Pulmonary manifestations of chronic granulomatous disease

Seyed Alireza Mahdaviani*, Seyed Amir Mohajerani†, Nima Rezaei‡, Davood Mansouri‡ and Ali Akbar Velayati§

Chronic granulomatous disease (CGD) is an inherited disorder, characterized by defects in superoxide-generating NADPH oxidase of phagocytes. The genetic defects in CGD induce failure to activate the respiratory burst in the phagocytes, leading to severe recurrent infections and unexplained prolonged inflammatory reactions that may produce granulomatous lesions. A noble advance in curative therapy for CGD is hematopoietic stem cell transplantation. Since the most common site of involvement in CGD is the lung, the pulmonologists (pediatrics or adult) may be among the first to recognize the pattern of infection, inflammation and granuloma formation, leading to diagnosis of CGD. Pulmonologists need to be aware of different lung manifestations of CGD.

Keywords: chronic granulomatous disease • manifestation • pulmonary • radiology • treatment

Chronic granulomatous disease (CGD) was first recognized as fatal granulomatosis disease of childhood in the 1950s. Later, it was named as chronic granulomatosis disease, in respect to clarification of the nature and pathophysiology of the disease [1]. In the last 50 years, advancement provided new achievements in diagnosis and treatment resulting in better outcome of the disease. Since then, a wider range of clinical manifestations were defined in these patients [2]. CGD is induced by a defect in NADPH oxidase of phagocytic and lymphocytic cells resulting in an inability to produce the superoxide anion necessary for killing of bacterial and fungal microorganisms, which predisposes the affected person to severe recurrent infections. CGD incidence has been estimated between 1 in 200,000 and 1 in 250,000 live births in the USA, but it differs from 1 in 1,000,000 to 1 in 160,000 individuals in other countries [3,4].

Genetics of CGD
CGD has at least five different mutations in genes involved in assembly and activation of the NADPH oxidase [5]. It seems that two-thirds of patients in Western countries have X-linked mutations in gp91phox (CYBB gene, Cytochrome b-[245], β subunit, OMIM*300481), on the X-chromosome. Other less frequent mutations are inherited in autosomal recessive forms that involve p22phox ([CYBA, Cytochrome b-[245], β subunit, OMIM*608508), p47phox (NCF1, OMIM*608512), p67phox (NCF2, OMIM*608515), or p40phox (NCF4, Neutrophil cytosolic factor 4, p40phox, OMIM*601448).

There is considerable disparity in the range and severity of clinical manifestations, which reflects the influence of genetic-based variation in different genes involved in innate immunity and inflammation [5,6]. X-linked forms are generally more prevalent in the world, whereas autosomal recessive forms are more prevalent in the countries with a high rate of consanguinity [7]. Notably, clinical outcome and manifestations could be hugely different in patients with similar mutations. On the other hand, X-linked mutations could be more devastating in CGD; for example, X-linked mutations involving gp91 have lower life expectancy [5,6,8].

Clinical presentations, diagnosis & therapy
CGD has a wide range of clinical manifestations presenting from early childhood to late adulthood. Mostly, CGD patients suffer from recurrent life-threatening bacterial and fungal infections and granuloma formation in multiple organs [2,9]. This disease involves multiple organs [3,10,11] including involvement of the lung, lymph nodes, bones, skin and GI tract. The most commonly involved organ in CGD is the lung [3,10,11], which can represent both infectious and granulomatous complications (Box 1). In general, the most common infectious agents in CGD are catalase-positive organisms including bacteria, such as Staphylococcus aureus,

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Box 1
- Staphylococcus aureus
- Pseudomonas aeruginosa
- Burkholderia cepacia
- Aspergillus
- Histoplasma capsulatum
- Coccidioides immitis
- Nocardia asteroides
- Kaposi sarcoma
- Thelazia callipaeda

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Box 1. Pulmonary manifestations of chronic granulomatous disease.

