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Pulmonary and Sinus Imaging in Common Variable Immunodeficiency: What Do We Expect to Find?

Yaygın Değişken İmmün Yetmezlikte Akciğer ve Sinüs Görüntülemesi: Ne Bulmayı Umuyoruz?

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Objectives: This study aims to evaluate the role of pulmonary and sinus imaging in common variable immunodeficiency (CVID).

Patients and methods: Between April 2001 and March 2011, 48 patients (30 males, 18 females; mean age 19 years; range 9 months to 58 years) who underwent pulmonary or sinus computed tomography (CT) and chest X-ray due to CVID in Masih Daneshvari Hospital, Tehran were retrospectively analyzed. Age and sex of the patients and procedure-related complications were recorded.

Results: The most common complications were bronchiectasis (52.6%) with the highest incidence in right lower lobe (39.5%), hilar adenopathy (39.5%) and mediastinal adenopathy (39.5%) in 38 patients who underwent CT scan. The main finding was parenchymal infiltration in 29 patients who underwent chest X-ray, indicating a higher trend in females than males (50% vs. 35%). A total of 30 patients were assessed by sinus CT and/or chest X-ray. These imaging modalities revealed sinusitis in 76.7% patients with a higher involvement of maxillary sinus.

Conclusion: Pulmonary and sinus complications are common manifestations of CVID which can be easily assessed by imaging modalities, such as CT, particularly. We recommend evaluating CVID patients for sinusitis in addition to pulmonary examination.

Key words: Chest X-ray; common variable immune deficiency; computed tomography; pulmonary complication; sinusitis.

Amaç: Bu çalışmada yaygın değişken immün yetmezlikte (CVID) pulmoner ve sinüs görüntülemenin rolü incelendi.

Hastalar ve yöntemler: Nisan 2001 - Mart 2011 tarihleri arasında Tahran Masih Daneshvari Hastanesi'nde CVID nedeni ile pulmoner veya sinüs bilgisayarlı tomografisi (BT) ve göğüs röntgeni çekilen 48 hasta (30 erkek, 18 kadın; ort. yaş 19 yıl; dağılım 9 ay-58 yıl) retrospektif olarak incelendi. Hastaların yaşı ve cinsiyeti ve işleme bağlı görülen komplikasyonlar kaydedildi.

Bulgular: Bilgisayarlı tomografi taraması yapılan 38 hastada en sık görülen komplikasyonlar sağ alt lobda en yüksek insidans ile bronşektazi (%52.6), hiler adenopati (%39.5) ve mediastinal adenopati (%39.5) idi. Göğüs röntgeni çekilen 29 hastada ana bulgu, erkeklere kıyasla kadınlarda daha yüksek oranda görülmek ile birlikte, parenkimal infiltrasyon idi (%35'e kıyasla %50). Toplam 30 hasta sinüs BT veya göğüs röntgeni ile değerlendirildi. Bu görüntüleme yöntemlerinde yüksek tutulum maksiller sinüste olmak üzere, hastaların %76.7'sinde sinüzit izlendi.

Sonuç: Akciğer ve sinüs komplikasyonları, BT başta olmak üzere, görüntüleme yöntemleri ile kolaylık ile değerlendirilebilen CVID'nin sık rastlanan bulgularıdır. Göğüs muayenesinin yanı sıra, CVID olan hataların sinüzit açısından değerlendirilmesini önermekteyiz.

Anahtar sözcükler: Göğüs röntgeni; yaygın değişken immün yetmezlik; bilgisayarlı tomografi; akciğer komplikasyonları; sinüzit.

The onset of common variable immunodeficiency (CVID), a group of approximately 150 primary immunodeficiencies (PIDs), usually occurs in adults between the ages of 20 and 40, but it is sometimes seen in childhood. These PIDS share common features, but their triggering mechanisms vary. Patients with CVID

have an increased susceptibility to infections along with reduced responses to protein and polysaccharide vaccines. This immune cell disorder is diverse in both its clinical presentation and types of deficiency that are present. Although decreased serum levels of immunoglobulin (Ig) G and IgA are characteristic, approximately 50% of patients also have diminished serum IgM levels and T-lymphocyte dysfunction. In addition, about 20% of patients with CVID develop an autoimmune disease.

The most common infections associated with CVID are sinopulmonary in nature and include *Streptococcus pneumonia, Hemophilus influenza,* and *Klebsiella pneumonia*. In some cases, mycoplasma infections have also been encountered.

