

1. Ambient pollutants as adjuvant for allergic sensitization: the emerging role of platinum group elements

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Vol. 23, no. 4, 207-215 (2009)

The prevalence of asthma and allergies often observed in urban metropolitan areas as compared to rural and farm communities is still an enigma. Westernized life styles, type of farming and exposure to environmental pollutants seem to simultaneously interact in the determination of this phenotype in genetically predisposed individuals. In this scenario, we asked whether and to what extent we could single out antropogenic airborne contaminants in general, and platinum group elements in particular as relevant causal factors in the generation and in the clinical expression of allergic immune responses in exposed individuals. To this aim, we evaluated epidemiological and basic immunology studies published on peer-reviewed journals indexed in Medline on this subject. We reviewed studies focused on effect of the exposure to platinum group elements on the allergic immune response, with specific reference to our own studies, on their influence on dendritic cells and on the consequent skewing of T-helper and T-regulatory lymphocyte functions. Our laboratory contributed to generate consistent evidence supporting the notion that antropogenic emissions in general, and platinum group elements in particular, can functionally modulate the immune response in a coordinated pro-allergic fashion. We conclude that in genetically predisposed individuals platinum group elements exert an adjuvant effect specifically leading to more severe allergic reactions.

2. Acute mercury intoxication and use of chelating agents

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There is a great hazard of mercury (Hg) intoxication in the third world for artisanal miners using Hg as amalgam for extracting and refining gold. In developing countries, there is the possibility of risk regarding exposure to Hg from amalgam tooth fillings, ethyl-Hg (thimerosal) added as antiseptic to vaccines and methyl-Hg in fish. In one case, a 41-year-old man attempted suicide by ingesting 100 mg of HgCl₂. After 8 hours, he developed hematemesis and entered the intensive care unit; his urinary Hg was 10.1 mg/l. Treatment with 2,3-dimercaptopropanol (BAL) was started by intramuscular route after 16 hours at the dosage of 5 mg/kg body weight every 4 hours (on days 2-3) and 3 mg/kg every 6 hours (on days 4-5) and then every 12 hours (on days 6-14) without adverse side effects. Acute Hg intoxication can be managed with BAL as first choice chelator, whereas the less toxic 2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercaptopropane-1-sulfonic acid (DMPS) should be reserved for cases of less severe inorganic Hg or methyl-Hg acute intoxication. Such agents, recommended only for the treatment of acute Hg poisoning, should not be used for patients suffering from neurological diseases in which environmental Hg exposure is hypothesised.

3. Recurrence of pleomorphic adenoma of the palate after sixteen years: case report and an analysis of the literature

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Pleomorphic adenoma or mixed tumour (MT) is a benign neoplasia of slow growth and epithelial histogenesis. We report a particular case of recurring MT of the hard palate. A 39-year-old man came to us with a swelling of the hard half-palate. The patient, 19 years earlier, had had a small formation in the same place that, over a period of three years had slowly grown. Histology showed that it was an MT and it was promptly removed. Sixteen years after the operation, a small recurrence reappeared, reaching a diameter of 12 mm. The patient underwent a new excision. The case reported is of particular interest due to many aspects: the outbreak from the minor salivary glands; the male sex; the young age of the patient at the first sign of the tumour; the appearance of a recurrence after 16 years, not contemplated in literature; and finally, the rapid growth of the second appearance.

4. Infections and mast cells

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Mast cells play a role in various physiological functions: innate and acquired immunity, epithelium remodelling and proliferation, angiogenesis, cancer, inflammation and infections. Mast cells are activated by cross-linking of FcεRI molecules, which are involved in the binding of multivalent antigens to the attached IgE molecules, resulting in a variety of responses including the immediate release of potent inflammatory mediators. In addition, mast cell biology consists in the capability to secrete preformed mediators which include biogenic amines and newly synthesized mediators, which include lipid-derived mediators and cytokines. It has been reported that parasite infections induce a systemic immunomodulatory network, including regulatory T cells, pro-inflammatory and anti-inflammatory cytokines, which might play a key role in the allergic phenotype. Here, in this article, we revisited the relationship between mast cells and infections.

5. Apoptotic effect of cyclosporin a and dexamethasone in malignant cells of patients with B-chronic lymphocytic leukemia

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B-chronic lymphocytic leukemia (B-CLL) is a malignant disorder characterized by the accumulation of the leukemic cells in the G₀-G₁ phase of the cell cycle and expressing high levels of the anti-apoptotic protein Bcl-2. Since we observed that the treatment of autoimmune complications with Cyclosporine A (CsA) determined in some CLL patients an improvement not only of the autoimmune phenomena, but also of the leukemic process, we evaluated the *in vitro* cytotoxicity of CsA as compared to Dexamethasone (Dex) on leukemic cells. Leukemic cells obtained from 32 B-CLL patients showed a heterogeneous pattern of spontaneous apoptosis at 24 h interval and this pattern permitted to identify: Group 1 (14/32) with high (>20%) apoptotic rate and Group 2 (18/32) with low cell death. CsA and Dex increased cell death in both groups with a different timing by an apoptotic mechanism that does not involve Bcl-2. Furthermore, in Group 2, CsA-induced apoptosis was significant higher than that observed with Dex both at 4 and 24 h. We suggest that, in B-CLL, CsA has a significant pro-apoptotic activity manifested also in patients with low spontaneous apoptosis. Our observations might be taken into account to consider new therapeutic strategies in B-CLL.

