

Low Grade Chronic Inflammation and Acute Lymphoblastic Leukemia as a Parameter of Air Pollution

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ABSTRACT

Environmental pollution is not only the cause of environmental degradation, but also represents a danger to our health. Industrialization and technological progress have brought prosperity social and economic but have caused an increase in toxic waste coming from the petrochemical, chemical and plastic manufacturing industries, causing pollution of the air we breathe, of the soil, of the subsoil, of the rivers, of the lakes, of the sea as well as of our water resources. Unfortunately, in these polluted sites an increase in the incidence of pathologies is observed Environmental impact [1,13], among which chronic-degenerative diseases are particularly relevant [2]. The polluting agents present in the environment in which we live are the cause of slow and progressive processes inflammation in our body, not only of the respiratory tract but also of various "target" organs. This process is called mild chronic inflammation. A clinical syndrome that is not easy to diagnose, because it is often correlated with various infections viral or bacterial, or frequently associated with diabetes, heart disease and obesity and often precedes tumors or autoimmune diseases. Most affected are the inhabitants who live in environments polluted by poles industrial plants that release multiple toxic substances (cancerous gases) into the surrounding air, or in cities with areas ports where they attract both cruise ships and merchant ships and with particularly airports trafficked [1,13]. This inflammatory process is acute by the clumsy and excessive use of drugs anti-inflammatories and antibiotics, which in addition to masking any preventive symptoms of serious diseases, they accentuate the bioaccumulation mechanisms in some organs. An example of the gravity of the combinations of environmental pollution and chronic low-grade inflammation (L.G.C.I.) in polluted sites and areas ports and airports is due to the increase in various neoplastic blood diseases. These pathologies are caused by an uncontrolled proliferation of blood cell precursors as occurs in Acute Lymphoblastic Leukemia (ALL) in children, where pluripotent stem cells undergo malignant transformations causing clonal myeloproliferation with subsequent hyperproduction and spread of immature cells that accumulate in the blood, bone marrow and in some organs. Our aim is to highlight a correlation between environmental pollution, in particular atmospheric pollution, and the incidence of neoplastic blood diseases, to place it as a paradigm for the identification of areas at high risk of air pollution (cancer gas) [13]. It is no coincidence that leukemic neoplastic diseases they are mostly present in those inhabited centers equipped with ports and airports as well as industrial hubs in the suburbs that release cancer gases and ionizing radiation into the atmosphere [1,13]. The increase in the incidence of Acute lymphoblastic leukemia in children should be considered as a benchmark of severe form of air pollution in an inhabited place, i.e. an increase in leukemia is found acute lymphoblastic infections in inhabited centers with ports where merchant ships and cruise ships dock, with an airport and often with industrial centers on the outskirts [1,13].

Keywords

Environmental pollution, Chronic inflammation, Stem cells.

Introduction

Environmental pollution can be caused by the qualitative and/or quantitative alteration of the environment, resulting from the direct or indirect action of various factors:

- **Natural:** volcanic eruptions, fires, earthquakes, tsunamis, coastal erosions; changes in the earth's axis.
- **Anthropic:** pollution of the air, water, land, extraction processes and treatment of minerals, industrial manufacturing and combustion processes, manufacturing processes management and disposal of waste, urban decay, migration and changes climate, wars (war events).

Toxic substances present in the environment can reach humans through inhalation, contact or ingestion, causing bioaccumulation mechanisms in different organs or systems over time, which fail to detoxify from exposure to constant and repeated polluting sources over time, causing tissue damage or genetic, with subsequent functional deficits and genetic mutations [1,2]. This inflammatory process is at basis of chronic or acute illnesses, often accompanied by viral, bacterial, or febrile episodes traumatic, and is characterized by a production of inflammatory biomarkers, carried out over time and often unjustified. In chronic-degenerative diseases, the toxicity threshold value is not decisive intended as reference data for the etiopathogenesis of the disease, but the correlation between the contact over time, even with minimal doses of pollutants, and possible mutation or organ damage. Very often, our clinical-therapeutic approach is aimed only at the acute phase of the pathology, without focus on the preclinical, almost silent, problems linked to the polluted environment in which the patient lives patient, thus not allowing the establishment of real threshold values of subjective toxicity. In fact, the damages caused by pollutants is related to the different bioaccumulation mechanisms in target organs and systems, correlated to various chronic-degenerative diseases. The bioaccumulation of pollutants in organs and systems together with viral and/or bacterial and/or traumatic insults can result in a process called **low-grade chronic inflammation** (L.G.C.I.) [3,4], which often represents the starting point of chronic-degenerative pathologies, such as tumors and in our case **Childhood Acute Lymphoblastic Leukemia** (A.L.L.) which causes the greatest clinical-diagnostic difficulties. This disease, initially silent and difficult to be diagnosed, occurs in inhabited areas adjacent to sites polluted by industries that emit cancer gas, in places adjacent to urban centers or in urban centers with ports for cruises or merchant ships or airports [5]. For this reason, there is an increase in the most polluted areas of the incidence of morbidity and mortality of various tumors: lung, colon, kidney, liver, prostate, pancreas, and nervous system, but also of blood cells such as Acute Lymphoblastic Leukemia. As said previously, this disease is difficult to identify because the symptoms are very non-specific it is often misjudged. The main symptoms may be general malaise, persistent tiredness, state of stress, hypersensitivity to odors, muscle pain, headache, dizziness, nausea, tachycardia, lacrimation, respiratory tract disorders and

