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Original articles

Clinical Perspective by Means of ARCHIVES

Luis M. Sarmiento Méndez^a and Diego Castillo Villegas^{b,*}

^aInternal Medicine Services, Esperit Sant Hospital, Santa Coloma de Gramenet, Barcelona, Spain

^bPulmonology Services, Respiratory Day Hospital, Santa Creu i Sant Pau Hospital. Barcelona, Spain

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ABSTRACT

This article discusses the current main clinical problems associated with thoracic surgery and pneumology by means of the articles published in 2008 in the "clinical notes" section of the journal *Archivos de Bronconeumología*. The 18 cases published, (dealing with topics ranging from pharmacologic toxicity to lung function) will enable us to discuss the main innovations in each of the various fields and highlight future areas for research.

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La clínica vista a través de ARCHIVOS

RESUMEN

A través de los artículos publicados en el año 2008 en la sección "Notas clínicas" de la revista *Archivos de Bronconeumología*, el presente artículo discurre por los principales problemas clínicos de la cirugía torácica y la neumología actual. Los 18 casos publicados, que abarcan desde la toxicidad farmacológica a la función pulmonar, nos permitirán discutir las principales novedades en cada uno de los diversos campos y señalar las futuras áreas de investigación.

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Introduction

ARCHIVOS DE BRONCONEUMOLOGÍA has always been a journal with a true translational mission. The product of this attitude was the fact that last year there was a drive to publish a review article that would shed light on the main clinical problems disseminated through this journal.¹ Due to the warm reception this article received, the journal decided to continue with this review section.

Even a quick reading of the articles published in 2008 provides a good overview of the main areas of interest: uncommon infectious diseases, surgical advances, pharmacological toxicity and, of course, the treatment of pulmonary hypertension.²⁻¹⁹ Without a doubt, the clinical notes highlight the most current research focus points: the development of new techniques that allow for better and less bloody

thoracic surgery, as well as the treatment of old diseases (infections) or 'new' ones (pulmonary arterial hypertension), without forgetting diffuse pulmonary disease, which continues to be one of the main "black holes" of our care activity.

Each one of these eighteen articles, with their main points of interest, are analysed below:

Infectious diseases

The first thing learned from the review of the 2008 "Clinical notes" is as follows: in modern society transmitted diseases spread with globalisation. The articles published show that germs we consider foreign to our population, in reality, are not as foreign as considered. This is owed to the fact that modern society is a product of one of the major migratory movements in history. At present, according to the provisional data from the 2009 census, 5,598,691 people live in Spain without having Spanish nationality.²⁰ Consequently, in the differential diagnosis of respiratory conditions we always need to make room for "imported" infectious diseases from endemic areas.

* Corresponding author.

E-mail address: dcastillo@santpau.cat (D. Castillo Villegas).

"Strongyloides stercoralis: an unusual form of flare-up in COPD"

A good example is the case published by Ortiz Romero et al.¹² in the August issue: an 85-year-old native Spanish man, without making trips to endemic areas, was diagnosed with GOLD stage II chronic obstructive pulmonary disease and chronic eosinophilia (eight years). He had clinical symptoms indicative of flare-up of his basic disease, for which he followed a conventional treatment, requiring two courses of orally administered antibiotics (claritromycine, moxifloxacin) and a third intravenously administered antibiotic (meropenem-amikacin) due to the isolation of enteric bacteria in the sputum. Nonetheless, the patient's condition did not improve, thus bronchial aspirate was performed in which numerous *S. stercoralis* larvae were observed in Gram staining. Following an anthelmintic treatment, the clinical symptoms went away.

Taking current migratory movements into account, helminthiasis, which are common in endemic areas, should not be excluded from the differential diagnosis in the normal medical practice. As the authors of this study have concluded, in patients with lower respiratory tract infections the unexpected presence of enteric bacteria in respiratory secretions (carried by the larvae as they cross the intestinal wall) and chronic eosinophilia of unknown aetiology should lead us to suspect a parasitosis.