- Infectious manifestations:
  - Pneumonia
  - Abscesses
  - Pleural effusion
  - Bronchiectasis
  - Bronchitis
  - Atelectasias
  - Respiratory failure
  - Mediastinal or hilar adenopathy
  - Lung tuberculosis
- Inflammatory and autoimmune manifestations:
  - Granuloma formations
  - Pneumonitis
  - Extensive fibrosis

Borkholderia cepacia, Serratia marcescens and Nocardia, and fungi such as Aspergillus. In some parts of the world, BCG, TB and salmonella also affect CGD patients [2,3,12]. Granulomatous formation induces other aspects of clinical manifestations that are more prominent in organs other than the lung such as the urinary tract and GI tract, resembling Crohn’s disease [13]. Since the most common site of involvement in CGD is the lung, the pulmonologists (pediatrics or adult) may be among the first to recognize the pattern of infection, inflammation and granuloma formation leading to a diagnosis of CGD. Figure 1 depicts different manifestations of pulmonary involvement in CGD patients.

Infectious pulmonary manifestations

The most frequent pulmonary manifestations arise from infectious complications that comprise almost 80% of the pulmonary involvements [3,14]. Infectious involvements are characterized by pneumonia in 40–60% and less frequently abscess in 3–6% [10,15]. Clinicians may encounter other less frequent infectious manifestations, which are listed in Box 1 [16–18]. Pneumonia could progress to atelectasia and abscess or extensive reticulonodular infiltration that may lead to respiratory failure or death [16]. In addition, mediastinal or hilar adenopathy, pulmonary fibrosis, honeycomb lung, pulmonary artery hypertension and pleural thickening are among complications that may be related to pulmonary infections with prolonged course [19,20].

Infectious agents involving the lung

Isolation of infectious agents from CGD patients with infectious pulmonary involvement is not always successful; in an NIH study, the success rate was 52% through different diagnostic procedures including needle biopsy or bronchial lavage [8]. Prophylactic antibiotic therapy in CGD patients might interfere with isolation success of infectious agents [12]. In other words, infectious agents involving lungs in CGD patients are often caused by organisms uncommon in normal hosts; therefore, a microbiologic diagnosis in every case before starting anti-infective therapy is crucial [14]. Thus, in order to target the accurate etiological agent in CGD patients, it is recommended to attain samples from serum and tissue cultures before initiating antimicrobial treatment [12]. The roles for serology, such as the B-D-glucan and galactomannan assays, are only vaguely defined in CGD patients, but positive results may be helpful in follow-up of patients [8].

The most commonly cultured organism that is a causative agent of pneumonia in CGD patients is Aspergillus. Based on published data, the following most commonly found agents after Aspergillus are variable among different countries; in published data from the USA, Staphylococcus species, Burkholderia cepacia, Nocardia species and Serratia species are the next following agents [3,21]. On the other hand, in the EU registry, second pathogens to Aspergillus were found to be slightly different. Sporadic cases included Candida, S. marcescens, B. cepacia, Cephalosporium and Staphylococcus epidermidis as the following most commonly detected agents after Aspergillus [15]. In summary, there is a general consensus on Aspergillus as the most commonly cultured causative agent in pneumonia, but there is a discrepancy in following commonly detected pathogens responsible for pneumonia between different regions and studies, which may be related to geographical and population variations or diagnostic...
Pulmonary manifestations of chronic granulomatous disease

Table 1. Pathogens responsible for pneumonia in chronic granulomatous disease patients extracted from different studies and registries.

