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Is Lymphoma Cancer, Auto-immune disorder, or Complicated Tuberculosis

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Introduction

I have been pre-occupied with a basic hypothesis regarding the true nature of lymphoma that I would like to present to an audience of health professionals in the hope of provoking informed discussion among colleagues in the medical community. My ultimate purpose is to bring greater clarity to the true nature of lymphoma, its diagnosis and treatment. I am on a difficult path in terms of challenging a prevailing view regarding this disease, and I am hoping for an open discussion and a reasoned approach to address the issues. It is my firm belief that sciences advance only by challenging the prevailing wisdom, even though not all challenges are well-targeted or technically justified. I base my views on focused personal observations and 8 years of literature review.

Initial Observations

The first set of issues are centered on Lymphoma as cancer

1. It is impossible to identify a single malignant lymphocyte based on morphology alone.

2. The morphologic appearance of typical CLL is not distinguishable from that of normal lymphocyte.

3. Clonality does not prove malignancy with certainty. More specifically,

4. A lymphocyte of reactive lymph node looks like lymphocyte from a lymphoma node.

5. There is growing evidence that MZL is associated with chronic antigen stimulation.

The second set of issues are centered on Tuberculosis (TB)

1. The *Mycobacterium* TB is a unique fatty shell (mycolic acid). It cannot be classified as a fungus or a bacterium, hence the composite name. It is also unique because it is not invasive.

2. It does not secrete toxins but enzyme that causes localized damage.

3. It replicates slowly in 20 hours, compared to other pathogens which occur in minutes or seconds.

4. It is difficult to diagnose among the elderly or when there is immunity failure (e.g., cryptic miliary TB). Diagnosis among elderly is possible only by therapeutic trial.

5. Infection is prevalent in certain populations, nearly 1/3 or more than one-half of the population I some countries test positive for TB, especially if we consider 20% to 50% of those who test negative are in reality positive. This means that more than 3/4 of people in some countries are positive or latent, i.e., TB is dormant or inactive.

6. The relationship between lymphoma and TB was originally suggested in 1832 by Thomas Hodgkin, world-renowned British pathologist (1798-1866), after whom this cancer is named, as well as others later.

7. A comparison between HIV/AIDS infection from chronic antigen stimulation and TB as an immune deficiency presents a somewhat analogous scenario, though not a replica. Moreover, they differ in terms of prevalence: HIV/AIDS among the young and TB in older age.

8. The role of MTb in the development of lymphoma:

a) Responsible for chronic antigen stimulation.

b) Provokes mutation in host cell (MTb is the pathogen responsible for the largest number of gene mutations).

c) MTb can also have access to MHC class1 (found on surface of host cells responsible for identification, if cell is own).

i. The first contagious contact with human body usually occurs via the respiratory system, but less frequently via the digestive system, mucous membranes or skin abrasions. The first contagion of Mtb spreads to all tissue in the human body (secondary TB is revived from an old or dormant primary nodule). During the first 3 weeks to 4 weeks of contagion, the immune system learns to resist the infection. Hence, another contagion cannot spread due to the body's competent immunity. Instead, it is destroyed or arrested in place (KOCH phenomenon) in the majority of cases, >90% stay dormant (latent, non-active) until it has the opportunity to revive and become patent, i.e., active or overt.

9. The onset of morbidity beginning during the first 3 weeks to 4 weeks of contagion is referred to as primary, which usually heals and transforms into latent. Later, it transforms to patent or secondary TB. But there is a risk for it to be continuous, especially in infants. Also, TB can be reactive immunity competent and non-reactive, defective immunity (cryptic miliary tuberculosis).

10. It is not wise to eradicate MTb, rather domesticated (by BCG) because like the herder taking care of the cattle (i.e., the human body); the MTb browses and protects from predators.

Why is lymphoma treated with immunosuppressive drugs rather than antibiotics? The standard treatment is directed toward auto-immunity, induced by MTb (a complication(, which is normally responsible for the acute features of the disease. However, this treatment leaves TB in the background as chronic indolent disease even though the cause is TB.

Due to inherent features of autoimmune disorders, TB can take 3 age-related forms.

1. At the age <65 years when immunity is optimal and laboratory ancillary are helpful.

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2. At the age >65 years when there is some immunity failure with difficult diagnosis.

3. Tb with auto immunity disorder (lymphoma), the emergence of gene mutation of host cells by TB, which becomes unrecognized by the immune system as body's own cells.

