Eur J Med Res (2004) 9: 573-574

EXTRINSIC ALLERGIC ALVEOLITIS WITH IGA DEFICIENCY

J. Sennekamp[1], H. Morr[2], J. Behr[3]

[1]Allergy Laboratory Prof. Sennekamp, Bonn,
[2]Hospital for Respiratory Diseases Waldhof Elgershausen, Greifenstein,
[3]Section for Pulmonary Diseases, Department of Internal Medicine I, Munich, Germany

Abstract: Up to now only 3 cases of extrinsic allergic alveolitis (hypersensitivity pneumonitis) with IgA deficiency have been published worldwide. We had the opportunity to detect two additional cases which will be presented here.

Summarizing all cases IgA deficiency is a risk factor for a severe course of the disease and an increased susceptibility to aquire allergic alveolitis by low dose antigen exposure.

Key words: extrinsic allergic alveolitis, hypersensitivity pneumonitis, IgA deficiency, IgE deficiency

INTRODUCTION

Antigen-specific IgG and IgA antibodies in the serum are acknowledged criteria of extrinsic allergic alveolitis (EAA)[7]. In most patients the IgG and IgA immunoglobulin levels in the serum are also elevated [9]. As formerly the IgG and IgA antibodies were regarded as the cause of EAA [9], a description of a case of farmer's lung missing any IgA immunoglobulin including the lack of antigen-specific IgA antibodies was a surprise [4]. The IgG level, however, was increased together with strong precipitins against Saccharopolyspora rectivirgula.

Also impressive was the second case of a home related alveolitis with lowered IgG and IgA levels [8]. The immunoglobulin G and A levels were lowered while IgM was within normal range. There were no antibodies detectable against a wide battery of bacteria and mold antigens. Also the number of B cells in the blood was low (12 cells/mm^3) while T cells were normal. The authors called their observation "an experiment of nature" pointing to sensitized T cells to be the cause of EAA.

Recently a pigeon fancier's lung lacking serum IgA was seen in a child [10]. IgG, IgG subclasses, and IgM were normal. There were high titered IgG antibodies against pigeon antigens.

Here we present a woman allergic to molds in her home, lacking IgA in her serum and a pigeon breeder's lung without IgA. Taking all patients together, we will give the first comprehensive survey of the clinical course of this subgroup of EAA patients in the discussion of this paper.

CASE 1

The never smoking 44-yr-old female developed cough, fever, dyspnea and weight loss. Her office in the basement of her house had become moldy. Microbial analysis detected Aspergillus ustus, Aspergillus versicolor, Cladosporium herbarum, Penicillium brevi compactum, Botrytis cinerea, and Paecilomyces variotii.

Working with bark mulch in her garden this expusure also provoked the symptoms. Bark mulch is plenty of mold [6].

The initial clinical examination showed the tachypneic patient with cyanotic lips and subcrepitant rales especially in the lower lobes area. Vital capacity was 85%, diffusion capacity Dco significantly reduced (52%). At rest hypoxemia was remarkable (pO_2 59.9 mmHg) and was completely compensated by oxygen supply. Radiologically there were marked regularly disseminated ground glass opacities and nodular densities.

Leukocytes were increased to 12 600 cells/mm^3, CRP to 8.6 mg/l (<0.5 normal), BSR to 80/110 mm. IgG antibodies were detected by ELISA against Aspergillus fumigatus, Aspergillus versicolor, and Cladosporium herbarum. No antibodies could be found against Penicillium brevi compactum, Aureobasidium pullulans, Botrytis cinerea, Paecilomyces, Saccharopolyspora rectivirgula, Thermoactinomyces vulgaris, pigeon serum, and budgerigar serum. Also no IgA antibodies could be found against Aspergilli and Cladosporium herbarum.

Immunoglobulin serum levels: IgG 14.4g/l, IgG1 10.60g/l (normal 4.9-11.4), IgG2 6.59 g/l (normal 1.5-6.4), IgG_3 0.34 g/l (0.20-1.10), IgG_4 0.08 (normal 0.08-1.4); IgA below 0.01g/l (normal 0.75-3.74); IgM 1.35 g/l; IgE: below 0.01g/l (normal 0.75-3.74). Thus this patient has an IgA and IgE deficiency. The secretory IgA level measured in the saliva fluid was in the normal range (86mg/l)(normal 42-292mg/dl).

In the basement of her house mold was eradicated and she moved her office upstairs in another room and improved. The initially given prednisolone (50 mg/die) could be withdrawn by tapering. However, 8 month later the IgG antibody levels were not diminished and we will control the further course of her disease.

Thus she suffered from a severe home related (indoor) allergic mold alveolitis.

CASE 2

The 28-yr-old male had suffered from sinusitis four times. The actual Roentgen of the nose and sinus was normal. There were no other signs of an immunodeficiency in his history.