<table>
<thead>
<tr>
<th>Pneumonia</th>
<th>USA [5]</th>
<th>EU [15]</th>
<th>UK (n) [59]</th>
<th>Italy (n) [10]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>368</td>
<td>429</td>
<td>94</td>
<td>60</td>
</tr>
<tr>
<td>Inheritance/molecular data</td>
<td>67% XL-CGD</td>
<td>70% XL-CGD</td>
<td>81% XL-CGD</td>
<td>65% XL-CGD</td>
</tr>
<tr>
<td></td>
<td>33% AR-CGD</td>
<td>22% AR-CGD</td>
<td>19% AR-CGD</td>
<td>10% AR-CGD</td>
</tr>
<tr>
<td></td>
<td>8% Uncertain</td>
<td>8% Uncertain</td>
<td>10% Uncertain</td>
<td>25% Uncertain</td>
</tr>
<tr>
<td>Aspergillus species</td>
<td>41%</td>
<td>18%</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Staphylococcus species</td>
<td>12%</td>
<td>2%</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Burkholderia cepacia</td>
<td>8%</td>
<td>–</td>
<td>5</td>
<td>–</td>
</tr>
<tr>
<td>Nocardia species</td>
<td>7%</td>
<td>&lt;1%</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>Serratia species</td>
<td>5%</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mycobacterial (BCG and Mycobacterium tuberculosis)</td>
<td>4%</td>
<td>&lt;1%</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Atypical mycobacteria</td>
<td>2%</td>
<td>&lt;1%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Candida species</td>
<td>2%</td>
<td>2%</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td>Cephalosporium</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Streptococcus species</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Actinomycyes species</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Neosartorya udagawa</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>3%</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Pseudomonas species</td>
<td>3%</td>
<td>–</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Paecilomyces species</td>
<td>1%</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Salmonella species</td>
<td>–</td>
<td>–</td>
<td>7</td>
<td>–</td>
</tr>
</tbody>
</table>

%: Percentage of isolated organism to total number of patients with pneumonia; AR-CGD: Autosomal-recessive chronic granulomatous disease; CGD: Chronic granulomatous disease; n: Number of cases that organism is detected; XL-CGD: gp91phox deficient.

approaches [10,12,15]. CGD as a prototype of phagocytic disorders is the only one known to be associated with invasive Aspergillus infection occurring in the absence of pre-existing lung damage [22,23]. Pulmonary Aspergillus infections mainly have a more indolent course than bacterial infection [24,25]. This explains why CGD patients rarely experience pulmonary cavitation or hemoptysis because of Aspergillus infection. Contiguous spread of Aspergillus infection from the lungs to the vicinity organs such as pleura or chest wall could occur in CGD patients and lead to osteomyelitis of the ribs or vertebral bodies [20]. Among Gram-negative bacteria, B. cepacia complex organisms are the most commonly found agent in pneumonia [3,26]. Surprisingly, in the EU studies, B. cepacia is rarely isolated from CGD patients [15]. The rarity of B. cepacia isolation in the EU papers may not reflect the actual role of this Gram-negative organism in pneumonia among CGD patients; hence, more studies are needed to clarify the role of environmental differences. The list of causative agents detected in CGD patients with pneumonia is depicted in Table 1.

Occurrence of emerging uncommon pathogens including Actinomycyes species [27] and Neosartorya udagawa [28] (a fungal agent) in CGD patients may lead us to identify new aspects of the NADPH oxidase pathway defect in this disease [8]. In other parts of the world such as China, Iran and Latin America, different infectious agents such as mycobacterial infections should also be considered and necessary work-ups should be performed in CGD patients [29,30]. Mycobacterial infections may also involve CGD patients and lead to severe pulmonary (not miliary) TB [7]. Interestingly, CGD patients are vulnerable to mycobacteria of the TB complex, such as BCG or M. tuberculosis itself, but not to other mycobacteria [30]. Moreover, some patients with specific mutations in CYBB that affect the respiratory burst in macrophages, but not monocytes and granulocytes, display a narrow phenotype of Mendelian susceptibility to mycobacterial disease [30].

