remains an open question. The study by Tice et al., which is based on the findings of the Breast Cancer Surveillance Consortium, showed considerable overlap in the risk estimates for women with atypical hyperplasia and the four density categories. It was only women with atypical hyperplasia and extremely dense breast tissue (12% of the entire group with atypical hyperplasia) whose risk did not overlap completely with the fatty-breast category; this group with high-density tissue had a substantially higher risk of breast cancer.

In response to Reimers et al.: their overall cohort consists of women with various risk features, especially a family history of breast cancer. In their most recent article on density, all benign breast disease is grouped together. In this letter, they refer to an unspecified number of women in a subgroup with atypical hyperplasia and suggest that such women with low breast density may not be at increased risk for breast cancer. They do not state how they handled the effect of age on density and breast-cancer risk.

To follow up on the question posed in both letters, we identified a subgroup of women in our atypical-hyperplasia cohort for whom we had readily attainable density information (Table 1). Although numbers are limited at this time, we see no significant difference in risk according to breast-density measurement in women with atypical hyperplasia, and thus suggest that this important question merits additional investigation.

Lynn C. Hartmann, M.D.
Amy C. Degnim, M.D.
Mayo Clinic
Rochester, MN
hartmann.lynn@mayo.edu

William D. Dupont, Ph.D.
Vanderbilt University
Nashville, TN

Since publication of their article, the authors report no further potential conflict of interest.


DOI: 10.1056/NEJMc1501046

Case 39-2014: A Girl with Crohn’s Disease and Pulmonary Nodules

TO THE EDITOR: Nelson et al. (Dec. 18 issue) report the case of a 9-year-old girl with familial Crohn’s disease and pulmonary nodules. Chronic granulomatous disease was considered and rejected by El Saleeby. We believe this rejection was based on insufficient data. Chronic granulomatous disease can be ruled out only by the measurement of reactive oxygen species (ROS) production by granulocytes. Testing for ROS production, which was not performed, could have had major clinical consequences in this patient, because Crohn’s disease is clinically and histologically indistinguishable from colitis related to chronic granulomatous disease, and in patients with chronic granulomatous disease, it would be essential to rule out infections with pathogens such as burkholderia, nocardia, granulibacter, and aspergillus before initiating immunosuppressive therapy.

Anti–tumor necrosis factor (TNF) treatment in patients with chronic granulomatous disease is associated with increased mortality. Therefore, testing ROS production to rule out this disease and evaluating the patient for opportunistic infections are needed before initiating anti-TNF treatment in cases such as the reported one. Finally, the exclusion of obvious mutations in the NADPH-oxidase complex that cause chronic granulomatous disease and NOD2 (indicating Crohn’s disease and Blau’s syndrome) would be equally useful before performing whole-exome sequencing.
Gastrointestinal manifestations rarely precede a diagnosis of chronic granulomatous disease\(^1\) and are less likely to occur with autosomal recessive inheritance of the disease. This patient is female, and her histologic examination revealed chronic colitis and poorly formed granulomas, which better support a diagnosis of Crohn’s disease. In contrast, the histologic examination of colitis in chronic granulomatous disease often lacks chronicity and shows more sharply demarcated granulomas.\(^2\) Furthermore, routine screening for chronic granulomatous disease in patients with inflammatory bowel disease has not been found to be informative.\(^3\)

Owing to the complexity of this case, bronchoalveolar lavage was completed before anti-TNF therapy was initiated. Testing was negative for sentinel organisms indicative of chronic granulomatous disease.

Chadi M. El Saleeby, M.D.
Jess L. Kaplan, M.D.
Benjamin A. Nelson, M.D.
Massachusetts General Hospital
Boston, MA
celsaleeby@mgh.harvard.edu

Since publication of their article, the authors report no further potential conflict of interest.


DOI: 10.1056/NEJMc1500453

---

**THE DISCUSSANTS REPLY:** Van de Veerdonk and colleagues correctly note that chronic granulomatous disease cannot be ruled out without measuring granulocyte production of ROS. However, in our opinion, such testing was not necessary in this case.

Many features of chronic granulomatous disease were incongruent with this patient’s history and presentation. Chronic granulomatous disease is a rare condition with significant male predominance.\(^1\) Although not universal, a large majority of patients with this disease have a history of chronic or recurrent infections,\(^4\) such as pneumonias and abscesses, neither of which were present.

**THE DISCUSSANTS REPLY:** Van de Veerdonk and colleagues correctly note that chronic granulomatous disease cannot be ruled out without measuring granulocyte production of ROS. However, in our opinion, such testing was not necessary in this case.

Many features of chronic granulomatous disease were incongruent with this patient’s history and presentation. Chronic granulomatous disease is a rare condition with significant male predominance.\(^1\) Although not universal, a large majority of patients with this disease have a history of chronic or recurrent infections,\(^4\) such as pneumonias and abscesses, neither of which were present.

**THE DISCUSSANTS REPLY:** Van de Veerdonk and colleagues correctly note that chronic granulomatous disease cannot be ruled out without measuring granulocyte production of ROS. However, in our opinion, such testing was not necessary in this case.

Many features of chronic granulomatous disease were incongruent with this patient’s history and presentation. Chronic granulomatous disease is a rare condition with significant male predominance.\(^1\) Although not universal, a large majority of patients with this disease have a history of chronic or recurrent infections,\(^4\) such as pneumonias and abscesses, neither of which were present.

**THE DISCUSSANTS REPLY:** Van de Veerdonk and colleagues correctly note that chronic granulomatous disease cannot be ruled out without measuring granulocyte production of ROS. However, in our opinion, such testing was not necessary in this case.

Many features of chronic granulomatous disease were incongruent with this patient’s history and presentation. Chronic granulomatous disease is a rare condition with significant male predominance.\(^1\) Although not universal, a large majority of patients with this disease have a history of chronic or recurrent infections,\(^4\) such as pneumonias and abscesses, neither of which were present.

**THE DISCUSSANTS REPLY:** Van de Veerdonk and colleagues correctly note that chronic granulomatous disease cannot be ruled out without measuring granulocyte production of ROS. However, in our opinion, such testing was not necessary in this case.

Many features of chronic granulomatous disease were incongruent with this patient’s history and presentation. Chronic granulomatous disease is a rare condition with significant male predominance.\(^1\) Although not universal, a large majority of patients with this disease have a history of chronic or recurrent infections,\(^4\) such as pneumonias and abscesses, neither of which were present.

**THE DISCUSSANTS REPLY:** Van de Veerdonk and colleagues correctly note that chronic granulomatous disease cannot be ruled out without measuring granulocyte production of ROS. However, in our opinion, such testing was not necessary in this case.

Many features of chronic granulomatous disease were incongruent with this patient’s history and presentation. Chronic granulomatous disease is a rare condition with significant male predominance.\(^1\) Although not universal, a large majority of patients with this disease have a history of chronic or recurrent infections,\(^4\) such as pneumonias and abscesses, neither of which were present.