Actually he complained of dyspnea, fever, chest tightness, and myalgias. The complaints were only in

Table 1. Essential data of all known cases of EAA with humoral immune deficiency.

	male 24 yr. Dalmasso 1980	female 44yr. Schkade 1996	female 5 yr. Yalçin 2003	female 44 yr. Sennekamp 2004 case 1	male 28yr. Sennekamp 2004 case 2
Ig deficiency	IgA + IgE	IgA + IgG	IgA	IgA + IgE	IgA
IgG antibody against:	Saccharopol. rectivirgula	no antibody	pigeon	molds	budgerigar
Diagnosis	farmer's lung	indoor alveolitis	bird breeder's lung	mold EAA	bird breeder's lung
Course	fibrosis, lethal course	strong, asymptom. by avoidance	symptoms already from indirect exposure	strong	symptoms already from indirect exposure

his flat. Frequently he left his house for business trips.

Vital capacity was reduced (69%), diffusion capacity Dco 67%, and there was an hypoxemia under exertion.

In the HRCT areas of ground glass attenuation were detectable.

In the BAL 62% lymphocytes were counted. CD4/CD8 ratio was markedly reduced to 0.2.

Using ELISA in his serum IgG antibodies against budgerigar serum proteins were detected, though he could not remember contact with birds.

Inhalation challenge by sleeping one night in his flat again resulted in fever (38 °C), decrease of vital capacity about 21%, pO_2 decrease of 19mmHg together with the same clinical symptoms as before.

Further inquiring showed the tenant living in the flat before had kept two budgerigars in these rooms. No new carpet was put in when the patient moved into the flat. The symptoms of the patient had been started two month after moving. So evidently he has become sensitized after moving.

After he was diagnosed he left these rooms and became completely asymptomatic in another environment without birds. This extraordinary "bird beeder's lung without birds" has already been published as an abstract [1].

Looking for the serum immunoglobulin levels lacking IgA (below 0.01g/l) was remarkable. IgG and IgM immunoglobulins were normal. IgE was within range of healthy nonatopic persons.

Discussion

IgA deficiency is the most frequent human humoral deficiency with one case/600 persons [2, 3]. Most of these IgA deficient humans are asymptomatic. Symptomatic IgA deficient persons suffer not only from infectious diseases but also from immune disorders as coeliac disease, autoimmune diseases, and allergies [2]. Vice versa in coeliac disease IgA deficiency is found much more frequently (12%) than in normal population (0.16%) [2]. The reason for this association will be genetic. Both IgA deficiency and coeliac disease have increased HLA frequencies of HLA B8, DR3, and DR7 [3]. Extrinsic allergic alveolitis shows the same HLA-pattern [9]. Therefore IgA deficiency could also be more frequently in EAA than in normal population.

Looking for the clinical courses of all five hitherto published cases of EAA with IgA deficiency (Table 1) there is a high susceptibility to EAA because two patients [Yalcin 2003, case 2 of this study] diseased already by indirect antigen contact, a very rare event in EAA [5]. The other 3 cases were serious [4, 8, 9]; the first published case [4] even died (Table 1).

In contrast to this fatal case of Dalmasso [4] lacking also secretory IgA, our case 1 has secretory IgA.

Whether the IgE deficiency, seen in only two patients (Table 1), has any clinical relevance cannot be judged today. We need additional observations concerning immunodeficiencies in EAA to discover the course of their allergic alveolitis and their prognosis.

References

1. Behr J. (1996) Vogelhalterlunge ohne Vogelhaltung? Allergologie 19: 527
2. Cataldo F, Marino V, Bottaro G, et al. (1997) Celiac disease and selective immunoglobulin A deficiency. J Pediatr 131: 306-308
3. Collin P, Mäki M, Keyriläinen O, et al. (1992) Selective IgA deficiency and celiac disease. Scand J Gastroenterol 27: 367-371
4. Dalmasso F, Cordola G, Sirkka M, Torghio R. (1980) Total selective deficiency of serum and secretory IgA associated with farmer's lung. Bronchopneumologie 30: 545-555
5. Greinert U, Lepp U, Becker MM (2000) Bird keeper's lung without bird keeping. Eur J Med Res 5: 124
6. Kirsten D, Kanzow G, Nowak D, Magnussen H. (1994) Aspergillus induzierte exogen-allergische Alveolitis bei einem Landschaftsgärtner. Internist 35: 182-184
7. Lacasse Y, Selman M, Costabel U, et al. (2003) Clinical diagnosis of hypersensitivity pneumonitis. Am J Respir Crit Care Med 168: 952-958
8. Schkade PA, Routes JM (1996) Hypersensitivity pneumonitis in a patient with hypogammaglobulinemia. J Allergy Clin Immunol 98 : 710-712
9. Sennekamp HJ. Extrinsic allergic alveolitis – hypersensitivity pneumonitis. Dustri, Munich, Orlando 2004
10. Yalçin E, Kiper N, Göçmen A, et al. (2003) Pigeon-breeder's disease in a child with selective IgA deficiency. Pediatrics International 45: 216-218

Received: October 1, 2004 / Accepted: November 23, 2004

Address for correspondence:
Prof. Dr. J. Sennekamp
Allergologisch-Immunologisches Labor
Weberstr. 118
D-53113 Bonn
Tel.: +49 228/213074
Fax: +49 228/219124
E-mail: sennekamp@t-online.de