Inflammatory & autoimmune pulmonary manifestations

Deregulated inflammation and inflammatory process is the main feature of CGD, which is initiated in response to a trigger and might be due to either increased proinflammatory or decreased anti-inflammatory mediators [12,31]. CGD patients experience inflammatory complications and some might have autoimmune problems [32]. Granuloma formations are typically one of the main manifestations of such dysregulation. Granulomas are typically noncaseating, composed of multinucleated giant cells that can be found in multiple organs, including the brain, lungs, liver, spleen and GI tract. The granulomas in the lung can manifest themselves as obstructive symptoms in pulmonary branches (Box 2) [31]. Granulomas in CGD are often found to be sterile, possibly underlining that granuloma formation does not require the continued presence of a microorganism [33]. The main pathogenesis of abnormal inflammatory responses and granuloma formation is not clear [2,3,21]. Inflammation can occur independently of infection, possibly owing to an inability to curb proinflammatory mediators; however, in some cases, incompletely resolved or recurrent infections have been proclaimed to induce chronic inflammatory responses [2,18]. Although the role of infectious pathogens in granuloma formation is controversial, it is difficult to exclude the presence of infectious agents, despite negative laboratory tests and lack of improvement in response to antimicrobial therapies [8]. Fungi could also elicit enormous inflammatory response in the lungs of CGD patients. Surprisingly, this role is
inflammation has been noted in the lungs and is characterized
by discrete infiltrates. The pathogenesis of such inflammation in lungs is difficult to prove by cultures, cytology and nucleic acid testing. In CGD mice (p47 and gp91phox deficient), progressive lung inflammation is induced with augmented NF-κB activation that causes increased proinflammatory cytokine levels after intratracheal challenge with zymosan or lipopolysaccharide [37]. Finally, lung involvement may be arising from the autoimmune process that has been mentioned in previous studies. In particular, association of sarcoidosis, rheumatic diseases and lupus-like syndrome are examples of this [2,5,21,38]. Polymorphisms in several components of the innate immune system, such as mannose-binding lectin and Fcγ receptors, are demonstrated to create autoimmune complications in CGD patients [39].

Radiologic findings of pulmonary manifestations
Radiologic findings of lung disease are of much importance as pulmonary manifestations are the most common findings in CGD. Some radiologic findings are nonspecific, but some of them could also be unique to the process of inflammation or infection in CGD. The most common findings of lung disease in chest radiography include consolidation, reticulonodular opacities and scarring [19]. Computed tomography (CT) findings can include consolidation, ground-glass opacity, tree-in-bud pattern, centrilobular or random nodules, bronchiectasis, septal thickening, air trapping or scarring [19,40]. Infectious complications of the lung can also be detected as focal consolidation or as a miliary pattern secondary to hematogenous spread. Lung infections in CGD patients tend to have a protracted course and may be complicated by granulomatous inflammation, persistent hilar or mediastinal lymphadenopathy, pulmonary fibrosis and honeycombing lung. In addition, pneumonia may be complicated by abscess formation or empyema, while pulmonary infections could involve previously scarred areas, which may delay radiographic detection [20]. Chest wall invasion is difficult to detect in a routine chest radiograph due to underlying lung parenchymal disease, but technetium-labeled bone scans and cross-sectional imaging with CT or MRI can be used to effectively diagnose this complication. Chest CT may reveal osseous erosion with periosteal or endosteal reaction. MRI could demonstrate abnormal bone marrow signal intensity, abnormal periosteum, cortical destruction and surrounding soft-tissue inflammation [20].

Treatment
Treatment of infectious complications
Long-term oral prophylaxis with cotrimoxazole and itraconazole has been shown to reduce the rate of infection among patients with CGD [41–43]. It is recommended that CGD patients avoid sources of *Aspergillus* spores (e.g., farms, mulch and construction sites) and refrain from smoking. Further broader antimicrobial agents may be needed if special organisms are isolated (e.g., *Nocardia* and *Aspergillus* species), but if culture results are not available, empiric antibiotic therapy has to be based on the most likely infectious agents expected. In fact, antibiotics should cover a broad range of bacteria including *S. aureus, Burkholderia, S. marcescens* and *Nocardia*. Oral ciprofloxacin and intravenous

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**Box 2. Radiological and CT scan manifestations of chronic granulomatous disease in the lung.**

- **Chest radiograph:**
  - Consolidation
  - Reticular nodular opacities
  - Scarring
- **Chest CT scan:**
  - Consolidation
  - Ground-glass opacity
  - Tree-in-bud opacity
  - Centrilobular or random nodules
  - Bronchiectasis
  - Septal thickening
  - Air trapping
  - Scarring
  - Mycetoma
  - Empyema
  - Milary pattern
  - Hilar or mediastinal lymphadenopathy
  - Pulmonary fibrosis
  - Honeycomb lung
  - Ground-glass pattern