"Chronic pulmonary histoplasmosis in a non-immunodepressed patient, previously living for ten years in an endemic area"

Similar to the previous publication, we find the clinical note of García-Marrón et al.¹⁵: a middle-aged male, heavy smoker and drinker, was medically examined for a lower respiratory tract infection with a pulmonary alveolo-interstitial pattern found in the chest X-ray. After administering a conventional antibiotic treatment, he did not show any clinical or radiological improvement. For this reason, bronchoscopy was carried out, in the culture of which *Histoplasma capsulatum* was isolated. From the previous epidemiological studies it was shown that the patient had been back from Venezuela for a period of ten years, although he did not remember having any serious diseases during his ten-year stay in that country.

H. capsulatum is a fungus with a behaviour similar to that of tuberculosis: it occurs as a primary infection with unspecific self-limited symptoms (from asymptomatic to variable general symptoms) and with reactivations or re-infections according to the patient's immunocompetence factors (in this case, alcoholism). Following a two-year antifungal treatment with itraconazole, the patient presented with a favourable progress, without new reactivations during a three-year follow-up period.

"Bronchial tuberculosis. A study of 73 cases"

Pulmonary tuberculosis is often diagnosed using direct sputum smears for acid-fast bacilli, thus avoiding carrying out invasive examinations. As a consequence, the endobronchial lesions caused by Koch's bacillus are not always assessed. This leads to the underdiagnosis of bronchial tuberculosis and to the variability of the prevalence in the case series reviewed.^{21,22} This consideration contributed to the study carried out by Miguel Campos et al.,⁸ in the retrospective review of which they obtained a prevalence rate of bronchial tuberculosis of 6.4% among the patients with tuberculosis who underwent bronchoscopy during a 27-year period. When reviewing the clinical and X-ray patterns they obtained unspecific results, similar to most studies carried out until then.^{23,24} Concerning the endoscopic patterns, granuloma was more common in young people, while granulomatous and ulcerous bronchitis was more common in adults.

Consequently, the bronchial tuberculosis lesions were probably more common than estimated. Taking into account that in most

cases they were present in the context of pulmonary tuberculosis that had already been diagnosed, and that their discovery did not entail changes in the therapeutic attitude adopted, this assessment does not appear to have clinical repercussions.

"Pleural empyema by microorganisms of the Gemella species: an uncommon complication"

In this journal's October issue, Senent et al.¹⁷ discussed one of the most extensive case series published to date on empyema caused by these unusual bacteria, in addition to reviewing all the case studies found in the medical literature.¹⁷ *Gemella* is a recently discovered Gram-positive coccus that is present in humans (in the pharynx, the intestines and the urinary system), which during immunocompetent situations can cause infections of the nervous system, endocarditis, arthritis and, in rare cases, pulmonary abscesses and empyema.²⁵ The case series presented consists of three pleural empyema cases of patients that tested positive for *G. morbillorum* (in two cases) and *G. haemolysans* (one case), all of whom were allergic to penicillin. Following antibiotic treatment, together with the placement of a thoracic drainage tube and the use of fibrinolytic agents, the clinical progress was satisfactory in all three cases.

"Isolation of Nocardia in patients with cystic fibrosis"

The clinical note published by Barrio et al.² shows the difficulty involved in the clinical interpretation of the results of respiratory secretion samples of patients with chronic pulmonary diseases, such as cystic fibrosis. A good example is that of *Nocardia spp.*, a germ the pathogenic role of which is unclear in this type of patient.²⁶ Its symptoms range from asymptomatic colonisation to severe systemic effects. In this case series 387 patients were evaluated, isolating *Nocardia spp.* in nine of them, three of whom were completely asymptomatic. Expectant management was chosen for two of these patients, while the rest received antibiotic treatment, namely cotrimoxazole, ranging from a period of two weeks to six months. Progress was favourable in all the cases.

As the authors of this study have concluded, the discovery of *Nocardia spp.* should be evaluated in every case to decide on the best management to be followed, since it is always necessary to establish the relationship between the patient's microbiological and clinical findings.

