

CASE REPORT**Hypersensitivity pneumonitis in a butcher**G. Gala Ortiz^a, J. A. Méndez López^b and R. Fernández Ordóñez^c*^aOutpatient Allergy Clinic and ^bOutpatient Emergency Section, "Begoña" Sanatorium, Gijón;
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Hypersensitivity pneumonitis or extrinsic allergic alveolitis is an inflammatory lung disease caused by multiple exogenous factors acting as allergens through environmental exposure at the working place or in the home environment. The disease is in most cases related to the working place environment or to the patients' hobbies. Although an extensive panel of complementary studies is available that may contribute in establishing the diagnosis, the identification of a possible antigenic source and the documentation of worsening clinical symptoms upon exposure are necessary for establishing a definitive diagnosis of this condition. The case is reported of a butcher with symptoms suggestive of hypersensitivity pneumonitis in which a controlled challenge test was imperative in order to establish a definite diagnosis, since exposure to other possible antigenic sources independent from the patient's working environment was recorded. The challenge test was performed at the butchery while he was handling and cutting bovine heads, with a positive result. It is likely that the antigen responsible for the patient's clinical symptoms of pneumonitis might be found in the pituitary glands of the cattle heads being handled. At present, a controlled challenge test, either in the workplace or in the laboratory if an extract of the presumably involved antigen and adequate equipment are available is one of the most important tools for confirmation of a clinically suspected hypersensitivity pneumonitis. The results of such tests may have a profound impact on the patients' future work activities.

KEY WORDS: Hypersensitivity pneumonitis / Butcher.

Neumonitis por hipersensibilidad en un carnicero

La neumonitis por hipersensibilidad, o alveolitis alérgica extrínseca, es una enfermedad inflamatoria pulmonar debida a múltiples factores que actúan como alérgenos por exposición ambiental, bien en el medio laboral o en el hogar. En muchos casos, la exposición se relaciona con el ambiente de trabajo o con las aficiones del paciente en sus períodos de ocio. Aunque existe una batería amplia de exploraciones complementarias que ayudan a realizar el diagnóstico, es fundamental demostrar una posible fuente antigénica y el empeoramiento clínico del paciente con la exposición para confirmarlo de manera definitiva. Se presenta el caso de un carnicero con síntomas que sugerían neumonitis por hipersensibilidad, en el que debido a que el paciente se encontraba expuesto a otras posibles fuentes antigénicas fuera del medio laboral, fue indispensable una provocación controlada para llegar a un diagnóstico de certeza. La provocación se llevó a cabo en la carnicería, manipulando y partiendo cabezas de ganado bovino. El resultado fue positivo. Probablemente, el antígeno responsable del cuadro de neumonitis de este paciente se hallaba en las hipófisis del ganado bovino. La provocación controlada, en el medio laboral o en el laboratorio cuando es posible disponer de un extracto del antígeno sospechoso y del equipo técnico necesario, es hoy en día una de las pruebas más importantes para confirmar una sospecha clínica, y tiene una enorme trascendencia para el futuro laboral de los pacientes.

PALABRAS CLAVE: Neumonitis por hipersensibilidad / Carnicero.

INTRODUCTION

The condition known as hypersensitivity pneumonitis or extrinsic allergic alveolitis is an immunologically mediated inflammatory disease of the lung parenchyma, secondary to the repeated inhalation by the susceptible host of a large variety of causative agents. The prevalence of this disease is unknown, and depends on the environmental exposure and on the involved antigen¹.

Clinically, the disease may present in an acute form in which the main symptoms are general malaise, myalgias, scarcely productive cough, dyspnoea, cephalaea and fever. The symptoms become manifest ca. four to six hours after exposure to the allergen and may persist for over 18 hours, with spontaneous recovery when the exposure ceases and reappearance of the symptomatology upon renewed exposure.

In the chronic form of the disease the exposure to the antigen is less intense but continuous. The disease does then not manifest itself as acute episodes but as an insidious clinical constellation of dyspnoea, chronic cough, general malaise and weight loss².

An intermediate, subacute form also exists, in which the clinical features are similar to those of the chronic form of the disease and which might be related to exposure to small quantities of the antigen over a long period of time.

