RELATIONSHIP BETWEEN NUMBER OF ALLERGIC SENSITIZATIONS AND IMMUNITY IMPAIRMENT: ANYTHING NEW IN IMMUNOTHERAPY FOR ALLERGIES AND VACCINES PLANNING?

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SUMMARY: To 106 14-56 year-old allergic people (30 monosensitized, 24 sensitized to 2 pollens, 52 polysensitized) we have evaluated the Global Immune Competence Status (GICS). That's a compound score, made of ten parameters, six regarding cell-mediated immunity (WBC/mmc, Gr/mmc, Ly/mmc, Ly CD3+/mmc, Ly CD4+/mmc, CD4/CD8 Ratio), four regarding nutritional status and humoral immunity (Tot. Protein mg/dl, Albumin mg/dl, Gammaglobulins mg/dl, IgG mg/dl). Each parameter is brought on a grid including 4 worth scores worsening from 4 to 1, related to different ranges of values; this way quickly leads to characterize type and grade of immune deficiency. So doing we found that in 30 monosensitized people 27 (90%) show a complete immune competence, while just 3 people (10%) have impaired GICS: in these 1 (3%) regards cell-mediated immunity, while 2 (7%) regard humoral immunity. In 24 patients sensitized to 2 allergenes, 18 (75%) showed complete immune competence, while 6 (25%) a GICS impairment regarding cell-mediated immunity. In leaving 52 polysensitized patients, 30 people showed complete immune competence (58%), while 20 (38%) showed a GICS impairment regarding cell-mediated immunity and 2 (4%) impaired humoral immunity. This work shows that the higher the number of sensitizations is, the stronger the cell-mediated immunity impairment in allergic people become.
Key-words: Allergic polysensitization - Cell-mediated immunity - Immune deficiency - Global immune competence status - Specific immunotherapy - Vaccination.

INTRODUCTION

Today the pivotal role of specific immunotherapy in the treatment of allergic diseases has been well established (1). The rate of success of this therapy is very high (near 80%) (2, 3, 4, 5, 6, 7) and the researchers' efforts are focused to point out and characterize the factors leading to residual resistance to this therapy with acknowledged efficacy; the aim of this work is to light this still obscure field of Allergology and Clinical Immunology. It's well known that the switch towards Th2 citokine profile polarization isn't characterized just for a IgE synthesis, but for a Th1 profile inhibition as well (8, 9, 10) and many data in literature show an increased risk of malignancies in allergic patients (11, 12, 13, 14), likely as a result of impairment of cell-mediated immunity and immune surveillance against tumours: the present work supports the thesis that the higher the number of allergic sensitizations is the stronger the Th1 inhibition. The Immune Deficiencies are a heterogeneous group of diseases, interesting aspecific, humoral, cell-mediated immunity and combined deficiencies; some of these diseases are genetically inherited (Primary Immune Deficiencies) and their impact on people is rare (1/5000=0,0002%), while acquired immune deficiencies have much higher frequency, due to malnutrition, viral diseases, chronic diseases, iron deficiency, tumours and iatrogenic agents. Recent evidences have shown a global incidence of acquired immune deficiencies in Apulia, an Italian region, on 1/6=17% of people (15), so that today we know these diseases have strong impact on clinical practice. We must confront ourselves with this knowledge in planning both specific immunotherapy to treat allergic diseases and vaccinations to prevent infectious diseases.

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MATERIALS AND METHODS

Apulia is one of the twenty Italian Regions; it's located in South Eastern Italy, facing the Adriatic and Ionian see, because of its location as heel of the Italian boot (that's why Italy cannot go around the world without Apulia).