asthma attacks, dyspepsia, mood disorders, depression, anxiety, cognitive disorders, memory disorders. Chronic degenerative diseases associated with viral diseases or bacterial over time can transform into: rheumatoid arthritis, fibromyalgia, scleroderma, sclerosis multiple, periartthritis nodosa, psoriasis, lupus, ulcerative colitis, autoimmune thyroiditis, allergic rhinitis, forms of asthma, food allergies, but also chronic fatigue syndromes, arterial hypertension, heart disease (heart attacks), diabetes, obesity, Parkinson's disease, some preclinical tumors (lymphomas, leukemia, etc.) [3,4], etc...

Discussion

Considering that it is impossible to escape environmental pollutants, but also various viruses and bacteria it is essential to recognize the subtle and harmful L.G.C.I. early and treat it to avoid it the onset of much more serious complications. Early diagnosis can occur through blood tests some inflammatory biomarkers such as adipocytokines which are produced by adipose tissue: I.L.-1, I.L.-6, I.L.-8, I.L.-19, Tnf-alpha, Ifn-gamma, Leptin, Resistin, which stimulate the production of C-reactive protein and fibrinogen by the liver. Other values to monitor are: ESR, erythrocyte sedimentation rate, this index increases in inflammatory and infectious pathologies, but also in tumors, heart disease and anemia.

Its increase is a sign of organ damage and regresses slowly. P.R.C., the C-reactive protein, is a good indicator of chronic inflammation and occurs both in acute and chronic inflammation. Other inflammatory markers are ferritin, serum amyloid as well as various proinflammatory cytokines produced by our body in response to inflammatory episodes [6]. Our goal is not only to create a correlation between environmental pollution, especially the atmospheric one, and the incidence of blood diseases, but to place it as a criterion reference point for the identification of areas at high risk for air pollution (cancer gas) [7]. A widespread example of this concept are leukemias and lymphoblastic leukemia Acute in children [7]. The etiology of Acute Lymphoblastic Leukemia (ALL) in children is complex and not fully understood which, like LGCI, begins in the womb and involves a combination of genetic and environmental factors and, probably, immunological.

Some of the key elements include:

1. **Genetic Factors:** Genetic predisposition plays an important role in correlations with leukemia, since it is frequently linked to a chromosomal anomaly called "Philadelphia" due to an improper union of part of chromosome 9 and 22 which gives rise to the production of "a protein" modified which is the cause of mutations in the leukocyte precursor cells. Some children, therefore, they appear to be born with already inherited genetic abnormalities that increase the risk of developing the disease A.L.L [8].
2. **Exposure to polluted sites:** Some environmental factors can increase the risk of developing A.L.L. For example, exposure to ionizing radiation or radiotherapy and some chemicals, such as benzene, nitrogen dioxide, glyphosate [1,9] and

some heavy metals (lead, aluminum, nickel, titanium, iron, phosphorus, zinc, copper, etc.), are often correlated with the onset of leukemia. In fact, an increased incidence of the pathology has been found in areas heavily polluted by dust ultrathin (PM 2.5). These pollutants can cause genetic changes in cells hematopoietic stem cells, leading to uncontrolled proliferation of lymphoblasts.

- 3. Early exposure to infections:** The hygiene hypothesis postulates that early and frequent exposure to infections during childhood can have a significant impact on the immune system. When children are exposed to common infections, their immune systems are stimulated respond and develop immunological memory. This early "education" of the system immunity appears to contribute to its long-term maturation and regulation. It is hypothesized that a well-trained immune system has a greater ability to recognize and control abnormal cells, thus reducing the risk of developing diseases such as ALL. On the other hand, a lack of early exposure to common infections could compromise it adequate development of the immune system [10].
- 4. Immune Alterations:** The role of the immune system in the development of A.L.L. Some studies suggest that genetic alterations of the immune system, both during pregnancy and in the first years of life, can contribute to immune failure cellular surveillance, which allows mutated cells to proliferate.
- 5. Correlation of air pollution:** Ultrafine particles PM 2.5, benzene, and carbon dioxide of nitrogen, but also from heavy metals, produced by vehicular or naval traffic, penetrating the cells they can bring about genetic mutations, already in the womb. This problem is particularly accentuated also in patients undergoing organ transplants.