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independent of whether the fungi are alive or dead, and such reactions could even be induced by boiled *Aspergillus* antigens in mouse models [34]. In humans, fungi antigens from aerosolized decayed organic matter, such as mulch, hay or dead leaves, may induce mulch pneumonitis and can either complicate previously recognized CGD or be its initial presentation [35]. The main features of mulch pneumonitis is closely related to pulmonary hypersensitivity, which presents as fever, dyspnea and hypoxia; chest radiographs show diffuse interstitial infiltrates; bronchoscopy may detect *Aspergillus* and lung biopsy shows acute inflammation with necrotizing granulomata and fungi. Therefore, mulch pneumonitis should be considered in CGD patients with sudden onset of fever, dyspnea and hypoxia, with bilateral infiltration in chest imaging [35]. The clinical and radiographic patterns seen in this syndrome are similar to that seen in association with other syndromes with significant host response to various environmental pathogens, including bacteria, mycobacteria, fungi, proteins, metals or chemicals, such as hypersensitivity pneumonitis. The pattern of inflammation in this syndrome could vary from bilateral interstitial infiltrates with necrotizing or non-necrotizing granulomas to patchy interstitial pneumonitis. The clinical symptoms may represent inflammation with or without infection, and patients may present with hypoxia, cough, fever and radiologic changes. Therefore, some aspects of these clinical pictures are probably induced by the host immune response, even in the absence of invasive fungal infection [35]. In some CGD patients, pulmonary manifestations could be hypoxia and functional limitation due to the granulomas and the extensive fibrosis of lung tissues [33,36]. In these patients, diffuse pulmonary inflammation has been noted in the lungs and is characterized

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meropenem are useful first-line agents. If fungal pneumonia is diagnosed, voriconazole needs to be initiated as the first choice antifungal agent for *Aspergillus*. Since infections often respond slowly, intravenous treatment must be followed by prolonged oral therapy [43]. IFN-γ was shown to be a safe and effective prophylaxis for CGD patients against infectious involvement [23]; however, these data have been obtained from different CGD patients in various countries that may have different standard medical practice and anti-infectious regimes [10]. The treatment of severe infections with transfusions of leukocytes is also very helpful [44].

**Treatment of inflammatory complications**

Treatment of autoimmune complications is a place of concern in CGD patients because most agents are immunosuppressive and immunity is already impaired. Immunosuppressive therapy, namely corticosteroids, are required for acute granulomatous exacerbation in the lung, bowel and urinary tract involvements as well as for inflammatory bowel disease. TNF-α inhibitors, such as infliximab, are effective anti-inflammatory agents but could increase the risk of severe and fatal infections [45]. CGD patients with invasive lung aspergillosis and nocardiosis profit from initial addition of steroids [46]. Patients with ‘mulch pneumonitis’ syndrome have benefited from simultaneous antifungals for the infection and steroids for the inflammation [8].

**Cell transplantation**

Currently, allogeneic hematopoietic cell transplantation is branded as the only definite cure in all patients with CGD who have an appropriate donor at the earliest opportunity. Outcomes of HLA-matched unrelated donors is close to those of HLA sibling donors, which implies that donor availability should not be a limiting factor for transplantation in patients with CGD. It has become a successful option for many patients with CGD that will probably treat and prevent both infectious and inflammatory complications. Even for those without a matched unrelated donor, cord blood products are proving to be a reasonable alternative and are being used more frequently.

Recent data have shown that patients with very low superoxide production had worse survival than those with higher levels of NADPH oxidase activity, notable particularly for the onset of increased mortality after age 20 years, suggesting that these patients should be considered appropriate candidates for early transplantation, particularly if a sibling-matched donor is available [6]. Infection and inflammation complications and their consequences could accumulate over time even after aggressive treatments, but transplantation outcomes are probably better before infectious and inflammatory damage progresses into end stage phases. In fact, transplantation may prevent or even reverse some of these CGD-associated complications [47]. Therefore, patients with significant inflammatory or autoimmune disease should also be encouraged for transplantation. With the advent of non-myeloablative regimens, the risks surrounding transplantation have decreased and have permitted transplantation in patients with active infections.

Although there has been tremendous progress in gene-based therapies, it has not been proven as a strong replacement curative therapy at this point [48]. Furthermore, even *in vitro* gene therapy appears to require conditioning via antiproliferative agents [49–51].

