Spontaneous regression of breast carcinoma: review of English publications from 1753 to 1897

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Abstract

Regression is an important phenomenon in oncology. Two reviews in 2011 dealt at length with what in modern parlance may be called its permutations and combinations. Specifically, in both 1982 and 1987, when its occurrence in breast cancer was presented from two centers, the oldest accounts of it were dated back to 1900. Therefore, a search for much older English literature was undertaken in order to widen current knowledge of this important problem. Consequently, a published long case dating back to 1897 is abridged and a short 1846 case is also noted. Furthermore, general etiological concepts are exemplified as far back as 1753. It is concluded that the history of cancer regression is like fishing in an ocean of this illness. However, the findings are deemed to complement what modern historical accounts lack.

Introduction

A most intriguing phenomenon in oncology is regression. Two 2011 reviews from India[1] and Taiwan[2] dwelt on the scientific theories behind it. The former concluded that *this review provides an insight into the benefits of fever and its role in prevention of cancer, the significance of common infections in cancer regression, the dual nature of our immune system and the role of the often overlooked primary innate immunity in tumor immunology and spontaneous regression of cancer.* According to the latter, *a complex interplay of mechanisms is involved in tumor growth and tumor regression. Better understanding of these mechanisms may give us a better ability to predict tumor behavior and for effective cures*.

Cures matter but it is evident from these excerpts that regression tends to be perceived from diverse dimensions. The same is true of the history of the subject. Thus, in 1982, Ross and associates presented a breast carcinoma that exhibited spontaneous regression.[3] Furthermore, they reviewed all such cases published in the English language since 1900. From their tabulation of 13 cases, it is apparent that two types were recognized, namely, cases which did not recur and the rest that recurred at a distance. Interestingly, back-dating to 1900 also featured in a 1990 review.[4] Therefore, this paper abridges the striking account of a non-recurrent case detailed by Gould in 1897.[5] Also included is the short recurrent case cited by Walshe in 1846.[6] Incidentally, that very case was also mentioned by Simon[7] in a *Course of Lectures in General Pathology* delivered in 1850. Thereafter, there is a review of other old generalizations recorded in the literature from as far back as 1753.

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Key words: breast cancer, review, history, spontaneous regression.

Conflict of interests: the author declares no potential conflict of interests.

Received for publication: 2 May 2012.
Revision received: 30 July 2012.
Accepted for publication: 4 September 2012.

Oncology Reviews 2012; 6:e22
doi:10.4081/oncol.2012.e22

Historical cases

Report of Gould

M.C., a single woman, a sick nurse, was until recently an inmate of one of the special cancer wards of the Middlesex Hospital. She states that in 1885 she noticed a small lump in the breast; this slowly enlarged, and in May, 1890, she was admitted into the London Temperance Hospital under the care of Dr. Collins, who diagnosed the case as scirrhus mammae, and excised the breast. The tumour was examined microscopically, and pronounced by two competent observers to be *typical scirrhous cancer.* Both the tumour itself and the microscopical sections of it have been mislaid.

In July, 1892, she noticed a lump in the left axilla. She returned to the hospital, and Dr. Collins removed the axillary glands.

In February, 1894, the patient noticed some lumps in the neighbourhood of the scar of the first operation, and also a lump above the right breast. For these lumps a third operation was undertaken by Dr. Collins, all the nodules being excised.

In December, 1894, she was again admitted to the Temperance Hospital, and was found to have several recurrent nodules round the scar and considerable dyspnoea. She was told that no further operation was advisable, and that she ought to seek admission to the cancer wards of Middlesex Hospital.

On January 17, 1895, she was admitted into Laffan Ward under care of Mr. Lawson. She was then forty-three years of age, and stated that for the past twelve months she had been getting thinner and suffering in her general health. Around the scar on the left side of her chest were numerous firm tubercles involving the skin and subcutaneous tissue, and in the left axilla were several hard, enlarged glands. Above the right breast was a linear scar two inches long, in the centre of

which was a hard nodule, and in the right axilla several hard enlarged glands were felt. Enlarged glands were also present above each clavicle. She continued in a very grave state with great dyspnoea and abundant expectoration for some months; then in the summer of 1895 she got somewhat better, but was worse again in the winter of 1895-6.

I saw her first in March, 1896. There were many hard nodules in the skin of the left side of the chest grouped around the scar, and one larger nodule in the scar above the right breast. Masses of enlarged glands were felt in each axilla and above each clavicle. She told me that she was suffering much pain in the left thigh, and on examination I found considerable deformity present. In addition to the external recurrent cancerous growths I believed that M.C. had secondary cancerous growths in the right lung and in the left femur, and I expected her death in a very short time.