Patients with CVID are also prone to repeated infections. For example, recurrent respiratory infections may lead to structural changes like bronchiectasis. Furthermore, these patients may clinically present without any symptoms, or mild-to-severe complications, such as lymphoid malignancy, may occur. Currently, radiological imaging plays an important role in the assessment of these complications.

In this study, we reviewed CVID patient images to determine the prevalence of sinopulmonary complications and analyzed them in terms of age and gender. We also compared chest X-ray and computed tomography (CT) findings to demonstrate their role in the assessment process.

PATIENTS AND METHODS

In this retrospective study, we evaluated 48 patients (30 males, 18 females; mean age 19 years; range 9 months to 58 years), with known cases of CVID who were admitted to the Masih Daneshvari Hospital over a 10-year period from 2001 to 2011.

The patients were assessed by either chest CT, chest X-ray, or sinus CT and/or or sinus X-ray at admission. Of the 48 total patients, 38 underwent chest CT, 29 had chest X-rays, and 30 underwent a sinus X-ray or CT. Based on this data, the study participants were then placed into one of three groups according to imaging procedure. An expert radiologist examined each image and reported the findings. All sinopulmonary complications of the patients were noted, including bronchiectasis, bullae or blebs, peribronchial wall thickening, parenchymal nodules, air trapping, hydropneumothorax, parenchymal infiltration, pleural effusion, pericardial effusion, mediastinal adenopathy, hilar adenopathy, consolidation, air bronchograms, ground glass opacity, and hepatosplenomegaly. Furthermore, we analyzed and compared the findings by age, with one group composed of the patients 20 years of age or younger (n=32) and the other made up of those over 20 years old (n=16). We also performed individual group age comparisons as well (25 younger patients vs. 13 older patients in the CT group; 24 younger patients vs. five older patients in the chest X-ray group; and 18 younger patients vs. 12 older patients in the sinus group). We also compared the patients according to gender (23 males vs. 15 females in the CT group; 17 males vs. 12 females in the chest X-ray group; and 20 males vs. 10 females in the sinus group).

Analyses was carried out using the SPSS version 16 for Windows software program (SPSS Inc., Chicago, Illinois, USA), and age and gender comparisons were performed using a chi-square test for bronchiectasis, pulmonary consolidation, parenchymal infiltration, and sinusitis. A p value of ≤ 0.05 was accepted as being statistically significant.

RESULTS

Of the 38 patients (100%) in the chest CT group, the most common finding was bronchiectasis, which was detected in 20 patients (52.6%). It was seen in all lobes, with the highest prevalence in the right lower lobe (RLL) (n=15, 39.5%). This was followed by an involvement rate of 36.8% (n=14) in the right middle lobe (RML) and left lower lobe (LLL), respectively. The third most commonly involved segment was the lingula with a prevalence of 13.2% (n=5). The chest X-ray findings are shown in detail in Tables 1 and 2.

In terms of gender, bronchiectasis was significantly more common in the males than the females (69.6% vs. 26.7%, respectively; p=0.01). Furthermore, regarding the lobar distribution, the RML, RLL, and left upper lobe (LUL) showed the greatest gender differences, but there were no notable differences in terms of age. In order of prevalence, bronchiectasis was seen in the RLL, RML, LLL, LUL, right upper lobe (RUL), and whole lung fields.

The second most common complications were mediastinal and hilar adenopathy, with each appearing in 39.5% (n=15) of the patients. These adenopathies were more common in the younger group of patients

TABLE 1

Chest X-ray findings of the 29 common variable immune deficiency patients

Chest X-ray findings	Frequency	Percentage
Bronchiectasis	8	27.6
Parenchymal infiltration	12	41.4
Lymphadenopathy	4	13.8

TABLE 2

A comparison of the chest X-ray findings in terms of gender and age

Chest X-ray finding	Age 20 (%)	Age >20 (%)	Male (%)	Female (%)
Parenchymal infiltration	37.5	60	35.3	50
Lymphadenopathy	16.7	0	5.9	25
Bronchiectasis	29.2	20	47.1	0.0

than the older group (44% vs. 30.8% for mediastinal adenopathy and 48% vs. 23.1% for hilar adenopathy, respectively; p=0.05).