6. IL-18 and Interferon-gamma in HCV-related hepatocellular carcinoma: a model of interplay between immune status and cancer

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Hepatocellular carcinoma (HCC) is a frequent malignancy with a high rate of mortality, and the hepatitis B and C viruses are considered major etiological factors associated with the development of chronic inflammation. Today, there is increasing evidence that the inflammatory process, mediated by the complex cytokine network, is inherently associated with many cancer types, including HCC. In this study we have assayed Th1 cytokines, such as IL-18 and IFN gamma, in the sera of 23 HCC patients with HCV infection, analysing their possible association with HCC in respect to 20 patients: 12 carriers for HCV infection and 8 healthy controls. We have also evaluated the possible difference on IL-18 and IFN gamma in HCC patients with respect to the number of hepatic nodules and rate of tumor differentiation. The mean values of serum IL-18 levels were significantly higher in HCC patients than in HCV carriers ($p < 0.001$) while IFN gamma serum levels were similar in cases and controls. No significant correlation was present between IL-18 and IFN gamma. In addition, IL-18 was higher in HCC patients with two or more nodules in respect to HCC patients with one nodule (372 ± 140 vs 109 ± 73 pg/mL; $p < 0.001$). There is no significant difference in HCC patients and no correlation between the cytokines and other evaluated variables such as HCV RNA, alpha-1 fetoprotein, genotype and demographics of HCC patients. Taken together, our data suggest that IL-18 may play a key role in the pathogenesis of HCC and its levels can be utilized as a possible marker in the diagnosis of HCC.

7. Immunohistochemical and transcriptional expression of the matrix metalloproteinases MMP-2 and MMP-9 in normal and pathological human oral mucosa

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The oral cavity is exposed to chronic or recurrent, physical and chemical trauma that could lead to mucosal reactions (e.g. hyperplasia, dysplasia and tumors). The objective of this study is to investigate the expression and the possible changes of the two matrix metalloproteinases MMP-2 and MMP-9 in normal and pathological human oral mucosa samples. Normal oral mucosa samples and three different types of pathological conditions (hyperplasia, dysplasia and carcinoma) were used for this study. Immunohistochemical analysis was used to evaluate protein expression for the two enzymes, while Reverse Transcription – Polymerase Chain Reaction (RT-PCR) was used to investigate gene expression. Image analysis was used to give a quantitative evaluation of the immunohistochemical data. In control samples we identified a weak expression of both MMP-2 and MMP-9 in the epithelial layers. In hyperplasia samples MMPs expression is limited to epithelial layers but the immunoreactivity is more intense than in the control. In dysplasia and carcinoma samples the two matrix metalloproteinases are expressed not only in epithelium but also in some cells of the connective tissue and in the vessel walls. Qualitative RT-PCR and image analysis confirmed the immunohistochemical data. The results obtained in this study suggest the existence of a possible relationship between the entity of morphological disorganization of the oral mucosa in different pathologies and the increase of MMP-2 and MMP-9 expression.

8. Severe intravascular haemolysis as delayed manifestation of perivalvular leak in patients with mitral valve replacement: a report of two cases

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Haemolytic anaemia following mitral valve replacement is uncommon, however in patients who suffer from some degree of perivalvular leak, severe and potentially fatal recurrent intravascular haemolysis can be an annoying problem. We report the cases of two patients with severe haemolytic anaemia observed some years after mitral valve replacement. In one of the two patients the presence of an association between a valvular leak after mitral valve replacement and a calcific atrial wall produced severe and recurrent haemolysis that required multiple blood transfusions. In the second patient the presence of a single valvular leak after mitral valve replacement induced an episode of haemolytic anaemia some years after the operation. These cases point out that in case of unexplained worsening anaemia, a transthoracic (TT) and transesophageal (TE) echocardiogram should be performed, and the possibility of atrial wall alterations in the producing of anaemia should be kept in consideration. In these cases reoperation resolved the recurrence of anemia.

9. Upper extremity deep vein thrombosis as an uncommon complication of pacemaker implantation: a case report

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Venous complications of pacemaker implantation rarely cause immediate clinical problems. An 89-year-old man, without thrombophilia, 4 weeks after a pacemaker implantation experienced functional impotence of the left arm that appeared warm, reddened, oedematous and painful. Color Doppler Ultrasonography revealed a thrombosis of the axillary vein extended to the proximal third of the ulnar vein. In our opinion, upper extremity deep vein thrombosis (UEDVT) represents an important complication of post-surgical pacemaker implantation that should be suspected early, even without specific symptoms and thrombophilia.

10. Human amniotic fluid stem cells culture onto titanium screws: a new perspective for bone engineering

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The use of titanium plates and screws for osteosynthesis is considered to be an effective treatment for different kinds of fractures in orthopedic surgery. The aim of the present study is to test the ability of titanium screws to promote the growth of osteoblasts obtained from human amniotic fluid stem cells (AFS). Osteoblastic differentiation was assessed by RT-PCR of specific markers such as COL1, ONC, OPN, OCN, OPG, BMP-4 and Runx2. Mineralization was demonstrated by the presence of red depositions. Adherent cells were found to cover the whole surface of titanium screw by Scanning Electron Microscopy (SEM). The result indicates the excellent growth of osteoblasts obtained from amniotic fluid on a titanium surface and could represent an important point in view of a possible therapeutic application of AFS cells.