Thanks to Istat dates related to 2003, we know that the residents here are 4,040,990 and represents 7% of the total Italian population (57,888,245); it's a very hetero-

geneous population, made of Italian and foreign residents, coming from southern and oriental countries (Africa, Balkans, Middle-East) and integrated in our social and economic web. We used a screening method to unmask immune deficiencies on the Apulian population, the GICS=Global Immune Competence Status (16); that's a compound score, made of ten parameters, six regarding cell-mediated immunity (WBC/mmc, Gr/mmc, Ly/mmc, Ly CD3+/mmc, Ly CD4+/mmc, CD4/CD8 Ratio), four regarding nutritional status and humoral immunity (Tot. Protein mg/dl, Albumin mg/dl, Gammaglobulins mg/dl, IgG mg/dl). Each parameter is brought on a grid including 4 worth scores worsening from 4 to 1; this way quickly leads to characterize type and grade of immune deficiency that may be shown graphically as well (Tab.1 and Fig.1). By using GICS characterization, we have studied 106 14-56 old-aged allergic patients to pollens; 30 patients were sensitized to just one pollen, 24 to 2 pollens and 52 polysensitized (>2 pollens). The data were collected on an excel table and graphically shown.

Immune Competence	4	3	2	1
WBC/mmc	>6000	>4500	>3000	<3000
Gr/mmc	>4000	>2500	>1500	<1500
Ly/mmc	>2000	>1300	>900	<900
Ly CD3+/mmc	>1400	>900	>650	<650
Ly CD4+/mmc	>600	>450	>300	<300
CD4/CD8 Ratio	>1.5	>1.3	>1.0	<1.0
Total Protein mg/dl	>6500	>5700	>5000	<5000
Albumin mg/dl	>3500	>3300	>3000	<3000
Gammaglob. mg/dl	>1200	>1000	>800	<800
IgG mg/dl	>1000	>850	>700	<700

Table 2: The Global Immune Competence Status (GICS).
The global score results from the addition of ten single scores (4-1) obtained from every parameter taken into account (complete immune competence: GICS=40).

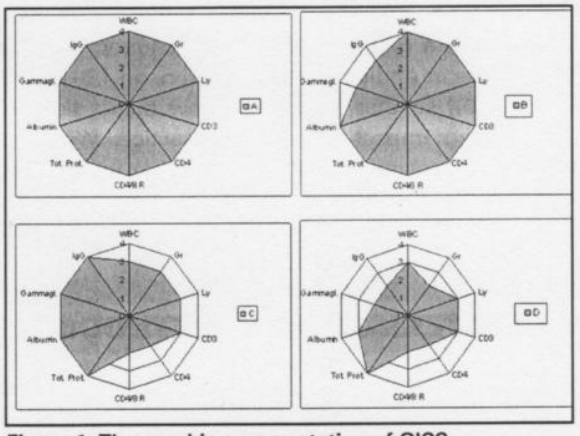

Figure 1: The graphic representation of GICS.
Patient "A" shows complete immune competence; Patient "B" has slight impairment of humoral immunity; Patient "C" shows impairment of cell-mediated immunity; Patient "D" shows bad impairment of both humoral and cell-mediated immunity. The covered area of the graphic is proportional to the global immune competence degree.

RESULTS

The allergic people showing complete immune competence are 75/106 (71%), while global incidence of immune deficiency in allergic patients is 31/106 (29%); 27 people out of these are suffering from cell-mediated immunity, while just 4 from humoral immunity impairment (Fig. 2). The evaluation in 30 monosensitized people shows a complete immune competence in 27 patients (90%), while GICS is compromised for just 3 people (10%): just 1 in these (3%) shows impairment of cell-mediated immunity, while 2 (7%) humoral immunity. As to 24 patients sensitized to 2 allergenes, 18 (75%) showed complete immune competence and 6 (25%) a GICS impairment regarding cell-mediated immunity; none of these shows impaired humoral immunity. In 52 polysensitized people 30 showed completeimmune competence (58%), while 20 (38%) showed a GICS impairment regarding cell-mediated immunity and 2 (4%) humoral immunity (Fig. 3)

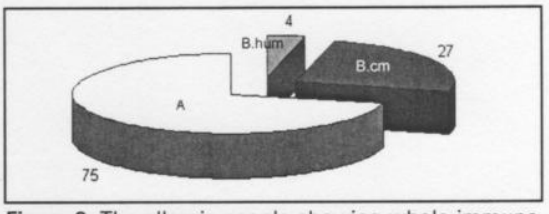

Figure 2: The allergic people showing whole immune competence (A) are yellow, those with cell-mediated immunity impairment (B.cm) are red, while those with humoral immunity impairment (B.hum) are blue.

