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Bronchiolitis obliterans organizing pneumonia: experience at three hospitals in Riyadh

Abdullah H. Alsaghir,* Abdullah F. Al-Mobeireek,* Hamdan Al-Jahdali,† Abdulsalam Al-Eithan,† Hadil Al-Otair,‡ Fouad Al-Dayel §

From the *Department of Medicine, King Faisal Specialist Hospital and Research Centre, ‡Department of Medicine, King Fahd National Guard Hospital, ‡Department of Medicine, King Khalid University Hospital, §Department of Pathology, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

Correspondence and reprint requests: Abdullah Al-Mobeireek, MD Department of Medicine King Faisal Specialist Hospital and Research Centre Riyadh, Saudi Arabia T: +966-1-442 7493 F: +966-1-442 7499 mobeireek@yahoo.com Accepted for publication November 2006

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BACKGROUND: Because reports of bronchiolitis obliterans organizing pneumonia (BOOP) are lacking from the Middle East, we conducted a retrospective review of of all histopathologically proven cases of BOOP over a 10-year period at three tertiary care hospitals in Riyadh and describe the clinical features and outcome.

METHODS: Charts at the three hospitals were searched using a specific code for BOOP or cryptogenic organizing pneumonia (COP). Lung specimens had to show histological proof of BOOP with a compatible clinical picture. Chest radiographs and high-resolution CT scans were reviewed.

RESULTS: Twenty cases of biopsy-proven BOOP had well-documented clinical and radiographic data. There were 11 males and 9 females (mean age, 58 years; range, 42-78). The clinical presentation of BOOP was acute or subacute pneumonia-like illness with cough (85%), fever (70%) dyspnea, (85%) and crackles (80%). The most frequent radiological pattern was a bilateral alveolar infiltrate. The most common abnormality on pulmonary function testing (n=14) was a restrictive pattern (11 patients). Most patients (70%) had no underlying cause (idiopathic BOOP). Other associations included thyroid cancer, rheumatoid arthritis, syphilis and Wegner's granulomatosis. Ten patients (50%) had a complete response to steroids, 6 (30%) had a partial response and 3 (15.8%) with secondary BOOP had rapid progressive respiratory failure and died.

CONCLUSION: The clinical presentation of BOOP in our patients is similar to other reported series. A favorable outcome occurs in the majority of cases. However, BOOP may occasionally be associated with a poor prognosis, particularly when associated with an underlying disease.

Though uncommon, bronchiolitis obliterans organizing pneumonia (BOOP) is now a well-recognized clinicopathologic entity. Most cases are idiopathic, but an underlying cause or association, such as a systemic disease, an infection, exposure to drugs or radiation may be implicated.[1,2,3] Despite many studies of BOOP in the literature, reports from the Middle Eastern region are lacking. The purpose of this study was to describe the local experience, including clinical, radiological features, treatment and outcome of patients with BOOP, and to contrast this with reported international series.

METHODS

Over a 10-year period (January 1992 to December 2002), all charts with biopsy proven BOOP at three large hospitals in Riyadh were reviewed. These hospitals included King Faisal Specialist Hospital and Research Centre, King Khalid University Hospital, and King Fahad National Guard Hospital. The charts were found by searching medical records by a specific code for BOOP or COP (cryptogenic organizing pneumonia). A second check was also done through the records of the pathology departments using the same search terms. For inclusion, lung specimens had to show histological proof of BOOP as the main feature (buds of granulation tissue [fibroblastic cells and connective matrix] within the alveolar lumen) with a compatible clinical picture. A pulmonary pathologist (FD) reviewed all lung specimens, which had been obtained either through open thorcotomy, video-assisted thoracoscopy (VATS) or by trans-bronchial biopsy.

The patient charts were reviewed to gather the following information: patient profile, symptoms at presentation, immunological profile, drug intake, routine laboratory results, treatment and outcome. The chest radiograph and high-resolution computed tomography (HRCT) scan films were reviewed by pulmonary radi-

ologists. Abnormalities were classified as patchy consolidation (unilateral or bilateral, migratory, associated abnormalities, nodules or reticulo-nodular or mixed pattern).

