

The Scientific Significance of the Role of the Thoracic Duct in Cancer Cell Carriage: A Review

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Abstract

This paper draws attention to the historical role of the thoracic duct in cancer cell carriage. It begins with the 1798 weighty work of the great Sir Astley Cooper who (i) believed that the thoracic duct was a vessel of much importance in the animal economy, (ii) carried out experiments on cadavers and dogs and (iii) autopsied a man who died with testicular cancer that had spread all the way through the lymphatics of the spermatic cord to the thoracic duct. Succeeding other eponymous giants like Paget, Hodgkin, Warren, and Andral contributed their own quota to the knowledge of cancer carriage through this conduit. No wonder that, by 1895, classical embolic metastasis was firmly on record. A weighty modern textbook was cited. Then, attention was drawn to the observations made on 40 coiled-up thoracic ducts. It was concluded that necrosis of cancer cells occurred naturally in some ducts during transportation from the abdomen to the neck and back to the chest by the moment of death. Consequently, it was hypothesized that, if the actively dying cells are retrieved from consenting patients by way of cannulation and videomicroscopy, the scientific replication of this normal phenomenon would in all probability point to target therapy and eventual cancer cure.

Keywords: Thoracic duct; History; Cancer; Carriage; Hidden Factor; Retrieval; Target therapy

Introduction

Academic interest was manifested in a Manchester University dissertation wherein it was stated that “Looking back over the history of the lymphatic system, it is clear that there have been periods of great activity followed by periods of rest” [1]. In an inaugural dissertation defended at the University of Zurich, Brunner [2] affirmed that the thoracic duct “shows itself to be of extreme importance as a path for metastasis in primary and secondary malignant tumours of the abdomen”. Earlier, Young [3] dissected the thoracic duct in 150 consecutive cases of tumor deaths, collected significant data and paid tribute to the account that Astley Cooper gave as far back as 1798.

Historical Texts

Therefore, it was gratifying to find, as regards that great man, that he had long and abiding interest in this duct. Thus, Cooper [4] had asserted that “The thoracic duct is a vessel of so much importance in the animal economy”. He had discovered by both quicksilver injection and disease observation “that nature, with a kind regard for our preservation, has provided security against this evil,” namely, through the provision of functioning collateral branches and anastomosing vessels. He gave detailed accounts of a postmortem case and three animal injection experiments. Here, it suffices to abstract his case of a 22-year-old man with right testicular cancer. He found that the lymphatics of the spermatic cord contained the same matter as that existing in the testis. Moreover, diseased coalesced lymph nodes exhibited the same matter. In particular, what of the thoracic duct? He extensively wrote:

The appearance of the thoracic duct was much altered: its coats were thickened and opaque, and it was rounder than usual, bearing more resemblance to a nerve than to the principal trunk of the absorbent system.

The receptaculum chyli was filled with matter of the same kind with that found in the tumour, in the absorbents of the spermatic cord, and in the body of the testis. It adhered with firmness to the inner coat of the vessel, which was thickened, opaque, and irregular.

The thoracic duct had undergone a similar change, for in its cavity a substance was obtained, resembling that in the other diseased parts, by which the tube was rendered impervious.

In his later lectures on breast cancer, Cooper [5] drew attention to some invaded lymph nodes present above the clavicle. As he put it, “by pressure on the thoracic duct they cause an interruption to the process of absorption: chyle is prevented from being transmitted into the blood ...”

Few years afterwards, Cooper [6] returned to the subject in his book on the testis. In particular, he mentioned placing, in St. Thomas’s Hospital Museum, the preparation of “thoracic duct obliterated by this disease, and at one part forming a tubercle as large as a walnut”. Incidentally, in those days, as I personally documented elsewhere [7], “tubercle” was interchangeable in the literature of both tuberculosis and cancer.

It is noteworthy that Cooper [6] had also taken the trouble to describe negative findings. Thus, in another cancer report, he was specific. “The thoracic duct,” he remarked, “was healthy; but there was a small gland attached to it, which appeared to have been attacked with the same diseased action”. In this connection, it is remarkable that Frerichs [8] observed that liver cancer could extend to the lymphatic glands in its fissure and “occasionally along the thoracic duct to the deep cervical glands”.

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Of some interest was purposive search of the thoracic duct for evidence of cancer carriage and its reportage even when this proved negative. Thus, concerning a pelvic primary tumor, Farre [9] wrote: "The lymphatic glands, in the direct line of absorption, were affected with the same disease; but the alimentary canal, the mesenteric glands, the thoracic duct, the pancreas, spleen, and kidneys were free from it".

Paget [10] also searched in vain. In his case report on a peculiar testicular tumor with marked lymphatic extension, he noticed that no deposit was present beyond the level of the renal veins: "Beyond this point no affection of the lymphatic system could be traced. The thoracic duct was healthy, and so were the lymphatic glands of the lungs".

A problem arose as regards the concept of cancer carriage by the thoracic duct. It was Dickinson [11] who discussed it in these words:

It might be inferred from what has been proved as to the independent life of the cancer-cell, that these bodies are taken up by the absorbents and deposited as seeds in the glands and organs traversed. I have, however, repeatedly examined the thoracic ducts in cases of this nature, and never could find anything abnormal either in the canal itself or its contents, and I have been almost led to believe that the cells are not taken up as such, but rather that fluid poison is conveyed.

