Review

Anomalous lung cancer cell carriage: A historical review with present prospects

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A R T I C L E  I N F O

Article history:
Received 16 May 2014
Accepted 19 May 2014
Available online 24 May 2014

Keywords:
Lung cancer
Contralateral lung
History
Anomaly
Explanation

A B S T R A C T

It is a scientific axiom that anomalous findings may imply imperfections in current concepts and are often a stimulus to discovery. Therefore, this article surveys the publications extending from 1818 to 1897 in order to quantify the experiences of the medical masters because they were perturbed that, at autopsy, lung cancer cells usually failed to cross the midline to the opposite lung. Accordingly, there is need to recognize that this is actually an anomalous phenomenon which requires explanation. In all probability, the anomaly is explicable on the basis of the workings of a hitherto hidden Factor which originates in lung parenchyma. Therefore, it is argued that the Factor would perform best in the contralateral lung. Finally, it is hypothesized that its conspicuous effect in the contralateral lung is what explains the anomaly of low or no colonization of that most eligible site in the body. Incidentally, surgical cannulation and videomicroscopic retrieval of dying and living cancer cells will provide subsets for research on the phenomenon proper.

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1. Introduction

Historical instances of the anomalous behavior of the lung cancer cell in scarcely invading the contralateral lung were reviewed [1–33]. Hence, following the academic interest manifested during the 1955 Harveian Oration concerning the role of anomaly in scientific research [34], these examples were put to good use not only as to why such oddities occur but also as to their possible utilization in the important search for a breakthrough in the target therapy of lung cancer.

2. Historical texts

The writings of the medical masters of the 19th century merit review. In particular, because lung cancer was new then in the scientific horizon, it was being observed with considerable interest and exactitude. Accordingly, it is important to present from 1818 to 1897 a series of them[1–27], especially as there was the general surprise that, against all expectations, the cancer cells in the one lung generally failed to cross over to the other lung.

Lung cancer cases have, therefore, been portrayed chronologically with regard to the year of publication, author(s), limitation to lung of origin, and access to the contralateral lung. See the accompanying table.

Table 1 presentation is not sufficient to properly portray the nuances of the descriptive words used in the individual cases. Thus, apart from invasion of the contralateral lung being outnumbered in the ratio of 6:1, the crisp comments concerning that lung were in terms of its being “healthy,” “sound,” “free,” “natural,” “normal,” or “not remarkable.”

Remarkable opinions are in themselves noteworthy. For instance, Stokes [4] differentially diagnosed tuberculosis from cancer on the firm basis that the cancer is associated with “the healthy state of the opposite lung.” Sims [2] waded into the debate on whether this growth arose in the mediastinal lymph nodes or in the lung itself by arguing that “the disease was nearly always unilateral, starting from the root and radiating inwards along the branches of the bronchus.” Similarly, with regard to the left lung cancer encountered by Finlay [21], he was surprised at the identical microscopical appearances found in it and in the associated numerous growths and remarked: “Another point of interest lay in the fact that the right lung presented not even a trace of nodular deposits.”

Deposits being mostly limited locally were portrayed also in monographs. On considering the 1846 Continental contribution of Hasse [28], he was conversant with the extant literature for he concluded thus: “Primary medullary infiltration is, as would appear from the few observations hitherto described with sufficient accuracy, characterized by one lung being exclusively involved, the other remaining exempt.” From England, Sutton [29] stated that
“One bronchus is chiefly involved, but the other perhaps a little also.” From USA, Flint [30] painted the picture of lung cancer “Occupying the greater part or the whole of one side (oftener the right), and sometimes encroaching more or less on the other side of the chest.” Another American [31] appreciated that “Primary cancer usually involves only one lung.”

3. Present prospects

The above assembled data exhibited graphic descriptions which have consistently been those of anomaly. Now, anomaly was emphasized in the 1955 Harveian Oration by Melville Arnott [32], who propounded thus: “Scientific principle requires us to be ever watchful for the unexpected and the anomalous; for these may imply imperfections in our concepts and are often a stimulus to discovery.” Therefore, it is instructive that from 1818 to 1897 painstakingly recorded autopsies revealed that most lung cancer cells anomalously failed to cross the midline to the opposite lung. Accordingly, the prevalence of this phenomenon deserves research especially because the contralateral lung occupies a premier position in lung cancer metastasis as follows:

1. The soil is similar.
2. The site is just across the midline.
3. The arterial blood supply is direct from the aorta.
4. The venous blood returns cancer cells from the various organs equally.
5. The thoracic duct directs cancer cells from the cisterna chyli equally.
6. The vertebral venous system provides rich interconnected networks to both lungs.
7. The invaded lymph nodes return cancer cells into both lungs.

Therefore, what is at stake? Assuredly, millions of lung cancer cells daily gain direct entry into the blood circulation [33–35], hence, in view of the above listed incontestably advantageous pathways, the contralateral lung is positioned so exceptionally as to be overwhelmed generally by the circulating cancer cells. Nevertheless, from all accounts, it is scarcely involved! The significance is necessarily worthy of explanation.

In all probability, there must be a natural Factor, a hitherto hidden Factor, that ensures that these cells reach but do not destroy the contralateral lung. In this context, if such a Factor exists, it is likely to be acting along predetermined principles.

Such principles were sought personally by using the monoblock formalin-fixation method [36] for investigating lung cancer cell dispersal in general. In particular, having with this method obtained 40 whole-length thoracic ducts [37], they were carefully coiled in Swiss-roll fashion. The giant paraffin blocks so formed were cut flat with the sledge microtome and prepared as single slides. On this account, I was able, in my British Journal of Cancer paper, to present the picturesque panorama of lung cancer cells as they were being carried up from the cisterna chyli at the moment of death. Propitiously, the most spectacular finding was clear as follows: “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.”

Another positive result of the investigation came from the study of inch-square pieces cut out from the base of the contralateral lung. In this location, necrosis was also demonstrated even among small clumps of cancer cells.

Clearly, necrosis of lung cancer cells occurs both in the thoracic duct and in the contralateral lung. The unknown Factor responsible for such necrosis must be keyed to lung tissue. Signaling, on this account, would perform best in the soil of the contralateral lung. Therefore, it is hypothesized that its conspicuous effect in the contralateral lung is what explains the anomaly of low or no colonization of that most eligible of all sites in the body. Incidentally, surgical cannulation of the thoracic duct [38] and videomicroscopy [39] will help to retrieve the necrotic material, thereby paving the way to recognize the underlying factor.

Ethical approval

Not required.

Author contribution

None.

Funding

Self funded.

Conflicts of interest

None.

References