I do not know if MTb induces mutation in host cells. Nonetheless, it is not unreasonable to expect the immune system to attack normal host cells when they are mutated. Karyotyping and cytogenetic in the diagnosis of lymphoma could potentially provide strong support for the hypothesis that lymphoma is a form of tuberculosis complicated by mutation, led by auto-immune disorders, or alternatively an immunodeficiency problem provoked by gene mutation, which leads to changes on the surface of host cells where MHC exist. The clinical symptom and blood profile are similar in the three forms of TB. However, tests for diagnosis differ by TST, X-ray, and cytology. They may be negative in some cases, as in type 2 above, and in all cases in type 3. This might explain disjuncture between lymphoma and tuberculosis as unique diseases. We now we know about the difficulty of diagnosing TB among the elderly. Some authors have added to the classical symptoms of TB: -shoulder pain, sore throat, bowel irregularity, and kidney malfunction. MTb is the first contact while spreading in all tissues of the body. They stay there for life, and can imitate a myriad of ailments, depending on area of residence, cardiac irregularity, and many other diseases and ailments among the elderly such as Parkinson's and others. They also act as a mimicker. Auto immunity induced by TB to the lymphatic system is typically labeled as lymphoma for the synovial, rheumatoid arthritis for thyroid (Grave, and so on for all autoimmune disorders). Some authors also defined HIV/AIDS (acquired immune deficiency syndrome) as being caused by: -1-HIV, 2-Non-Hodgkin, 3-Caposi Sarcoma. The first cause is the destruction of CD-4 lymphocyte, the second and third explanations go in the opposite direction. I propose another cause, namely old age with chronic antigen stimulation by MTb as the other possible pathogen. The core of the problem is immune deficiency. Simulation by MTb provokes damage to genetic structure resulting in autoimmune disease or cancer. The target in type 2 TB is a deficient immune system. Although elementary, I believe it is important for us to understand why a successful treatment for TB does not work for lymphoma. TB attacks the immune system by making changes in host cells gene, thereby resulting in damaged gene, which makes it no longer recognizable by the body's immune system. All this results in a situation whereby TB is no longer on the front scene, it becomes indolent. Hence, the priority for treatment is for lymphoma later, whereas treating TB may prevent the relapse of lymphoma. What encourages me in the study of lymphoma when TB may be suspect is the presence of bits and pieces of information in the medical literature that can be combined to form a coherent and meaningful picture regarding a suspect disease. Indeed, I found similar views in the literature regarding autoimmunity and gene mutation. Accordingly, views provided by different authors can be joined together to form a meaningful and logical picture, namely that lymphoma is a manifestation of an autoimmune disorder provoked by TB (forming a complicated TB). One cannot believe that the immune system would attack normal cells when there are mutated host cells. The use of karyotyping (cytogenetic) for the diagnosis of lymphoma supports this view. in brief, (1) the immune system does not attack normal host cells; (2) all lymphomas constitute one unique disease; (3) in (TST+) among patients, not only 5% to 10% develop active TB among the aged, but all by one of the unusual diverse manifestations of the disease (acting as a mimicker or pretender), thereby rendering the diagnosis of TB difficult. In essence, my perspective on the misdiagnosis of lymphoma is based on the fact that the immune system does not attack normal host cells. Gue provided further support for this view on the basis of similar arguments, as follows: (1) uniqueness and ubiquity of MTB; (2) all lymphomas are one unique disorder or disease; (3) the immune system does not attack normal host cells; (4) similar to HIV, the revival of TB nodules already exists at any age, whereas in TB, the revival of TB nodules typically occurs in old age. AIDS results from an HIV infection. Adenopathy from TB needs much more than 6 months to regress while adenopathy from lymphoma needs few days; (5) if healing of MZL (MALT) by elimination of *Heliobacter* why can't be the same for MTB and other lymphomas? (6) The presence of MTb on the scene is not as a spectator, but an essential player to induce autoimmunity; (7) lymphoma is atypical tuberculosis (Ewing).

Conclusion

In conclusion, a scrutiny of the extant literature on TB and lymphoma supports the view that lymphoma is an autoimmune disorder provoked by cell mutation. In essence, it is a form of TB. Hence, contrary to professional wisdom, it is an infection not cancer. I hope the views presented in this short article would provoke reasoned discussion and vigorous debate among interested colleagues in order to arrive at a better understanding of this disease and its appropriate treatment. TB originated in the Fertile Crescent and areas neighboring Africa, and has been considered as a grave predicament to the world. It is time we correct the diagnosis and treatment of lymphoma.

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