Thoracic surgery*"Usefulness of omentoplasty in the treatment of poststernotomy mediastinitis secondary to myocardial revascularisation surgery"*

Poststernotomy mediastinitis is a serious postoperative complication of heart surgery, with a mortality rate of up to 50%.²⁷ The rate described varies according to the case series reviewed (from 0.4 to 5.1%).²⁸ Its treatment was and still is subject to continuous review, since it entails enormous technical difficulties and long periods of time are needed to observe clinical improvement. The therapy ranges from traditional hygienic and aseptic measures (specific antibiotic treatment, debridement of necrotic tissue, closure by secondary intention, drainages, washing fluids, dressings, etc.) to the use of vascular grafts (myoplasty, omentoplasty) in the anterior mediastinum.

Quiroga Martínez et al.³ presented in the February issue two interesting cases that required omentoplasty through supra-umbilical midline laparotomy. The progress was satisfactory in both cases. However, the authors noted that this technique is not free of complications (ileum, hernias, infections, etc.) and they explained that the laparoscopic approach will be an option for reducing these complications.

"Bronchogenic cyst of the mediastinum. Video-thoroscopic resection in eight cases"

The clinical note of Jiménez Merchán et al.⁶ comprised a generous case series of eight patients diagnosed with bronchogenic cyst of the mediastinum, who were operated on using video-thoracoscopy with excellent results. Bronchogenic cysts are the most common cystic lesions of the mediastinum, representing 18% of all primary tumours in this area.^{29,30} They constitute a congenital anomaly which is often diagnosed by accident, although it can also result in symptoms caused by the compression of neighbouring structures (cough, dyspnoea, thoracic pain, haemoptysis, etc.). The test chosen for its diagnosis and localisation is magnetic resonance. Despite the fact that there are some authors who defend a conservative treatment in asymptomatic patients, the rest of the studies are in favour of surgical extirpation as treatment of choice.³⁰ Unlike what is described by other authors,³¹ the patients of this study underwent complete aspiration of the mucoid fluid of the cyst at the start of the intervention, which greatly facilitated its dissection and extirpation. There were no intraoperative, postoperative or recurrent complications. In the case series published, the approach chosen was video-thoracoscopy. According to the authors, taking into account the parity of the results with respect to traditional thoracotomy and the postoperative advantages it offers, video-thoracoscopy should be the first choice of approach.

"Contribution of thoracoscopy to the diagnosis and treatment of complicated thoracic endometriosis (regarding two cases)"

Thoracic endometriosis is a condition with an incidence rate less than 1%, which was described for the first time in 1958.³² It consists of a growth in the endometrial tissue in the bronchial tree, the pulmonary parenchyma and/or the pleural tissue. Clinical suspicion is very important in its diagnosis. It affects women at a child-bearing age, who may present with chest pain, haemoptysis and/or haemopneumothorax, coinciding with menstruation. The definitive diagnosis is the histological one. The first line of treatment is the hormonal block; however, due to a high recurrence rate and the variable tolerability to the treatment, in many cases it is necessary to carry out surgical treatment.

Martínez Somolinos et al.,⁷ who presented two cases of endometriosis in the diaphragmatic pleura, stress the usefulness of video-thoracoscopy both for the diagnosis (direct view of brownish-grey flat plaques with a central haematoma, with a subsequent histological confirmation) and the treatment (electrocoagulation and scarification of pleura).

Diffuse interstitial pulmonary disease

It is important to state that from the four articles published on this topic in 2008 in *Archivos de Bronconeumología*, three were about the pulmonary damage caused by medicines. This shows the growing sensitivity of pneumology with regard to pharmacological toxicity. This sensitivity is also associated with the feeling that new medicines are more pneumotoxic than those previously used.

"Desquamative interstitial pneumonia and respiratory bronchiolitis associated with interstitial pulmonary disease: data from the Spanish registry"

In 2008 an excellent clinical note was published on desquamative interstitial pneumonia (DIP) and respiratory bronchiolitis-associated interstitial lung disease (RBILD).¹³ The note described the data of the Spanish registry, in which there were a total of 19 cases. The total number concerns the low prevalence rate of the disease and it shows the importance of collaborating with different centres.

The data confirm a relevant fact: the characteristics of the disease in Spain appear to be similar to those described in other countries. Both conditions only appear in middle-aged smokers with symptoms of cough and dyspnoea. In the computed tomography of the thorax we found ground-glass areas (DIP) or centrilobular nodules (RBILD). The progress is usually benign and the majority of the patients respond to the treatment (corticoids and giving up smoking).