Regarding the diagnosis, a detailed anamnesis that discloses an environmental exposure is highly suggestive.

Among the complementary procedures for establishing the diagnosis, the most salient ones are lung function measurements, radiologic explorations, bronchoscopy and bronchoalveolar lavage, and transbronchial biopsies.

Further to these diagnostic procedures, it is important to try to demonstrate the environmental exposure to an allergen that might explain the patient's symptoms of pneumonitis, and also to document a clinical worsening of the condition upon controlled exposure to that antigen either in the patient's workplace environment or in an allergy laboratory, as well as the improvement and recovery of the patient when he is isolated from the antigen for an adequate period of time.

The list of possible responsible antigens is quite long, and comprises serum proteins (from pige-

ons, chicken, turkeys, bovine and porcine cattle), microorganisms (*Micropolyspora faeni*, *Thermoactinomyces vulgaris*, *Th. sacchari*, *Th. viridis*, *Th. candidus*, *Cryptostroma corticale*, *Graphium* spp., *Penicillium frequentans*, *P. casei*, *Mucor stolonifer*, *Aspergillus clavatus* and *Trichosporon cutaneum*, among others), chemical products (isocyanates), metals (gold) and drugs (thiazides, penicillin, tetracyclin, hydroxyurea, etc.), among others³.

We report the case of a butcher who had started evidencing clinical manifestations suggestive of hypersensitivity pneumonitis three years earlier. The complementary diagnostic procedures performed are discussed, as well as the results of a controlled challenge test in the patient's workplace environment, which were considered to be highly helpful in establishing the definitive diagnosis.

CASE REPORT

The patient was a 58-year-old male who had been a butcher for the last 23 years. He consulted because of evidencing, since three years earlier, episodes of nasal blockage, sneezing, scarcely productive cough, general malaise, tiredness and dyspnoea upon moderate exertion, which remitted during absences from his work and sick leave. Over these three years he had repeatedly tried to resume working, but the same symptoms reappeared about two days thereafter, remitting after about 72 hours when the patient remained at home.

In the butcher's shop he had been working with all kinds of meats and viscera, and he stresses the large amount of "brains" and "jawbone meats" they sell. Among the three butchers working at the shop, the patient is the one who generally strips the meat from the cattle skulls and opens up the skulls in order to remove the inner organs. He carried out this task one or two times every week.

The patient lives in a farm, where he also attends personally to the bovine cattle; he also handles and manipulates dry hay and also cares for rabbits and chickenfowl. He does not handle pigeons or any other type of fowl, nor does he work with ovine or porcine cattle. The patient reports no contact with wood, cheeses, mushrooms or fungi, or with paints, varnishes or other chemical products.

His home is an old house in a rural environment, humid but sunny, and he does not have any indoor pets.

The patient's previous history did not disclose any medical or surgical antecedents of note; he does not smoke. When he first came for consultation he had been on sick leave since two months previously, he was concluding a tapering methylprednisolone schedule prescribed because of his last episode and was under treatment with inhaled budesonide (400 µg b.i.d.) and terbutaline p.r.n.

In the physical examination, the pulmonary auscultation revealed isolated end-inspiratory wheezes; the patient was eupnoeic and reported no subjective sensation of dyspnoea. He did not have cough, and both the rhinoscopy and the examination of the pharynx yielded normal findings.

Analyses and complementary explorations provided by the patient. The CBC and the blood biochemistry evidenced no abnormalities.

A panel of precipitin tests (with pigeon serum, *Thermoactinomyces*, *Micropolyspora faeni*, pigeon faeces and *Aspergillus fumigatus*) had been negative two years earlier and again when it was repeated in the present year.

The plain chest film disclosed a diffuse interstitial pattern in both lung bases.

A thoracic CT scan revealed a very faint patchy pattern in the parenchyma of both lungs, with thickening of the bronchial wall in the proximal bronchi. There were no lymphadenopathies, nodular lesions or condensations.

A bronchoscopy revealed erythema and inflammation of the bronchial mucosa.