This disease manifests itself with sudden and repeated febrile episodes over time, sometimes poorly evaluated since not correlated with the slow and insidious signs that precede the acute phase of A.L.L. childish. Such symptomatology is characterized by deficiencies of normally functioning red blood cells, platelets and lymphocytes by recurrent infections, frequently viral or sometimes bacterial traumatic, supported by often non-specific symptoms with: pallor, asthenia, weight loss, tiredness, night sweats, bruising, easy bleeding, joint pain, loss of appetite, headache, nausea, and enlargement of the lymph nodes and sometimes of the spleen and liver. Bruising and easy bleeding represent a full-blown state of A.L.L. The correlation between environmental pollution, low-grade Chronic Inflammation, and blood diseases, so much so that we could use this data as a reference criterion in identifying particularly polluted environments. Our considerations consist of starting from epidemiological data regarding diseases blood cancers to highlight the excessive air pollution of certain areas which may be closely linked to low grade Chronic Inflammation. So, you must pay attention pay attention to infections and recurrent feverish episodes in children, especially those who live

in environments polluted. For this reason, in environments with intense air pollution, this clinical condition it must immediately be investigated with specific diagnostic tests, and in doubtful cases up to a biopsy bone marrow and genetic tests. In addition, in these patients suffering from blood disorders may result.

It is useful to measure certain toxic substances such as benzene, nitrogen dioxide, glyphosate, and some heavy metals (lead, aluminum, nickel, titanium, iron, phosphorus, zinc, copper, etc.), dioxins and PCBs which affect the birth and proliferation of tumor cells, but also on the success of experimental therapeutic programs or on a possible lack of response therapeutic [11]. Our proposal consists in starting from epidemiological data regarding diseases of blood and specifically L.L.A.I. to highlight the excessive air pollution of certain areas. In fact, the study of genetic mutations is bringing about great reevaluations both etio-pathogenetic and therapeutic of various diseases, especially tumors, and new implications therapeutic in cases of lack of or reduced therapeutic response.

Conclusions

In conclusion, the L.G.C.I. it is a silent killer that slowly wears away tissues and organs in our body changing our state of health. Our body has a well-tested defense mechanism that is the inflammatory reaction against trauma, bacterial, viral, fungal infections, and such reaction it can be immediate or acute or progressive over time or chronic. The latter represents one sort of failure of our immune defenses and is the basis of chronic-degenerative pathologies such as those of tumors, cardiovascular, diabetes, obesity, etc. The connection with pollutants atmospheric diseases and chronic-degenerative diseases, especially blood tumors, is evident. In fact, the case of A.L.L. childhood, described by us, represents the air pollution-disease combination that we can (highlight) in evaluating the presence of polluting sources the air we breathe, for the presence of ports, airports, cancer gas industries, adjacent to population centers. In fact, we need to evaluate the presence of these substances in the atmospheric matrix, but also in other environmental matrices, which follows both qualitative and quantitative evaluation of toxic substances in different human matrices, to discover any clinically silent diseases such as L.G.C.I. Therefore, it could be useful to evaluate any correlations with foods (both of plant origin and animal) and with clothing worn, especially by younger people, such as nylon, acrylic, polyester with phthalates, etc., all petroleum derivatives, which may contain many toxic substances as well dyes which, if absorbed, can cause allergic reactions, skin or organ inflammation e can interfere with the endocrine system (fertility, obesity, diabetes, asthma, etc.) of our body, to evaluate a possible bioaccumulation in some organs of these toxic substances or their metabolites, evaluating the harmful effects or the diseases related to them. This would allow the processing of primary and secondary prevention measures in risk areas. Therefore, it is essential to quantify the presence of toxic substances in polluted areas and in the biological matrices of the people they live in these polluted places to discover any clinically silent or already paucisymptomatic diseases L.G.C.I.