However, the analysis of the data also gives rise to numerous questions on which we need to continue working: What is the relationship between DIP and RBILD? Is it a systemic disease? Is smoking the only aetiological factor? Why is there clinical improvement and no radiological improvement? What role does giving up smoking play in the progression of the disease?

"Organising pneumonia associated with treatment with peginterferon alpha"

Interferon is a cytosine produced by the immune system itself as a response to aggression caused by a virus or tumour cells. It contributes to the destruction process of infected cells and prevents virus replication. Various types have been described (up to three groups) with different protein isoforms. Its initial therapeutic use was in chemotherapy; however, at present it is also used in multiple sclerosis or hepatitis C. Within the pneumology field, interferon-gamma has been tested as a treatment for idiopathic pulmonary fibrosis due to its antifibrotic effects.³³

On the other hand, the clinical case published in this journal shows how a variant of this protein, peginterferon --2b, is able to cause an inflammatory reaction consistent with organising pneumonia.⁵ We therefore learn which medicines of the same family cause totally opposite conditions. This proves the complexity of the inflammatory condition and how far we are from understanding the entire complex system of symptoms that govern the condition in question.

"Hypersensitivity pneumonitis associated with venlafaxine"

It is well known that many medicines can cause pulmonary damage, and that histological findings are similar to those described in other diffuse interstitial pulmonary diseases.³⁴

In October, Borderías Clau et al.¹⁶ published a case of hypersensitivity pneumonitis associated with venlafaxine. This medicine is used as an antidepressant treatment under the inhibition mechanism for the recapture of serotonin, noradrenaline and dopamine. Following the exhaustive description of the case carried out by the authors, the association between the symptoms and the medicine appears to be proven. As a result, the discussion does not concern this association but the nomenclature, since the latter is confusing. If we understand that hypersensitivity pneumonitis (or extrinsic allergic alveolitis) is caused by the inhalation of an organic antigen (and rarely inorganic), it is difficult to include in the same group a medicine that acts through oral administration. Although the histological findings are similar, the clinical behaviour is different and, therefore, it appears more correct to use the term of pulmonary toxicity due to venlafaxine.

"Etanercept as a possible trigger for fatal pulmonary fibrosis"

The article published by Díez Piña et al.¹⁰ describes another case of pulmonary toxicity, although with important differences from the abovementioned case. The medicine causing this condition, that is, etanercept, has been used in the treatment of systemic diseases, and has also been suggested as an antifibrotic treatment for idiopathic pulmonary fibrosis, given that it is a tumour necrosis factor antagonist. Therefore, a product that in theory is favourable can produce a devastating effect. In this case, the patient presented with

many complex diseases, including chronic respiratory diseases (asthma) that can render the diagnosis difficult and can influence the prognosis. However, the main underlying difference is that in this case it is more difficult to establish the causal relationship.

The patient presented with both a respiratory disease and a systemic disease (psoriatic arthritis), was a heavy smoker and had been treated with methotrexate. It is well known that methotrexate can cause interstitial pulmonary disease, including years after stopping the treatment. However, the main contribution of this article is to warn us about the possible toxicity of etanercept.

Pulmonary hypertension

“Severe pulmonary hypertension and Takayasu disease”

Takayasu disease is a type of vasculitis of the great vessels with a low prevalence rate in Spain. García-Olivé et al.⁴ presented a case in which the pulmonary effects were more prevalent than the systemic one. This is an even more uncommon fact that justifies the importance of this case.

Pulmonary hypertension secondary to Takayasu disease should be included in group V of the clinical classification of pulmonary hypertension.³⁵ At present, the use of anti-proliferative medicines is not accepted in the therapeutic treatment. Stent implantation, such as in this case, should be carried out in selected patients and always by groups with experience in the management of said technique.

“Experience in the treatment of pulmonary arterial hypertension with imatinib”

Pulmonary arterial hypertension is one of the respiratory diseases with the worst prognosis. Moreover, idiopathic pulmonary arterial hypertension affects young people. This is why at times measures adopted by doctors are so “dramatic”.

