

The Relative Fewness of Renal Metastases in Lung Cancer is Probably Explicable with the “Erythrocyte Associated Necrosis Factor” which may be an Oncobiomarker

Keywords: Cancer; Spread; Thoracic duct; Necrosis; Cannulation; Pabulum; Retrieval; Translational research; Oncobiomarkers; Target therapy; Cancer cure

Abstract

There is profundity of lung cancer cells thrown into the circulation with each heart beat and the quantity of the quarter of the cardiac stroke volume being delivered to the kidneys. Despite both of these attractive attributes, renal deposits are so few as to constitute an anomaly asking for solution through recondite research. Such a situation was clearly pointed out in his 1955 Harveian Oration by Melville Arnott who mentored the profession by promoting the theory that an anomaly is actually Nature's own way of pointing to the researchable phenomenon of lung cancer spreading preferentially to the ipsilateral adrenal gland. This was acknowledged in Professor Cappell's 1958 Edition of Muir's Text-Book of Pathology. Thereafter, during fully fledged training at his Department, the author realized that a Mono-Block Formalin-Fixation Method was ideal for lung cancer investigation. As serendipity would have it, the 45 cm long thoracic duct was coiled up in Swiss-roll fashion and therefore became processable on a single microscopic slide. This opened up a panorama, namely, that lung cancer cells were being carried more or less leisurely through this curious conduit at the moment of death. In particular, there was cogent conclusion that “Necrosis of the cancer cells was apparent in 3 cases, but it was clear that this had occurred in association with large aggregates of the malignant cells and that among such aggregated cells red blood corpuscles abounded”. This 1967 conclusion awaited the revolutionary development of the intravital videomicroscope in the realm of human research. Thus, on obtaining consent from lung cancer patients, cannulating them would ensure the retrieval of the above necrosis-associated pabulum. Thereafter, the performance of translational research would follow, especially as funding has reportedly been generous. In other words, Nature has offered opportunity to obtain materials for that target therapy which could be geared towards cancer cure. To this end, it has been hypothesized that there is an underlying “Erythrocyte Associated Necrotic Factor” (EANF). Moreover, to counter the usual problem of doubt, such a hypothesis needed to have supporting data with an explanatory power. Such data were, therefore, provided at some length. Here, the hypothesis is grounded on the unique position of the glomerulus. In addition, there is the closing emphasis on pursuing whether EANF is an oncobiomarker whose usage can be expedited with the help of consenting patients from whom the vital pabulum would be retrieved and its intrinsic nature identified and utilized.



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Introduction

Lung cancer is so supremely situated as to drain directly into the pulmonary veins [1]. On this account, millions of these cells have been quantitated in the circulation [2]. Accordingly, the anomaly arose naturally as to why an organ such as the kidney does not brim with metastases [3] while taking a quarter of the aortic output [4].

On the personal side, the author had the opportunity to get trained under Professor D. F. Cappell at the famous Glasgow Western Infirmary [5]. As the fate would have it, the British Medical Journal had been offered to students at a reduced price. Since the author had opted for this, he soon noticed that many articles were based on just 100 cases. Soon, it was realized that lung cancer usually spreads preferentially to the adrenal gland on its own side. This led to amassing 1000 cases which were published in 1957 in the British Journal of Cancer [6]. Moreover, Professor Cappell bolstered matters by highlighting this result in the 1958 edition of the world famous Muir's Text-Book of Pathology [7].

During personal Residency training that followed, the ensuring experience in the Dissection Room soon led to abandoning the cutting of parts and displaying them separately on the Table. Therefore, this encouraged the formulation of the “Mono-Block Formalin-Fixation Method” for investigating lung cancer spread [8]. Moreover, since serendipity surfaced, on coiling up of the 45 cm long duct in Swiss-roll fashion, there was the very visualization of lung cancer cells as they more or less wended their way up the thoracic duct at the moment of death. Thereafter, it was concluded: “Necrosis of the cancer cells was apparent in 3 cases, but it was clear that this had occurred in association with large aggregates of the malignant cells and that among such aggregated cells red blood corpuscles abounded”. The sublimeness of this observation led naturally to the phase of hypothesizing.

Past Hypotheses

The author's first hypothesis appeared in Medical Hypotheses in 2013 [9]. Therein, it was argued that the above conclusion merited the recognition of the natural work of an underlying “Erythrocyte Associated Necrosis Factor” (EANF). Since one way of substantiating a hypothesis is the formulation of supportive hypotheses i.e., the

“operational power” which Brandon Reines spotted, the author made appropriate use of it in several Journals [10], via, (i) Single Cell Biology [11], (ii) International Journal of Surgery [12], (iii) Translational Medicine [13], (iv) Translational Medicine [14], (v) Journal of Cancer Prevention & Current Research [15], (vi) International Journal of Clinical Chemistry and Laboratory Medicine [16], (vii) Pulmonary & Respiratory Medicine [17], (viii) Immunochimistry and Immunopathology [18], (ix) Translational Medicine [19], (x) Research Chronicles in Health Sciences [20], (xi) Translational Medicine [21], (xii) Archives in Cancer Research [22], and (xiii) International Journal of Cell Science & Molecular Biology [23].

Present Hypothesis

The kidney merits consideration as regards its low capacity for developing cancer metastases. As stated earlier [3], this is an organ very well supplied with blood. However, its anatomy ensures close admixture of cancer cells and red cells in the glomeruli. In this context, whereas in the thoracic duct, the medium is lymph, in the kidney, it is blood. However, the enabling element of close proximity is the same, this being a requisite aspect of the “Erythrocyte Associated Necrosis Factor”. In other words, the close interactions in this miniature histopathological unit are responsible for the infrequency of renal metastasis.

Discussion

The famous German pathologist, Julius Cohnheim held that the findings at autopsy “are all in a manner experiments instituted by nature, which we need only rightly interpret to get a clear idea of the causes, laws of growth, and significance of the tumor” [24]. Elsewhere, the author showed that the medical masters of the past were conscious of Nature’s norms in cancer carriage [25].

Not averse to animal experimentation, the author did some work on the Brown-Pearce carcinoma of the rabbit and produced the cognate in the paper on the surgical significance of mediastinal metastases in lung cancer [26]. It illustrated “the right testis of the rabbit with bilateral metastasis of the contiguous lymph nodes and tissues”. As was continued, “ipsilateral preponderance of the secondary deposits is apparent”.

In the context of the importance of the autopsy in advancing knowledge, there is the overlooked bonus concerning the author’s 1963 special method [27]. In it, the centrifugally metastasized lymph nodes in the abdomen were carefully traced as regards the earliest deposits arriving from lung cancers. In doing so, newly formed lymphatic channels were mentioned six times. Now called “lymphangiogenesis” it was reviewed [28]. Lymphangiogenesis is today a prevailing target in cancer therapy [29]. Regarding such potential therapeutic targets, Australian researchers provided 231 references [30]. There was no reference, however, related to the author’s initial publication! Hopefully, EANF gains more ground, and receives sufficient funding [31]. With proper referencing, translational laboratories could do some good work in regard to target therapy that could conduce to cancer cure soon.

In conclusion, let the very nature of EANF be determined as to whether it is an oncobiomarker or not. This can surely be obtained by simply cannulating the thoracic duct of consenting lung cancer

patients and then using the intravital videomicroscopy not only to retrieve the named necrosis-based material but also to use it as a breakthrough in the proclaimed war on cancer. As Mehlen and Puisieux lamented, metastasis is a question of life or death. Perhaps, this paper is capable of helping to answer in the direction of life! [32].

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