On June 15, 1896, I examined M.C. again, and found one tiny nodule in the skin above the left scar. The right scar was keloid, and thicker in the centre. There were no enlarged glands to be felt in either axilla or above either clavicle. The patient's general condition was much better. The left thigh was deformed as before, but was less painful.

Since this she has steadily progressed. She has gained flesh, has a good colour, and enjoys life. She walks with a limp, but can rest her weight upon the left leg. The bone is not notably enlarged. The scar on the left side is quite soft and supple, and the skin around it is absolutely free from all nodules or signs of cancerous growths. The right scar is still rather keloid, and in its centre is thicker than elsewhere. There are no enlarged glands in either axilla or the neck.

It is difficult, if not impossible, to account for the change that has occurred in this patient's femur in any other way than by the development of a tumour in the bone, destroying its rigidity and then itself undergoing absorption, and new bone forming to consolidate the weakened and deformed femur. It is noteworthy that the history points to the primary growth starting at the age of thirty-seven, and then running a rather slow course; this is contrary to what we generally observe, that the earlier in life carcinoma arises, the more rapid and malignant is its course. The case is one of such interest and importance that, although incomplete, it seems worthy of being shown to this Society.

Walshe's 1846 cited report and Simon's 1850 version

…The perfection of the seed is not enough to secure the development of the plant; the soil, in which it is sown, must be capable of feeding it.

Intimately allied with the present questions, is the subject of the so-called *metastasis* of cancerous tumors, a doctrine which has on the evidence of certain cases on record met with not a few advocates. The following is an abridged account of one of these, related by Recamier, on the authority of Parent-Duchatelet. A woman, after having for a length of time suffered from a tumor in the breast possessing all the characters of non-ulcerated scirrhus, and presented the symptoms of the cachexia in so marked a manner that Dupuytren not only refused to remove the diseased organ, but dissuaded M. Parent from the use of leeches, was seized with remittent cephalalgia of intolerable violence: at the same time the mammary growth ceased to be painful, and eventually disappeared almost completely. Apoplectic symptoms with hemiplegia supervened, were combated by the ordinary means, and recurred twice before the patient's death, which took place ten weeks after the first apoplectic seizure, and two years after the supervention of the symptoms in the mamma. On post-mortem examination a tumor the size of a nut, and possessing the characters of carcinoma, according to the testimony of Cruveilhier, was discovered floating, as it were, in a quantity of diffluent brain.

Now, of the accuracy of the facts of this case no fair doubt can be raised; but the interpretation given them wears a more questionable form. In truth, that a tumor can have been conveyed in proper person, particle by particle, from the breast to the brain, and remodeled into shape in its new habitat, is beyond the limits of the credible. In such piecemeal migration it is allowable to have no faith. The only feasible explanations of the circumstances are either that the mammary growth was wholly eliminated by absorption and excretion, and that this removal gave an indirect impulse to the development of a pre-existing tumor in the brain; or that in the course of absorption certain elements of the formation in the breast may have been transferred entire to the brain and there germinated into a mass.

Historical hindsights

Mass of meaningful materials dating back to distant domains are necessarily worthy of review. On scrutinizing them, it is apparent that the possible occurrence of spontaneous regression had actually long been contemplated. Thus, by 1793, John Pearson[8] considered some cancerous complaints and generalized that *Sometimes the disease in the breast disappears completely.* However, it is to be noted that he was circumspect thus:

> I must decline attempting any induction from the preceding narrative of facts: they are too few in number, and not delineated with minute exactness, which could alone justify us in forming general conclusions. When the combined experience of enlightened practitioners shall have enlarged the number of well authenticated particulars, we may perhaps be able to form principles of the most extensive utility. I would only beg leave to call the attention of the reader to the circumstance I have mentioned, of the spontaneous disappearance of tumors seemingly scirrhous; for this fact may assist us in forming a correct judgment of the merit of a variety of medicines, the efficacy of which is apparently supported by the most incontestable evidence.