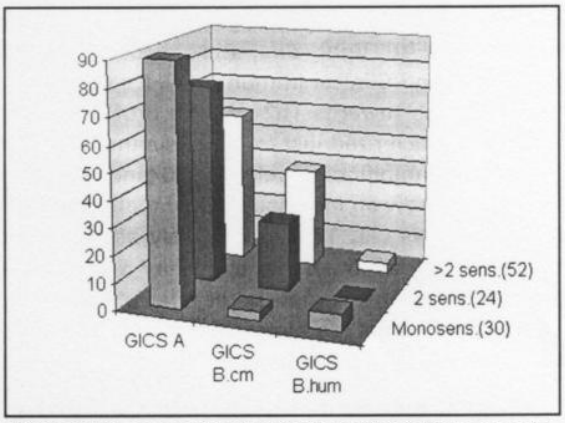

Figure 3: Monosensitized allergic patients have complete immunocompetence (GICS A) in 90% of people, while the more often cell-mediated (GICS B.cm) than humoral (GICS B.hum) immunodeficit worsens with the increasing number of sensitizations.

DISCUSSION

The global incidence of immune deficiency in the Apulian people is 17% while in a cohort of 106 allergic people this incidence is 29%. The impairment is mainly related to cell-mediated immunity and fits well the literature data showing impairment of Th1 citokine profile in allergic people. But when we analyze the single patients' groups we see that this impairment regards 3% (1/30) of monosensitized patients, 25% (1/4) of those sensitized to 2 pollens and 38% (1/3) of polysensitized patients. There are some considerations to do here. First: there is the lower incidence of impairment of cell-mediated immunity in people monosensitized compared with the global people in Apulia; this means that the allergic sensitization to just one allergen seems to be protective against impairment of cell-mediated immunity in population. Second: the addition of a second sensitizing allergen leads to stronger impairment of cell-mediated immunity and polysensitized patients have the strongest immunity impairment. As to the first consideration, it seems that the sensitization to just one pollen may be protective against cell-mediated immunity impairment, perhaps because of the fact that just one sensitization induces a too light Th2 stimulation and may result in Th1 stimulation as well; on the other hand, the increasing number of sensitizations seems to worsen the cell-mediated immunity involvement. These findings can account for conflicting data regarding the incidence of malignancies in allergic patients: as to the incidence of malignancies in allergic people, we don't have any selection of the patients by the number of allergic sensitizations.

Moreover, we know that in allergic diseases the specific immunotherapy leads to the desensitization thanks to a switch from Th2 to a Th1 polarized response to the involved allergens (17, 18). A simultaneous cell-mediated immunity impairment may lead to a slower and worse response to the immunotherapy; so that to reach the aim to optimize the immunotherapy clinical outcomes, it may be useful to restore the cell-mediated immunity as soon as possible before starting immunotherapy. This goal may be achieved characterizing the pathogenesis of immunity impairment and acting to correct the causes leading to immune defect (iron deficiency, malnutrition, vitamin deficiency, etc.) (19, 20, 21, 22, 23, 24, 25, 26); on the other hand it cannot be forgotten that iron overload may be dangerous for the immune system (27, 28). Clinical studies show that immune system function recovery is helpful in the prophylaxis and getting over many viral and bacterial infectious diseases (29, 30, 31); the global immune competence status may be useful even as element to decide on vaccines in infectious diseases (32), because if GICS is impaired living vaccines which can repeat the disease in immunonodeficient host shouldn't be used. With regard to allergic diseases, in our experience the likelihood of successful immunotherapy is better after the GICS improvement, especially in polysensitized people: thanks to this knowledge we hope in the future to see the specific immunotherapy failures in allergic people more and more minimized.

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