**Prognosis of pulmonary involvement**

The prognosis of CGD has been improved dramatically during the last decade. Many patients survive into their adulthood by applying prophylactic regimen, early diagnosis and aggressive treatment of infectious and noninfectious complications. Pulmonary involvement in patients with CGD is the most important cause of death; it may not necessarily be the initial manifestation but it grows in severity over time [18]. Longer survival of the patients with CGD has indisputably lead us to identify cumulative effects of repetitive pulmonary infectious and noninfectious inflammatory disorders [5,32,52,53].

One major consequence of severe infections, particularly in lungs, is predisposition to subsequent infections [54,55]. Furthermore, the exaggerated inflammatory responses of CGD results from a defect in NADPH oxidase [49,50]. CGD patients with invasive lung aspergillosis and nocardiosis profit from initial addition of steroids [46]. Patients with ‘mulch pneumonitis’ syndrome have benefited from simultaneous antifungals for the infection and steroids for the inflammation [8].

**Conclusion**

CGD results from a defect in NADPH oxidase of phagocytes and lymphocytes, resulting in an inability to produce the superoxide anion necessary for killing of bacterial and fungal microorganisms. In the last 50 years, due to achievements in diagnosis and treatment of this disease, we meet a broad range of clinical manifestations in affected patients compared with earlier observations. The most commonly involved organ in CGD is the lung, manifested as both infectious or granulomatosis involvement. Infectious complications are characterized by pneumonia and, less frequently, abscess. The most common causative agent of pneumonia in CGD patients is *Aspergillus* followed by *Staphylococcus*; *Burkholderia*, *Nocardia* and *Serratia* species. CGD patients may experience granuloma...
formation in the lung. The exact pathogenesis of atypical inflammatory responses leading to granuloma formation is not clear. Appropriate antibiotics and antifungal agents are the mainstay of long-term treatment of CGD patients. Acute infections should be treated by early and aggressive therapies with antimicrobial agents. The pathogen cannot be isolated in all infective complications, particularly in lung involvements. Thus, in patients with CGD, it is almost impossible to target the etiological agent precisely. Stem cell transplants, such as bone marrow stem cell transplantation, are the phenomenal restorative treatment plan for these patients. Pulmonary manifestations could be either ambiguous or misleading, particularly if not enough attention and clinical impression is made. In other words, since the most common site of involvement in CGD is the lung, the pulmonologists (pediatrics or adult) may be among the first to recognize the pattern of pulmonary manifestation leading to a diagnosis of CGD.

Expert commentary
Research on various manifestations of pulmonary involvement could help in revealing extra-leukocytic functions of NADPH oxidase in tissues, such as in increasing pulmonary vascular permeability. Future genetic studies could be a useful tool in detecting genes that instigate pulmonary involvement.

With new antifungal therapies, CGD-induced mortality is less of a concern compared with morbidity and end organ damage.

Five-year view
Future research may be required to discover the grounds for higher noninfectious (granulomatous) involvement of pulmonary and extra-pulmonary organs in CGD. Although bone marrow transplant is the technique of choice for stable remission of CGD patients, we have to apply new criteria for patients who could truly benefit from bone marrow transplant. Gene therapy is the attractive future treatment for CGD, which should be considered for further research that contains gene studies in vivo and in vitro.

Financial & competing interests disclosure
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Key issues
- During the last decade, our knowledge of chronic granulomatous disease (CGD) has been improved significantly due to extensive research, which inspired a better outcome of this disease.
- The most commonly involved organ in CGD is the lung, which could present with both infectious and granulomatous complications.
- Radiologic lung manifestations contain a wide range of aspects such as consolidation, reticulonodular opacities and scarring.
- Residual reactive oxygen intermediate production is more predictive of survival than the specific NADPH oxidase gene mutation.
- Nowadays, CGD has a better outcome due to early diagnosis and aggressive treatment of infectious and noninfectious complications.

References
Papers of special note have been highlighted as:
• of interest
• of considerable interest

One of the largest cohort studies in this field.


One of the largest cohort studies in this field in Europe.


One of the best studies in the field of imaging findings in adults.