Evidence was sought during the next century. In fact, several horizons were envisaged in the 1806 publication[9] which had appeared in the *Edinburgh Medical and Surgical Journal.* That era followed the death of John Hunter whose students and colleagues gathered together into the *Society for Investigating the Nature and Cure of Cancer*. Constituted in this way, they drew up 13 research questions. Interestingly, the last question was: *Is cancer under any circumstance susceptible of a natural cure?*

Cure concerned James Paget very much (Figure 1). Elsewhere, in portraying his eponymous expertise, his portrait was appended in my historical paper.[10] On turning from that aspect to his monumental *Lectures in Surgical Pathology*,[11] we find that that meticulous maestro pointed in 1853 to the difficulty inherent in regression studies thus:

> We may perhaps refer the occasional withering of a cancer under

Figure 1. Sir James Paget (1814-1899).

the influence of some fever, and the more rarely occurring complete death of one, so that during an attack of acute fever the whole mass may slough off; and this whether the feverish condition of the blood be produced by some miasma, or by medicinal means. Such, I fear, is all that can be, at present, safely regarded as matter of fact in relation to the nature of the peculiarity of cancerous blood; and it must be admitted that these facts are scarcely more than indications of the direction in which inquiry should be made.

Made in this direction of inquiry was a great *Discussion on Cancer* that took place at the Pathological Society of London in 1874. The leading discussant, Campbell de Morgan,[12] exemplified not with fever *per se* but with specific diseases proper. *Syphilis and scrofula*, he averred, *after years of activity, will often exhaust themselves and die out*. As he continued, *this is an extremely rare event even in primary cancer, but almost an unknown one when the disease has become extended to distant parts*. As he generalized further, *another remarkable and not very explicable phenomenon is the arrest of cancerous growth and the gradual wasting of the diseased mass. This is an occasional event which is very important, as it encourages us to hope that a cure may yet be found for the disease*. Continuing the Discussion, he expatiated thus:

We must look elsewhere for an explanation. It only shifts the difficulty back a stage or two, as I have so often done before, to suggest that the recession of cancer takes place in obedience to the law under which local atrophy, independent of inflammation or disuse, may occur, or that it may be due to some want of organising power inherent in it from the first, as some cancers seem born to be atrophic.

It is under any circumstances a most important subject for investigation.

Investigation of regressive cancer was all along being undertaken. In this context, Benjamin Travers,[13] when he was the President of the Medico-Chirurgical Society, reminisced that *a sudden and extensive gangrene has been known to eliminate the disease completely*. No less an authority than Theodor Billroth[14] held that *it never or very rarely, happens that a complete, spontaneous, cicatricial healing up of the cancer takes place*. Or, as John Bell[15] of Glasgow gleaned:

Again, we must give credit to the reports of trustworthy pathologists, that such tumours not only have the productive power of the cell suspended or destroyed, but even occasionally the growths are transformed into perfectly harmless saponified or osseous masses. There is nothing in the nature of cancer to render the notion unwarrantable, that the cells may be deprived of their reproductive power, and that the progress of the disease may thus be checked or suspended.

Suspended or healed was obviously long the question. For example, very much earlier, William Norford[16] in 1753 appreciated that *even in the worst of (cancer) cases, Nature does, sometimes, relieve herself in a manner absolutely above our knowledge*.

Knowledge grew when gathered from the experience of authorities. For instance, Laurence,[17] who won The Liston Prize Essay for 1854, referred to the work of a differently spelt Lawrence. The latter's own case went thus:

…a tumour of the right upper jaw, clinically and anatomically innocent, recurred and was removed successively four times in the course of fourteen months. After the fourth operation it grew again, and at the same time some new growths made their appearance - one on the left upper jaw, and two on the cranium. It was removed for the fifth time, when, strange to say, the three others disappeared spontaneously.

Spontaneously did a tumor vanish, as it were, in the personal experience of Semon.[18] Thus, as regards an obstructive tumor of the windpipe, there was commensurate amazement:

On laryngoscopic examination I hardly trusted my eyes when I saw that the subglottic tumour which Mr. Butlin, Dr. Wright, and I had so clearly seen (I myself on a good many occasions) had completely disappeared, and that it was now possible to see a long way down into the trachea.

Trachea may now give way as we turn to the phenomena manifested at other sites. For instance, Sir Spencer Wells[19] himself considered how well it will be for the patient if regression could occur. In his own words:

Can we encourage the forlorn hope of the patient that even yet growth may be stopped; that some benign alteration may take place in its structure - something like the 'spontaneous involution' of Virchow - some retrograde fatty change in the cells or elementary components of the tumour, while extension or growth of new cancer cells is stopped?

Stopped was the growth of liver cancer in the experience of Oppolzer and Bochdalek, according to Frerichs.[20] Apparently, they had observed cases *in which they believe they have traced, both clinically and anatomically, the process of spontaneous cure of cancer of the liver*. Unlike their short opinion, Thomas[21] was expansive.