The transbronchial biopsy specimens were reported as septal thickening with fibrosis and with presence of lymphoid cells, but without granulomata or desquamative signs.

The bronchoalveolar lavage fluid yielded 3% polymorphonuclear leukocytes, 2% eosinophils, 67% lymphocytes and 28% macrophages; the T4/T8 ratio was 0.82 and increased contents of activated and NK cells were noted, as well as increased IgG levels.

The spirometry showed a Vital Capacity (FVC) of 3610 ml /84% of the predicted value), a forced expiratory volume in the first second (FEV₁) Of 2730 ml (79% of the predicted value), and a 76% FEV₁/FVC index.

On the basis of these results the patient was referred to our allergy outpatient clinic with the diagnosis of extrinsic allergic alveolitis with unknown causative agent, which agent might be present in his workplace environment or in his farmstead.

Complementary studies carried out at the Allergy Outpatient Clinic. Skin prick tests were performed with the airborne allergens usual in our environment (ALK-Abelló, Madrid, Spain), with negative results for mites (*Dermatophagoides pteronyssinus* and *D. farinae*), storage mites (*L. Destructor* and *T. putrescentiae*), moulds (*Alternaria*, *Aspergillus*, *Cladosporium* and *Penicillium*), cat and dog danders and grass pollen mix.

The therapy with oral methylprednisolone was withdrawn with a tapering schedule and the peak expiratory flow (PEF) was monitored during 23 days while the patient was at home and absent from his work, carrying out his normal household chores. For this monitoring, the patient performed three consecutive measurements and recorded the highest value, three times each day. The inhaled

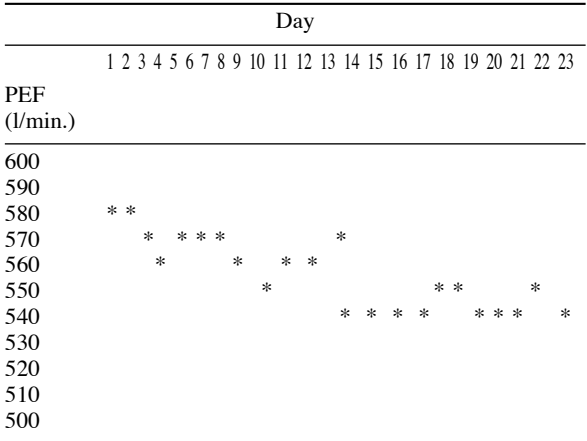


Fig. 1. Peak Expiratory Flow rate (PEF); maximal daily values while the patient was monitored at home.

Table I. Baseline spirometry recorded after the PEF monitoring days

	Predicted value	Actual measured value	Proportion (%)
FVC (ml)	4,190	3,360	80
FEV ₁ (ml)	3,320	2,250	68
FEV ₁ /FVC (%)	79	67	84

	Day				
	Monday	Tuesday	Wednesday	Thursday	Friday
PEF (l/min.)					
600					
590					
580					
570					
560				+	
550			+		+
540	+				
530					
520					
510					
500		+			

Fig. 2. Peak Expiratory Flow rates (PEF); maximal daily values on the days the patient returned to work (Monday and Tuesday) and on the three following days when he remained away from his work and resumed oral corticosteroid therapy.

corticosteroid treatment was maintained. The highest values recorded for each day are shown in Figure 1. The patient remained asymptomatic throughout this period.

Table I summarises the results of a baseline spirometric study performed after completion of the PEF monitoring.

The patient returned to his work and the PEF was again monitored, with measurements every two hours from 8:00 in the morning to 12:00 midnight (Fig. 2). The patient's working day is from 08:00 to 15:00. The patient returned to the Outpatient Clinic every day after completing his work stint.

During his first morning at work the patient "stripped" eight bovine heads and removed their inner organs. About noon (12:30) he started presenting sneezing and nasal blockage, without dyspnoea or cough. The physical examination revealed rhonchi in both lung bases and slight

oedema of the nasal mucosa in both nasal fossae, with no other significant findings. The PEF while at the Outpatient Clinic was 490 l/min.