However, there were other old observers who firmly noted an aspect of this "fluid". This was because they were able to notice the coloration of the transported cancer matter. For example, Earle [12] encountered one such case. As he wrote, "The large lymphatic trunks passing between those abdominal glands, which exhibited the bloody colour in the most remarkable degree, were distended with a reddish fluid". "The thoracic duct," he continued, "contained a similar fluid, and was pervious throughout".

Also fortunate was Hodgkin [13] himself in his classical paper. In Case I, he found the coats of the thoracic duct "perfectly transparent and healthy". The duct in Case III also "presented nothing unusual". As regards Case IV, the lymphatic vessels "were enlarged and distended with a bloody serum" while "A similar fluid less deeply tinged was found in the thoracic duct". The same tinctorial characteristics were so striking in Case V that Hodgkin expatiated as follows:

The remarkable appearance of blood in the thoracic duct and some of the absorbents, observed in the case of Thomas Westcott, (No. IV.,) although it sufficiently attracted my attention to induce me to have a drawing immediately made, was only regarded as an accidental occurrence; but the recurrence of the same phenomenon to a much considerable and striking extent in the recent case, (No. V.,) induces me to suppose that it is intimately connected with this glandular disease.

Little wonder that, not long afterwards, Hodgkin [14] appreciated the exact sequence of events in cases of encephaloid cancer. According to him, such a cancer "like true scirrhus, also extends to the lymphatic glands, through which the absorbent vessels pass, in their way to the thoracic duct or right trunk.

Subsequently, great authorities such as Warren [15], Hasse [16] and Macewen [17] affirmed that spread occurred through the lymphatics to the thoracic duct and beyond. In the explicit words of Paget [18], "The lymphatic glands usually become cancerous in direct succession from the primary disease to the thoracic duct".

In the case of carried tumor tissue, it was microscopical observation as well as animal experimentation that finally led to the discernment of this process. In this respect, the work of Langenbeck [19] stood out. He not only performed animal experiments but also exemplified with

human uterine cancer. From such a primary site, he observed that "the cancerous cellules are quickly taken up, but, being arrested in some point of their course, such as in the thoracic duct, or the capillaries of the lungs, quickly form cancerous masses". In that decade, too, Andral [20] documented his first experience after avowing that he knew of no previously recorded case. As it transpired, when he dissected the thoracic duct of a woman dying from uterine cancer, he found it to be considerably enlarged while "its internal surface was studded with an infinite number of round white bodies".

Walshe [21] was aware of a long standing disturbing problem, namely, whether the communicating lymphatics must show visible evidence of their transportation role or not. He put the two issues squarely:

Now, when the tubes are themselves loaded with cancerous substance, and are, for example, traceably so loaded from the diseased organ even to the thoracic duct, (the latter tube has been found to contain the morbid matter by Andral, A. Cooper, Hourmann, and others), without any evidence existing of the matter being a product from the walls of the tubes themselves, the implication of the lymphatic system is evidently the result of absorption. But when the glands are cancerous, and the connecting tubes in the natural state, the condition of the former is not thus so satisfactorily explicable.

Explication arose satisfactorily before the end of the 19th century. Thus, Pepper and Stengel [22] in 1895, put the stamp of authority on the issue when they accepted that "there may be embolism through the thoracic duct to the chest".

Discussion

As knowledge and technology progressed, the natural pathway offered by the thoracic duct in cancer carriage was so well understood that Willis [23] devoted a whole chapter to it in his massive monograph on "The Spread of Tumours in the Human Body". Hitherto, the problem with doing research on the thoracic duct was the sheer length of it. For example, Young³ dissected the duct, while a Japanese [24] worked laboriously on its cross sections. Personally, I documented this easily by using the Swiss-roll method [25] to so coil the duct that each prepared microscope section revealed the progression of cancer cells at the moment of death.

Both solitary and clumped cancer cells were in evidence. Indeed, one oat-celled growth exhibited, as it were, a procession of cancer cells almost throughout the entire duct. In particular, I concluded significantly 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".

A complementary aspect of the work was that I determined the fate of the cancer cells carried from the thoracic duct to the base of the contralateral lung. For this purpose, each-square blocks were studied. This maneuver revealed that "necrosis was evident even among small clumps of cancer cells". Perhaps, more elaborate studies may disclose the fate of even the single lung cancer cell. Certainly, my study [26] of the most important Pathologic Unit of the kidney, the glomerulus, showed evidence of "the destruction of entrapped cancer clumps". Here again, closer investigation may also elaborate on the fate of the single cancer cell.

If necrosis of the cancer cells occurs when commingled with red cells, I hypothesized that this is due to the presence of a hitherto hidden natural Factor [27]. I named it as the "Erythrocyte Associated

Necrosis Factor” (EANF). Therefore, I postulated that the duct should be cannulated as hitherto practiced [28]. Then, with the aid of the new technique of intravital videomicroscopy [29], the retrieved single cells or larger materials should be manipulated and replicated in leading laboratories for designing the target therapy of cancer [26]. However, the proviso is to follow what a Memorial Lecturer [30] said, “Ideas must be sought after and cultivated. We must not be afraid to attempt the impossible; no device or technique that holds out the faintest hope of discovery can be put aside ...”.

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