RESULTS

Over the 10-year study period, 20 patients were identified at the three hospitals. There were 11 males and 9 females, with an age range of 42 to 78 years. Smoking history was available in 16 patients; 13 patients had never smoked and only 3 patients were smokers. The most common presenting symptoms were cough, dyspnea, and fever, and the most common clinical finding was bilateral crackles (Table 1). Their clinical presentation varied from acute to subacute and the duration of symptoms ranged from 1 to 3 months.

The underlying etiologies were idiopathic in 14 patients (70%); in two patients disease was due to rheumatoid arthritis, in one patient each it was associated with thyroid cancer, syphilis, Wegener's granulomatosis, and liver cirrhosis. The most common abnormalities on the chest radiograph were patchy consolidation in 14 patients (70%), bilateral in 11 patients, and unilateral in 3 patients. Three patients (15%) had associated pleural effusion; and 2 patients (10%) had cavities. Migration was observed in 2 patients (10%). HRCT scan was done for 17 patients and showed a patchy consolidation with pleural-based character in most patients. A ground glass appearance was detected in 17.7% and mixed pattern in 41.2% (Table 2).

The white blood cell count (WBC) was above 10×10^3 mm in 30% (range, 5.8-20.4). The erythrocyte sedimentation rate was over 30 mm the first hour in 55% (range, 25-104). Most of the patients showed hypoxemia with a mean PaO2 of 66 mm Hg (range, 53-81). Pulmonary function tests before treatment were available in 14 patients. Eleven patients (78.5%) showed a mild to moderate restrictive pattern, while the reminder (3 patients, 21.5%) had normal values. The diffusion capacity (DLCO) was reduced to <70% of predicted in 78.5% of patients.

Transbronchial biopsy (TBB) was performed in 12 patients, and was diagnostic in 9 patients (75%). In eleven patients (55%), including the 3 patients who initially had a non-diagnostic TBB, the diagnosis was established through either video-assisted thoracoscopy in 3 patients (27%) or open lung biopsy in 8 patients (73%). Bronchoalveolar lavage for WBC differential analysis was performed for 5 patients. Neutrophilia more than 5% was observed in all the patients, while lymphocytosis of more than 25% was observed in only one patient.

Table 1. Patient characteristics (n= 20).

Age range (mean) (years)	42-78 (58)
Male sex (%)	11 (55)
Smokers	3 (15)
Cough	17 (85)
Fever	14 (70)
Dyspnea	17 (85)
Chest pain	6 (30)
Weight loss	5 (25)
Haemoptysis	4 (20)
Crackles	16 (80)
Wheezes	2 (10)

Values in parenthesis are percentages, except for age .

Table 2. Radiographic and high resolution computed tomograpghy findings.

Pattern of opacity	Chest radiograph	High resolution computed tomography
No. of patients	20	17
Patchy consolidation:		
Unilateral	3 (15)	1 (5.9)
Bilateral	11 (55)	7 (41.2)
Reticulonodular	1 (5)	1 (5.9)
Ground glass	-	3 (17.7)
Mixed	5 (25)	7 (41.2)
Associated finding:		
Pleural effusion	3 (15)	3 (17.7)
Cavity	2 (10)	2 (11.8)
Migration	2 (10)	-

Values in parenthesis are percentages.

The majority of patients (95%) received prednisone; 17 patients (85%) were started with a dose of 40-60 mg per day for 4 to 6 weeks, which was then tapered slowly to a lower dose over 6 to 12 months. A 43-year-old male patient with idiopathic BOOP who presented with acute respiratory failure received pulse steroid therapy initially (methylprednisone 1500 mg per day for 3 days) as well as cyclosporine. In addition to a corticosteroid, 5 patients (25%) received cytotoxic drugs, including cyclosporine, cyclophosphamide, methotrexate, gold, and azathioprine. Ten patients (50%) had a complete response, 6 patients (33 %) had relapses (one patient had 3 relapses, one had 2 relapses, and three patients had 1 relapse). Patients with relapses responded after restarting or increasing the dosage of corticosteroid, but in two patients cytotoxic drugs were added. One patient with focal BOOP recovered after surgical resection.