and the possible correlations with the pollutants present in that area. Biomonitoring, even at a young age, can be a useful and well-validated tool for evaluating the individual accumulation of pollutants and the related risk of possible diseases both as LGCI and therefore of LLAI. Populations and matrices must be selected based on specific objectives and criteria scientific and within adequately structured study protocols, preferably born from paths participatory initiatives that involve communities, researchers, but mainly institutions. Obviously, the results obtainable with biomonitoring are today correlated to the available resources (funding, availability of competent laboratories and researchers). The commitment of scientific and political organizations, but also of health system, academia and research should be aimed at protecting the health of people inhabitants and promote the prevention of diseases and the remediation of polluted environments. In particularly polluted places, personalized, predictive, preventive medicine must be introduced, participatory, with collection of clinical, diagnostic, genetic, molecular data and with a clinical approach multipurpose, which involves all health guardians from epidemiologists to general practitioners and others specialists to allow prevention programs for the various pathologies occurring in that place in such a way preventative medicine must be implemented with global participation and consensus. In conclusion, the increase in acute lymphoblastic leukemia in population centers with ports and airports is the sign pathognomonic of a serious form of air pollution, for which both children and adults, in addition to traditional clinical-instrumental diagnostics (image diagnostics) that normally comes performed to ascertain an ongoing pathology, it is important to start quantifying the presence of substances toxic in different biological matrices (in blood, hair, urine, breast milk and others organic liquids) of individuals who live in environments with strong air pollution, whether sick or clinically healthy, this could help to discover pathologies that are not yet clinically manifest, as well as evaluate the pollutants [12] present in these territories and their correlation with certain diseases, this is valid also for neoplastic blood diseases and in particular for A.L.L. The presence of repeated and frequent feverish episodes in children should make us think about the possibility of possible blood diseases and in this case of forms of leukemia. Unfortunately, it is not always easy to make the right to health prevail on economic interests. In conclusion, it would be appropriate to consider some pathologies as an index of air pollution in urban centers with ports, airports, and with heavy car traffic (city gases) this may make us suspect the possibility not only of chronic-degenerative diseases (L.G.C.I.), but also of blood diseases and in this case leukemic forms such as A.L.L [13].

References

1. Ruffolo P. Environmental pollution and causal link: From early diagnosis to prevention of tumors: Manual on pollution and possible damage to health.
2. Ruffolo P. Report entitled Therapeutic Problems of Toxic and Remediation Substances. Environmental at the Conference on Risks from Environmental Pollution: Characteristic Pathologies. Healthcare. Risk Assessment and Insurance Transfer Issues. The Code of Medical Ethics. Conference Room of the Order of Doctors of Naples. 9; 23: 23.
3. Ruffolo P. Report entitled Environmental Pollution and Low-Grade Chronic Inflammation at I Care Conference... Low Grade Chronic Inflammation. Mostra d'Oltremare Naples. 29; 10: 23.
4. Ruffolo P. Report entitled Environmental Pollution and Low-Grade Chronic Inflammation at Low Grade Chronic Inflammation Conference in Family Medicine. Grand Hotel Salerno. 2; 12: 23.
5. <https://www.anconatoday.it/attualita/pollution-ancona-dati.html> Article published on Ancona Today with the title Nitrogen Dioxide, environmentalists raise the alarm: "Ancona's air? Sick".
6. Alain Menzel, Hanen Samouda, Francois Dohet, et al. Common and Novel Markers for Measuring Inflammation and Oxidative Stress Ex Vivo in Research and Clinical Practice—Which to Use Regarding Disease Outcomes? Antioxidants (Basel). 2021; 10: 414.
7. McNally RJ, Parker L. Environmental factors, and childhood acute leukemias and lymphomas. Leuk Lymphoma. 2006; 47: 583-598.
8. www.aieop.org Acute Lymphoblastic Leukemia: Disease Fact Sheet.
9. <https://www.rsi.ch/info/mondo/Glifosato-e-leukemia-trovato-un-legame-1996747.html> Article published on RSI entitled Glifosato and Leukemia: a link found by ATS/RSI info. 21; 11: 2023.
10. Birch JM, Alexander FE, Blair V, et al. Space-time clustering patterns in childhood leukaemia support a role for infection. Br J Cancer 2000; 82: 1571-1576.
11. Ruffolo P, Acquaviva O, Capece P, et al. From the Histological Model to the Mutational Model: The Study of Heavy Metals and Other Substances in New Antineoplastic Therapies Glob J Med Res 2023; 23: 7-9.
12. Ruffolo P, Acquaviva O, Di Giacomo R, et al. Lung tumors: "vox clamantis in desert".
13. <https://www.ilfattoquotidiano.it/2023/12/14/gravissimo-il-danno-alla-salute-pubblica-in-provincia-di-napoli-ma-passa-tutto-sotto-silenzio/7381053/> Article published on the Fatto Quotidiano Blog by Antonio Marfella.