In our evaluation, parenchymal infiltration was detected in 36.8% (n=14) of the patients in the RML, LLL, RLL, RUL, LUL, and both lung fields, with the involvement in the RML being the highest at 26%. There were no notable differences with regard to gender or age, but all of the lobes showed higher involvement in the males than the females.

Regarding lung consolidation, 23.7% (n=9) were affected, and considerably more patients in the older group had this complication compared with the younger group (38.5% vs. 16%, respectively; p>0.05). However, there was no significant difference regarding gender as the rate was almost identical between the males and females. In order of prevalence, lung consolidation was seen in the RLL, LLL, RML, LUL, and RUL.

We found air trapping in 21.1% (n=8) of patients, with a higher rate occurring in the younger group. In addition, six patients reported ground glass opacity (15.8%), two had air bronchograms, (5.3%), and two presented with bronchiolectasis on their CT. Furthermore, 23.7% had hepatosplenomegaly, and 28.9% had hepatomegaly. Pleural effusion and pulmonary nodules were each found in five patients, pericardial effusion and bullae were each noted in three patients, and hydropneumothorax was reported in one patient. The chest CT findings are shown in Tables 3 and 4.

In the 29 patients who had chest X-rays (17 males and 12 females), the most common finding was infiltration, which was seen in 41.4% of the study participants while bronchiectasis was found in 27.6%. In terms of gender, 47.1% of males presented with this lung condition, but it was not seen in any of the females.

We also evaluated lymphadenopathy, and it was identified in 13.8% of patients, all of whom were in the younger group. Additionally, the rate was considerably higher in the females than the males (25% vs. 5.9%, respectively).

In the group who underwent sinus images, sinusitis was detected in 76.7% of the patients, with the most involved sinus being the maxillary sinus at a rate of 76.7%. This was followed by ethmoid and frontal sinusitis, which were each seen in 50% of the patients. In addition, there was evidence of pan-sinusitis in 46.7%. No significant differences were reported with regard to age and gender; however, sinusitis was more common in the females than the males. The sinus findings are given in Tables 5 and 6.

TABLE 3

Computed tomography findings of the 38 common variable immunodeficiency patients

Computed tomography findings	Frequency	Percentage
Bronchiectasis	20	52.6
Pan-bronchiectasis	5	13..2
Right middle lobe bronchiectasis	14	36.8
Right upper lobe bronchiectasis	6	15.8
Right lower lobe bronchiectasis	15	39.5
Left upper lobe bronchiectasis	7	18.4
Left lower lobe bronchiectasis	14	36.8
Lingular bronchiectasis	5	13.2
Bullae or blebs	3	7.9
Peribronchial wall thickening	4	10.5
Parenchymal nodules	5	13.2
Air trapping	8	21.1
Hydropneumothorax or pneumothorax	1	2.6
Infiltration	14	36.8
Diffuse infiltration	2	5.3
Lingular infiltration	4	10.5
Right middle lobe infiltration	10	26.3
Right upper lobe infiltration	6	15.8
Right lower lobe infiltration	7	18.4
Left upper lobe infiltration	3	7.9
Left lower lobe infiltration	8	21.1
Pleural effusion	5	13.2
Pericardial effusion	3	7.9
Mediastinal adenopathy	15	39.5
Hilar adenopathy	15	39.5
Lung consolidation	9	23.7
Right middle lobe consolidation	3	7.9
Right upper lobe consolidation	1	2.6
Right lower lobe consolidation	4	10.5
Left upper lobe consolidation	2	5.3
Left lower lobe consolidation	4	10.5
Air bronchogram	2	5.3
Ground glass opacity	6	15.8
Hepatomegaly	11	28.9
Splenomegaly	9	23.7
Hepatosplenomegaly	9	23.7