Three patients with BOOP associated with another systemic illnesses died despite steroid therapy; the cause of death was probably secondary to underlying disease. These included a patient with papillary thyroid cancer and lung metastasis with respiratory symptoms for 4 months who died 17 days after diagnosis of BOOP despite steroids, a patient known to have Wegner's granulomatosis for 3 years who was symptomatic for 2 months and died with progressive respiratory failure, and a patient with liver cirrhosis who died rapidly with respiratory failure within one week of his symptoms despite treatment with steroids. Adverse effects of treatment were seen in 3 patients (15%) who developed diabetes mellitus and one patient who developed osteoporosis.

DISCUSSION

This report documents the first local experience with BOOP. Although our study was not designed to estimate the incidence of BOOP, we were surprised to find only 20 cases in the three main hospitals in Riyadh, which has a population of nearly 5 million. This is possibly due to the fact that most cases are treated empirically without histological confirmation, which was a requirement of our study. Furthermore, it is likely that patients who present to the hospital are more symptomatic and more severely ill, and many milder cases are treated by general practitioners or improve spontaneously without being recognized.[4,5,6]

Most patients in this study were found to have idiopathic BOOP. The clinical presentation was similar to descriptions in other series[4,7,8] with a picture like an acute or sub-acute infectious pneumonia. The radiological picture in our study was also classical; the most common presenting radiographic abnormality was a sub-pleural patchy consolidation (70%).[4,5] Migratory infiltrates have been reported in BOOP,[4,7] but this was seen in only two patients in our study (10%). HRCT showed abnormalities similar to the chest radiograph. However, as in other studies,[4] HRCT was more sensitive in detecting a ground glass appearance. Such abnormalities on the chest radiograph or HRCT scan are non-specific and other diseases that give similar abnormalities should be entertained when the clinician is suspicious of BOOP.[9] Pulmonary function test abnormalities (a restrictive pattern with reduced diffusion capacity in most of our patients) were again consistent with other reports.[10,11]

As the pathological changes of BOOP are focal, TBB specimens may not be diagnostic. In a series of 112 patients by King et al,[8] only few patients underwent bronchoscopy, and the authors recommended open lung biopsy to diagnose BOOP. However, in another series by Cazzato et al the diagnosis were established by TBB in 58 cases (74%).[4] In our study, bronchoscopy was also rewarding, with a diagnostic yield of 75%.

BOOP is a disease that usually responds well to corticosteroids, which remain the first-line treatment. Efficacy and optimal dosing and duration of steroid therapy have not been determined yet by controlled studies. Many experts recommended starting therapy with prednisone at a dose of 1 to 1.5 mg/kg per day.[12,13] Most of our patients (90%) received a steroid with a dosage within this range and had a good response. However, nearly a third had relapses shortly after reduction of the dose or discontinuation of their therapy. The relapse rate (30%) is similar to previously published large studies, where it varied between 9% to 39%.[14,15,16] As to the factors associated with a relapse, we found no differences in age, sex, smoking history, clinical presentation, ESR, white blood count, and pulmonary function between groups with and without relapses. The duration of symptoms prior to presentation was also similar, which is in contrast with another study that showed that a delay in treatment may predict relapse.[17] In addition, there was no difference between patients who had one relapse as compared with patients who had multiple relapses. Amongst our patients, five (25%) received cytotoxic drugs because of inadequate response to steroids or as steroid sparing therapy as the dose could not be tapered. Another reassuring factor is that all patients with idiopathic BOOP survived; death occurred only in patients where BOOP was secondary to significant systemic disease that carried by itself a poor prognosis.

In conclusion, the clinical profile of BOOP in our

series is similar to what has been previously described in the literature, showing a good prognosis in the majority of cases, except in the presence of an underlying systemic disease. BOOP still poses challenges, namely better understanding of the pathogenetic mechanisms and the need to find more effective therapies.

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