Case history

A.P. residing at Shennington in Oxfordshire, age 43 years, of a corpulent but irritable habit, was, about six weeks previous to her application to me, attacked with a tumor in her left breast, which had during that time gradually increased in size, and had at length become knotty and irregular, and was attended with severe lancinating pains extending into the axilla, with every other appearance of scirrhus, and such had it indeed been pronounced by the surgeon who had been called upon for his advice. Under the above circumstances, and without any hope of success, I must acknowledge, I directed her to rub in, morning and night, about the size of a bean, of an ointment composed of an ounce of the unguentum hydrargyri mitius, and the same quantity of the unguentum ceræ, in which two drachms of camphire were dissolved, and to take, twice a day, two of the pills advised below, washing them down with half a pint of the decoctum sarsaparillæ compositum, with the addition of thirty drops of thevinum antimoni. She was likewise enjoined to keep her body open, to make use of a spare diet, consisting principally of vegetables and milk, and to abstain from all spirituous and fermented liquors. After a pursuance of this plan for about three weeks (someslight affection of the salivary glands having taken place during that period) the tumor wholly disappeared, as well as every other symptom.

Discussion

Symptom free life has always been what the patient and the practitioner have craved. But, there has been the underlying question as to whether the illness itself was cancer or not. In particular, was there microscopic confirmation? In this context, it is well to remember that it took many years for microscopy to be accepted. Consider that a debate on it took place at the French Academy of Medicine during the 1854/1855 Sessions.[22] A major question on microscopy cropped up: *Is its use indispensable for the diagnosis of cancer?* In fact, Velpeau, who dominated the discussion, was reported to have given a balanced opinion as follows:

The microscope has rendered service to science, and will probably render still greater service; but it has committed, and still commits errors. M. Velpeau did not oppose the use of the microscope; but he questioned its facts when they disagreed with his own observations. In malignant tumours, there is some specific element with which we are unacquainted. Perhaps there are several kinds of cells. Such questions can only be determined by long experience and clinical observation. We must not, in accepting the doctrines of the microscopists, set aside the accumulated experience of ages. Well-observed facts must be accepted; and it is thus only that we shall promote the advancement of science.

Science that investigates cancer has been growing for decades with the accumulation of information gathered with or without the microscope. In effect, cancer history cannot be held to ransom by insisting on

microscopic diagnosis. A good illustration of not depending on microscopy is apparent in Handley's Presidential Address to the Section of Surgery of the Royal Society of Medicine in 1972.[23] He bolstered his personal overview of breast cancer by approving one important old publication as follows:

Their source was the records of the Middlesex Hospital Cancer Charity, carefully kept from the inception of the charity in 1794 to relatively recent times. In each of these 250 patients, the date of the first symptom, the progress, the date of death and the post-mortem report were available, though (there being no histology over most of the period) very few microscopic reports were available.

Conclusions

Available data detailed above emanate from the ideas of yester years with regard to the etiology of cancer regression. Indeed, Pearson[8] had by 1793 called for remembering *the combined experiences of enlightened practitioners*. Hence, let these experiences be itemized hereunder with pertinent selections thus:

- any circumstance susceptible to a natural cure[9]
- undergoing absorption[9]
- influence of some fever[11]
- peculiarity of cancerous blood[11]
- gradual wasting of the diseased mass[12]
- sudden and extensive gangrene[13]
- cicatricial healing up[14]
- deprivation of their reproductive power[15]
- natural relief[16]
- disappeared spontaneously[17]
- completely disappeared[18]
- benign alteration[19]
- the process of spontaneous cure[20]and
- affection of the salivary glands.[21]

Glands that are full of cancer may regress. This has clearly been an intriguing issue. Little wonder that, even of late, Lowy's associates[24] had to concede that *only an occasional practicing physician has had the pleasure of seeing such a case during his medical lifetime*. Consequently, in all probability, as Saleh's group[25] canvassed, when they relied on histopathological evidence, regression is associated with immune surveillance. Hence, as to the future, its study, which was greatly pioneered by Macfarlane Burnet,[26] should progress so well as to foster the wellbeing of suffering mankind. Incidentally, as was presented recently in this Journal,[27] the quality of life outcomes in patients with breast cancer should be investigated with a salient search strategy. Indeed, such a search strategy is what I employed in the present paper. I have not seen any mention of the phenomenon in modern historical works.[28-32] In other words, this review is like fishing for tumor regression in the ocean of cancer history! It is hoped that what we caught represents a cogent contribution to cancer classics.

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