TABLE 4

Comparing computed tomography scan findings in terms of gender and age

Computed tomography finding	Age 20 (%)	Age >20 (%)	Male (%)	Female (%)
Bronchiectasis	52	53.8	69.6	26.7
Pan-bronchiectasis	12	15.4	17.4	6.7
Right middle lobe bronchiectasis	32	46.1	52.1	13.3
Right upper lobe bronchiectasis	12	23.1	21.7	6.7
Right lower lobe bronchiectasis	36	46.1	56.5	13.3
Left upper lobe bronchiectasis	16	23.1	26.1	6.7
Left lower lobe bronchiectasis	36	38.5	43.5	26.7
Lingular bronchiectasis	16	4	21.7	0.0
Bullae or blebs	8	7.7	4.3	13.3
Parenchymal nodules	8	23.1	17.4	6.7
Airtrapping	24	15.4	21.7	20.0
Hydro pneumothorax	0	7.7	4.3	0.0
Diffuse infiltration	4	7.7	8.7	0.0
Right middle lobe infiltration	24	30.8	34.8	13.3
Right upper lobe infiltration	12	23.1	17.4	13.3
Right lower lobe infiltration	12	30.8	26.1	6.7
Left upper lobe infiltration	8	7.7	8.7	6.7
Left lower lobe infiltration	16	30.8	26.1	13.3
Lingular infiltration	12	7.7	8.7	13.3
Pleural effusion	20	0	17.4	6.7
Pericardial effusion	12	0	8.7	6.7
Mediastinal adenopathy	44	30.8	39.1	40.0
Hilar adenopathy	48	23.1	34.8	46.7
Consolidation	16	38.5	17.4	26.7
Right middle lobe consolidation	8	7.7	8.7	6.7
Right upper lobe consolidation	4	0	4.3	0.0
Right lower lobe consolidation	12	7.7	8.7	13.3
Left upper lobe consolidation	0	15.4	4.3	6.7
Left lower lobe consolidation	8	15.4	8.7	13.3
Air bronchogram	0	15.4	4.3	6.7
Ground glass opacity	16	15.4	8.7	26.7
Hepatomegaly	36	15.4	26.1	33.3
Splenomegaly	28	15.4	26.1	20
Hepatosplenomegaly	28	15.4	26.1	20

DISCUSSION

Common variable immune deficiency is one of the most common primary immune deficiencies and features a wide variety of complications, especially infections. Sinopulmonary infections are seen most often. Since recurrent infections are very common in CVID, structural disorders can occur after these infections. Most of these changes can be identified via chest CT, but some are detectable on chest X-rays.

In the chest CT group in our study, 20 patients (52.6%) had bronchiectasis, the most frequent complication. This rate was very similar to what was previously reported by Martínez García et al.[1] in a study that involved 19 patients, 58% of whom reported bronchiectasis. In addition, our results also corresponded with the study by Bondioni et al.[2] in which out of a total of 40 patients, bronchiectasis was found in 65.38% (n=26) via chest CT. Furthermore, in 2010, Touw et al.[3] reviewed 26 articles that included 1,047 patients (587 patients with CVID), and they concluded that chronic structural pulmonary complications occurred in up to 73% of the CVID

TABLE 5

Sinus imaging findings in 30 common variable immune deficiency patients

Sinus imaging findings	Frequency	Percentage
Sinusitis	23	76.7
Pan-sinusitis	14	46.7
Maxillary sinusitis	23	76.7
Ethmoid sinusitis	15	50
Frontal sinusitis	15	50

TABLE 6

A comparison of sinus complications in terms of gender and age

Sinus complications	Age 20 (%)	Age >20 (%)	Male (%)	Female (%)
Pan-sinusitis	50	41.7	45	50
Maxillary sinusitis	72.2	83.3	75	80
Ethmoid sinusitis	55.5	41.7	50	50
Frontal sinusitis	55.5	41.7	50	50

patients, with the most common being bronchiectasis and peribronchial wall thickening.

In our study, mediastinal and hilar adenopathy were the second most prevalent complications after bronchiectasis. In a study by Curtin et al.[4] in 1995, they reported that 11 out of 27 CVID patients had enlarged mediastinal lymph nodes (41%), which was similar to what we identified. It was also the most common finding in the CVID patients in their study. Additionally, Ardeniz et al.[5] demonstrated a high prevalence of lymphadenopathy in CVID patients.

The third common finding in the CT group in our study was parenchymal infiltration, found in 36.8% of the patients. It was also the most common finding in the chest X-ray group, with a prevalence of 41.4%. Even when taking into account the higher accuracy of CT, the similar results of these two groups demonstrates that chest X-ray is helpful for diagnosing lung parenchymal infiltration in CVID patients.

Another significant result in our study was related to parenchymal pulmonary nodules, although they were seen in just five patients (13.2%). In a five-year follow-up study by Bondioni et al.[2] there was a very high incidence of pulmonary nodules. They evaluated 40 CVID patients by CT. Additionally, 20 of these were followed up via CT scans over a period of five years, and 38.4% had pulmonary nodules that correlated with splenomegaly, which presented in 70% of these patients. This varies considerably from the 23.7% of patients with this complication in our study.