The nasal blockage worsened during the night, but without cough or dyspnoea. The patient again returned to work on the next morning, and "stripped" a further three bovine heads. About 11:00 in that morning he urgently telephoned the Outpatient Clinic and reported dry cough, malaise, subjective dyspnoea and severe nasal blockage. The physical examination one hour later revealed disperse rhonchi in the pulmonary auscultation, tachypnoea (28/min), repetitive dry cough and severe nasal blockage. There was no fever, nor other salient findings. The PEF at that time was 480 l/min.

A new spirometry was carried out on the second morning at work (Table II).

The patient was thereupon separated from his workplace environment and oral therapy with methylprednisolone was again instituted. The patient's PEF was monitored for three more days.

DISCUSSION

The patient whose case is here reported was referred to our Outpatient Clinic with the diagnosis, oriented by all the complementary study procedures, of hypersensitivity pneumonitis caused by an undetermined allergen. Considering that he was a farmer, the most likely possibility would have been that the antigen responsible had been one present in his farmstead (fowl, hay, etc.). However, the clinical history suggested that the patient's clinical manifestations worsened on the days he went to work. For this reason, and in order to clarify his working future, the most important consideration was to objectively assess to what extent his workplace environment was harmful for him.

Table II. Spirometry recorded in the second day after the patient returned to work

	Pre-bronchodilation			Post-bronchodilation		Δ %
	Predicted value	Measured value	% Of the predicted value	Measured value	% Of the predicted value	
FVC (ml)	4,190	2,860	68	2,870	68	-
FEV ₁ (ml)	3,320	2,090	63	2,060	62	-1
FEV ₁ /FVC (%)	79	73	-6	72	-7	-1

The monitorisation of the Peak Expiratory Flow rate while the patient remained at home showed a fall in the maximal daily value of about 8% up to day 12 of the assessment. This might be explained by the fact that the oral corticosteroid therapy had been withdrawn some two weeks earlier. From that moment the measured maximal flow rates stabilised, with very little variation; the patient was at that time asymptomatic while under exposure to the eventual antigens in his household.

On the first day he returned to work the PEF fell some 10% and the patient experienced nasal symptoms, which were not typical for a pneumonitis, without pulmonary symptoms. The nasal symptoms worsened throughout that night and on the following morning the patient already evidenced symptoms of pulmonary involvement and general malaise, together with a worsening in his lung function tests. The spirometry showed a restrictive pattern with a 15% drop in the Vital Capacity as compared to the levels recorded prior to the return to work, and a 23% drop as compared to the best values recorded one month before that. The variations in the FEV₁ were less significant, with a 7% drop as compared to the level recorded immediately before returning to work and a 17% one as compared to the best level one month earlier.

It is striking that, in the two days when he resumed work at the butchers' shop, his actual occupation was to strip and open up bovine cattle heads. A review of the causes of hypersensitivity pneumonitis showed that an allergen in the pituitary gland of ovine and porcine cattle has been described in this context⁴. This might explain the patient's manifestations, although until now this allergen had been mainly related to the therapeutic inhalation of powdered bovine or porcine pituitary as a drug for the management of diabetes insipidus⁵. The confirmation of the aetiological diagnosis would require a specific bronchial challenge test in the laboratory using heterologous powdered pituitary, or skin tests and/or determination of precipitins with bovine pituitary as the antigen. It must be remembered, however, that in the present case the main objective of the study was to establish whether a relationship existed between the patient's symptoms and his workplace environment.

The results of the challenge test in the work environment confirmed such a relationship and led to the conclusion that the causative agent for

the pneumonitis was a bovine antigen. However, it was not possible to fully confirm that the antigen was located in the pituitaries.

The changes observed in the baseline spirometry, despite permanent therapy with inhaled corticosteroids, might be due to the fact that the patient had repeatedly tried to return to his work over the previous three years in spite of his symptoms. This would lead to the classification of his pneumonitis in the subacute-chronic group.

As the prognosis of this patient would have worsened if his workplace exposure continued, he was removed from the butchers' shop after the study had been completed. In the following months the oral corticosteroids were withdrawn while maintaining the inhaled corticosteroid therapy, and the patient's lung function has progressively improved.

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