The review of four cases published by García Hernández et al.¹⁹ is an example of this paradigm. Imatinib is an antagonist of platelet-derived growth factor. Its success would therefore lie in its antiproliferative activity, which has been demonstrated in vitro. In vivo, a case series has been published where its activity could be beneficial. However, as shown by the case series published in *ARCHIVOS DE BRONCONEUMOLOGÍA*, we need to include its secondary effects with the poor results.

In short, the need to find new medicines is of paramount importance concerning such a devastating disease. However, given the fact that it is also a disease that rarely occurs, it is necessary to combine the data in order to be able to obtain better results. At present, except for clinical trials, the use of imatinib is not justified in pulmonary arterial hypertension.

Miscellanea

“Acute respiratory failure in the immediate postoperative period of surgery for morbid obesity”

It is well known that patients with sleep apnea-hypopnea syndrome can have more perioperative complications than the general population. However, few thorough studies regarding this relationship have been carried out.^{36,37} This observation gains importance if we take into account that up to 50% of the patients with morbid obesity scheduled to have bariatric surgery present with a moderate to severe sleep apnea-hypopnea syndrome (many times underdiagnosed). Del Campo Matías et al.¹¹ mentioned in their clinical note published in August that despite the evidence of this relationship, in many occasions this is an undervalued clinical situation. The authors place a great emphasis on the early diagnosis

and treatment prior to surgery and in the immediate postoperative period, which would prevent a large number of postoperative complications. In the case published, the patient, who had not been diagnosed prior to the intervention, presented with acute hypercapnic respiratory failure as an immediate postoperative complication, and responded satisfactorily to non-invasive bi-level positive airway pressure ventilation.

As a result, we need to continue to insist that if we intend to decrease the morbidity and mortality rate of this surgical intervention, it is necessary that patients receive a multidisciplinary care.

“Endovascular management of a lesion in the left subclavian artery following thoracoplasty for bronchopleural fistula and empyema secondary to Aspergillus fumigatus”

In the June issue Ramos et al.⁹ presented the difficulties that are currently associated with the treatment of pulmonary aspergillus. We refer to probably the most common type of pulmonary aspergillosis.³⁸ It can appear to be asymptomatic for years, without needing to be treated, until being manifest as massive haemoptysis, in which case surgical treatment is the standard of choice, combined with antifungal medicines. This approach is associated with significant postoperative morbidity and mortality. In many instances, as in the case presented by the authors, various surgical interventions (pulmonary resection, thoracoplasty, vascular surgery, etc.) are necessary to overcome possible complications (air leak, empyema, thrombosis, arterial haemorrhage, etc.). The authors suggest using endovascular techniques in cases of complications of the great vessels.

“Spirometric evaluation of the respiratory effects in asymptomatic multinodular goitre with an intrathoracic component”

Perhaps the most groundbreaking clinical note published last year was the one by Ríos et al.¹⁴ Thanks to the results of their study, the authors suggested early surgery for asymptomatic intrathoracic goitre. They evaluated 21 patients diagnosed with asymptomatic intrathoracic goitre from the point of view of respiratory function. None of the patients presented with chronic respiratory disease. However, 10% already presented with some degree of obstruction in standing position and 20% in supine position. These disorders had disappeared during an examination carried out three months after surgery. As a result, goitre should not necessarily be expected to be symptomatic. Therefore, the morbidity and mortality of the surgery is probably higher.

To conclude, the article reminds us of the need to carefully evaluate all patients with asymptomatic intrathoracic goitre and, depending on the results, suggest surgical intervention.

“Necrotic lipoma of the posterior mediastinum”

In the November issue Andreu et al.¹⁸ described the case of an uncommon tumour. Although intrathoracic lipoma is already an individual rarity,^{39,40} the authors presented a case in which the area of the lipoma (posterior mediastinum) and its appearance (fat necrosis) were exceptional. In general, treatment is conservative, given the benignancy of the condition and the lack of associated symptoms. However, in some instances we need to opt for surgery due to the size, the presence of compressive symptoms and the diagnostic doubts raised by the heterogeneous aspect of the lesion, as in the case presented in this clinical note, in which the imaging techniques could not differentiate between a lipoma, a liposarcoma or a thymolipoma.

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