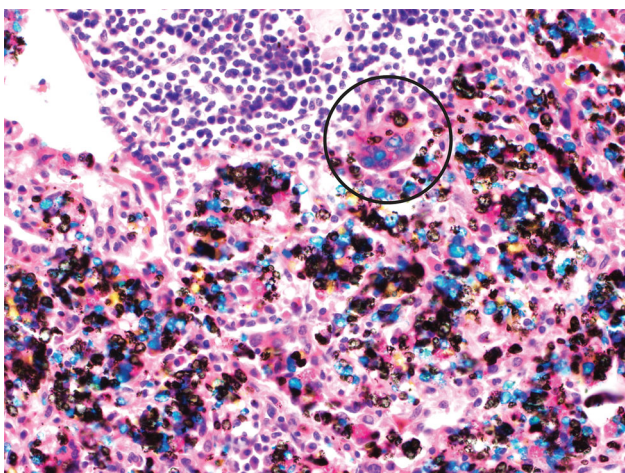
unusual combination of pathologies in patients exposed to paper toner (both patients) and paper dust (one patient), suggesting a role for these exposures in the development of the unusual pathology, including giant cell interstitial pneumonia, desquamative interstitial pneumonia, and toner particles within the lung.

The toner cartridge used for laser printing contains carbon (organic and elemental) as the main black pigment. The other pigments used are benzimidazolone compound which imparts the yellow color, quinacridone compounds for magenta, and copper phthalocyanine for blue. In addition to the pigments, the products contain nanoscale metals and metal oxides. The nanoparticles are external additives and adhere to the surface of toner.<sup>10</sup> The mean particle diameter of these particles is 5 to 10 microns, thus, enabling the toner dust to penetrate deep into the lungs.

In rat models, the printer emitted particles caused genetic changes and changes in cell viability in macrophages, small airway epithelial cells and microvascular endothelial cells at doses which are comparable to an 8-hour exposure of a human to these particles.<sup>3,4</sup> Bai et al<sup>12</sup> reported that exposure of mice to printer toner particles resulted in an increase in the number of cells in bronchoalveolar lavage fluid, as well as changes in pulmonary NO synthase, IL 1, and IL 6.

In a study done by Pirela et al,<sup>4</sup> it was observed that intratracheal instillation of printer emitted particles caused an increase in the number of neutrophils in the lung and in Leukemia Inhibitory Factor (LIF), a cytokine presumed to protect the lung from injury. They also noted upregulation of pro-inflammatory cytokines, an increase in oxidative stress and, epigenetic changes like downregulation of DNA methyltransferase. The finding across the various studies in rat models showed that the toner exposure to lungs causes chronic inflammation, and mild to moderate fibrosis.<sup>6</sup>

In 1994, Gallardo et al<sup>7</sup> reported siderosilicosis due to photocopier toner dust exposure. The histopathologic examination



**FIGURE 7** Patient 2. Giant cells (circle) associated with cyan, yellow and black pigment particles. Magenta pigment is harder to appreciate (see Figure 8)

showed iron particles, macrophages containing iron, located in the peri-vascular, peri-bronchial parenchyma and also in alveoli and bronchial spaces. The silicon content was presumed to be responsible for fibrosis seen. The patient had occupational exposure to photocopier toner dust for 6 years. X-ray microdiffraction detected iron and silicon.<sup>7</sup> Another case report<sup>8</sup> described findings from a patient with an occupational exposure to photocopier dust of 18 months. He was found to have pulmonary infiltrates and mediastinal lymphadenopathy due to photocopier dust. Histology showed nonnecrotizing granulomas with epithelioid cells and giant cells of Langerhans, and foreign-body-type; and pigment-containing macrophages.

One of our patients had fairly classic features of giant cell interstitial pneumonia (GIP), while the second had some giant cells present, but the features were less classic. GIP is a rare disease and often considered synonymous with hard metal lung disease caused predominantly by cobalt and tungsten carbide exposure.<sup>13,14</sup> However, there are some case reports describing GIP with no exposure to hard metals.<sup>13,15-19</sup> Exposures include environmental dusts, drugs as well as idiopathic cases.

We present two cases of lung damage associated with printer dust and toner, one with prominent GIP and DIP features. Both the cases lacked exposure to hard metals. Histories revealed continuous exposure to paper dust and toner particles in a poorly ventilated environment. Also, both patients were nonsmokers, with no history of intake of any pneumotoxic medications known to cause reactions like those described, or other systemic disease. The histopathologic examination in both the cases also revealed interstitial inflammation and interstitial fibrosis. There was no polarizable material found. The unusual combination of findings in these two patients is very suggestive that toner particles with or without paper dust exposure were responsible for the signs, symptoms and pathologic changes in the lungs of these patients. This possibility should be explored further by studying additional patients who work in print shops and are exposed to paper dust and paper toner who present with signs or symptoms of diffuse lung disease. They also suggest that patients working in these environments may want to use respiratory protection until more information is known about the ability of paper toner and paper dust to produce disease.