On the other hand, van de Ven et al.[6] evaluated 54 children, and 24-25% of them presented with multiple lung nodules, which differs from the Bondioni et al.[2] study. However, in our study, we saw no statistically significant difference in the prevalence of nodules in the two different age groups.

We also analyzed the lobar distribution of bronchiectasis, lung consolidation, and infiltration, and the RLL was the most commonly involved lobe for bronchiectasis, whereas infiltration was seen more in the RML and consolidation more in the RLL and LLL at the same prevalence rate. The lowest rate of lobe involvement for bronchiectasis and infiltration occurred when there was simultaneous involvement of all lobes (pan-bronchiectasis and diffuse infiltration). However, the RUL showed the lowest rate of lung consolidation.

In reviewing the chest X-rays of 29 patients, we evaluated the findings as they related to bronchiectasis, lymphadenopathy and infiltration and determined that the most common finding was infiltration, with a prevalence rate of 41.4%. This was followed by bronchiectasis and lymphadenopathy with rates of 37.6% and 13.8%, respectively.

As previously mentioned, this suggests that chest X-rays should play a more diagnostic role when attempting to assess the presence of parenchymal infiltration, though CT has always been thought of as the more accurate technique.

Taking into account the higher sensitivity of CT and notable difference between the prevalence of bronchiectasis in the chest X-ray (27.8%) and CT (52.6%) groups in our study, it is obvious that chest X-rays are not reliable for diagnosing structural changes in CVID patients. Therefore, CT is strongly recommended due to the high incidence of this complication in CVID patients.

In addition, we evaluated 30 patients for sinus involvement via CT or X-rays, and 76.7% had sinusitis. This high prevalence rate confirms the benefits of sinus assessment in CVID patients.

In a study by Bondioni et al.[7] 41 out of 45 patients were identified as having sinusitis on CT. We believe that the lower rate in our study was probably because of the low diagnostic value of X-rays compared with CT as some of our patients underwent a sinus X-ray without undergoing sinus CT.

The most commonly involved sinus in our study was the maxillary sinus. Lesser involvement was seen in the frontal sinus. It is notable that the frontal sinus was not mature in some patients, which could explain the lower rate. Aghamohammadi et al.[8] reported that 66.2% of their CVID patients had a history of sinusitis, which was similar to our findings. Therefore, because of the

high prevalence of sinusitis in all age groups in both genders, sinus evaluation is strongly recommended for CVID patients.

The most notable difference associated with lobar involvement as it related to bronchiectasis between genders was seen in the RML and RLL. In addition, there was no lingular involvement in the females. The patients' CT findings revealed a notable difference in genders between the pulmonary nodules and pleural effusion (17.4% in the males vs. 6.7% in the females) and ground glass opacity (26.7% in the females vs. 8.7% in the males). None of the other complications showed any significant differences related to gender.

In the chest X-rays, bronchiectasis was only seen in the males, but infiltration and lymphadenopathy were more common in the females. In addition, with lymphadenopathy, a notable difference was seen in the incidence rate in the females (25%) versus the rate in the males (5.9%). When these results are considered along with the lower cost and reduced radiation exposure of chest X-rays, it is reasonable for patients with acute infections to undergo chest X-rays before CT. In addition, this type of X-ray is widely available throughout the world. However, in cases with recurrent infections with the resultant structural changes, patients should undergo CT instead.

In the chest X-ray group, the greatest difference according to age was related to lymphadenopathy, which was more common in females and those 20-years-old or younger. Lymphadenopathy via chest X-ray was only found in the younger patient group younger than 20-years-old patients with a prevalence of 16.7%. There was not significant difference regarding sinusitis prevalence rate in terms of age.

In other study by Ogershok et al.[9] in 2006 on 12 patients with mean age of eight years old at presentation time, sinusitis was reported in 75% of patients, which was similar to the finding in our result. It shows that sinusitis incidence is almost similar between children and adults.

Conclusion

We believe that our data points to the fact that chest X-rays are a beneficial imaging technique for evaluating pulmonary complications associated with CVID. In fact, they should be the preferred technique for examining structural changes that take places due to recurrent respiratory infections. In addition, because sinus changes and infections are so prevalent in CVID patients, sinus imaging should be conducted as part of any assessment.

Declaration of conflicting interests

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