#### ACKNOWLEDGMENTS

Special thanks to electron microscopy personnel at Mayo Clinic Rochester who performed the testing including Jon Charlesworth and Dr Alberto Fernandez for helpful clinical details.

#### CONFLICTS OF INTEREST

Henry D. Tazelaar is a consultant with Paraxel Inc.

#### DISCLOSURE BY AJIM EDITOR OF RECORD

John D. Meyer declares that he has no conflict of interest in the review and publication decision regarding this article.

#### AUTHOR CONTRIBUTIONS

All authors contributed to the study design, execution, and writing of the manuscript.

#### ORCID

Henry D. Tazelaar  <http://orcid.org/0000-0001-5721-2336>

#### REFERENCES

1. Khatri M, Bello D, Pal AK, et al. Evaluation of cytotoxic, genotoxic and inflammatory responses of nanoparticles from photocopiers in three human cell lines. *Part Fibre Toxicol.* 2013;10:42.
2. Schneider J, Walter D, Bruckel B, Rodelsperger K. Primary particles and their agglomerate formation as modifying risk factors of non-fibrous nanosized dust. *J Toxicol Environ Health A.* 2013;76(2): 131-141.
3. Sisler JD, Pirela SV, Friend S, et al. Small airway epithelial cells exposure to printer-emitted engineered nanoparticles induces cellular effects on human microvascular endothelial cells in an alveolar-capillary co-culture model. *Nanotoxicology.* 2015;9(6): 769-779.
4. Pirela SV, Miousse IR, Lu X, et al. Effects of laser printer-emitted engineered nanoparticles on cytotoxicity, chemokine expression, reactive oxygen species, DNA methylation, and DNA damage: a comprehensive in vitro analysis in human small airway epithelial cells, macrophages, and lymphoblasts. *Environ Health Perspect.* 2016;124(2): 210-219.
5. Pirela SV, Lu X, Miousse I, et al. Effects of intratracheally instilled laser printer-emitted engineered nanoparticles in a mouse model: a case study of toxicological implications from nanomaterials released during consumer use. *NanoImpact.* 2016;1:1-8.
6. Muhle H, Bellmann B, Creutzenberg O, et al. Pulmonary response to toner upon chronic inhalation exposure in rats. *Fundam Appl Toxicol.* 1991;17(2):280-299.
7. Gallardo M, Romero P, Sanchez-Quevedo MC, Lopez-Caballero JJ. Siderosilicosis due to photocopier toner dust. *Lancet.* 1994; 344(8919):412-413.
8. Armbruster C, Dekan G, Hovorka A. Granulomatous pneumonitis and mediastinal lymphadenopathy due to photocopier toner dust. *Lancet.* 1996;348(9028):690.
9. Nakadate T, Yamano Y, Adachi C, et al. A cross sectional study of the respiratory health of workers handling printing toner dust. *Occup Environ Med.* 2006;63(4):244-249.
10. Yanagi N, Kitamura H, Mizuno M, et al. A 4-year follow-up cohort study of the respiratory functions in toner-handling workers. *Saf Health Work.* 2014;5(4):222-226.
11. Karrasch S, Simon M, Herbig B, et al. Health effects of laser printer emissions: a controlled exposure study. *Indoor Air.* 2017;27(4): 753-765.
12. Bai R, Zhang L, Liu Y, et al. Pulmonary responses to printer toner particles in mice after intratracheal instillation. *Toxicol Lett.* 2010; 199(3):288-300.
13. Moriyama H, Kobayashi M, Takada T, et al. Two-dimensional analysis of elements and mononuclear cells in hard metal lung disease. *Am J Resp Crit Care Med.* 2007;176(1):70-77.
14. Nemery B, Abraham JL. Hard metal lung disease: still hard to understand. *Am J Resp Crit Care Med.* 2007;176(1):2-3.
15. Reddy PA, Gorelick DF, Christianson CS. Giant cell interstitial pneumonia (GIP). *Chest.* 1970;58(4):319-325.
16. Kakugawa T, Mukae H, Nagata T, et al. Giant cell interstitial pneumonia in a 15-year-old boy. *Intern Med.* 2002;41(11): 1007-1012.

17. Hargett CW, Sporn TA, Roggli VL, Hollingsworth JW. Giant cell interstitial pneumonia associated with nitrofurantoin. *Lung*. 2006;184(3):147-149.
18. Menon B, Sharma A, Kripalani J, Jain S. Giant cell interstitial pneumonia in a 60-year-old female without hard metal exposure. *Respiration*. 2006;73(6):833-835.
19. Khor A, Roden AC, Colby TV, et al. Giant cell interstitial pneumonia in patients without hard metal exposure: analysis of three patients and review of the literature. *Hum Pathol*. 2016;50:176-182.

**How to cite this article:** Sarwate M, Vrbenska A, Cummings K, Tazelaar HD. Unusual pneumoconiosis in two patients with heavy print toner, and paper dust exposure. *Am J Ind Med*. 2020;63:821-827. <https://doi.org/10.1002/ajim.23147>