Iatrogenic Implantation of Cancer Cells During Surgery

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Abstract

In the late 1800s, the concept of iatrogenic implantation of cancer cells during surgery was put forth. The most dramatic example is a recurrence in a donor graft site, which is often distant to the primary site of excision. This eliminates the possibility of incomplete removal as the etiology of recurrence. However, in addition to direct transplantation to the graft site via gloves or instruments, several other possibilities exist, including de novo *lesions of squamous cell carcinoma in the graft, as well as systemic metastases. This article reviews 15 published case reports of cancer recurrence in graft donor sites in which the authors considered seeding via gloves or instruments. Viewing these cases in the context of a 2018 study demonstrates the varying opinions of surgeons on the possibility of cancer seeding. This article strongly advises the changing of gloves and instruments following resection of any suspicious or established cancerous tumors.*

Keywords

cancer seeding, graft site, iatrogenic, sterile field, tumor implantation

Abbreviation

SCC = squamous cell carcinoma

Introduction

In 1896, Lack first penned the consideration that cancers may disseminate iatrogenically via "direct transplantation, as distinguished from dissemination by means of the blood and lymph channels."[1] This was an important progression from Gerster in 1885, who was the first to caution surgeons on the risk of iatrogenic dissemination of cancer. Gerster's focus, however, was on the avoidance of massaging tumors, resulting in tumor cells "propelled through the lymphatics and veins into the general circulation."[2] Lack's belief was echoed by Ryall in 1907.[3] Over a century later further clinical observations were made of this phenomena. In 1954, Ackerman and Wheat called for surgeons to change instruments, gloves, and drapes in cases requiring grafting for malignant tumors.[4] However, in 2018, Berger-Richardson, et al, found in a survey of 351 Canadian general surgeons, only 52% changed gloves during cancer excisions to prevent seeding. When asked about beliefs, 58% thought it was "possible or probable" (vs unlikely, definitely not, definitely) that gloves could harbor malignant cells, but approximately 57% thought it "unlikely" they could lead to locoregional or wound recurrence.[5] Surgeons are often faced with the need for concurrent incisional or excisional biopsies of two or more lesions from different sites in the same individual that are suspicious of cancer.

As seen by the opinions expressed, there is no standard of care dictating the changing of gloves and instruments. This review aims to answer the question whether, in the literature, there is evidence of patients undergoing cancer excisions where iatrogenic implantation of cancer cells via gloves or instruments has occurred. To isolate these instances from recurrence due to imperfect removal, this literature review will focus on known cases of iatrogenic implantation of graft sites, as they present the most compelling example of iatrogenic seeding and make the case for the consistent practice of changing gloves and instruments following the excision of a specimen suspected to be cancerous.

Methods

A literature review was conducted using PubMed and the University of Hawai'i at Mānoa Library's OneSearch from January 15, 2019 to April 14, 2019. OneSearch is a tool used to search Primo Central Index, Hawai'i Pacific Journal Index, Scholarspace, and eVols. PubMed search terms in "all fields" included "seeding cancer to skin graft site," "tumor seeding gloves," "iatrogenic tumor implantation," and "iatrogenic tumor seeding." Sources found in PubMed also provided references. In addition, searching for referenced articles via OneSearch and Google provided additional journal articles. No date range was placed on the search, in order to find both the earliest referenced studies as well as the most recent.

Case Reports

In 1986, Carr and Gilbert described an early example of iatrogenic tumor implantation to a graft donor site. It occurred at the temporalis muscle flap donor site from squamous cell carcinoma (SCC) excised from the right retromolar fossa. Carr and Gilbert postulated the implantation most likely occurred by introducing an orally contaminated glove or instrument when the flap was transferred to the mouth by passing it through the infratemporal fossa, or during the raising of the flap. Lymphatic drainage of the tumor was deemed unlikely as there was no known drainage from the mouth to the implanted area. Incomplete removal of the tumor was not considered, due to the distance from the primary site.[6]

In 1988, Nielson, et al, described a patient presenting with SCC on the right ring finger, treated with wide excision and a split thickness skin graft from the right thigh. At 3 months follow up, the patient presented with SCC on the margin of the graft

donor site. The authors cited the possibility of the SCC on the graft being a new primary lesion, due to neoplastic change secondary to the scarring.[7]

While proving iatrogenic implantation of SCC in a skin graft is an arduous task, given the propensity for *de novo* lesions, the examination of other tumors can eliminate that possibility. In 2001, Sadahira et al. encountered a patient with evidence of a recurrent malignant meningioma in the abdominal fat pad, which had been used to pack the orbital defect secondary to curettage of the tumor. Although the authors had not conducted the surgery, it was suspected that iatrogenic implantation occurred based on the history and histological review.[8]

In 2003, Hoopmann, et al, described what they believed to be the first ever recurrence of breast cancer in a musculocutaneous flap. The patient presented with a mass in the right upper outer quadrant of the left breast, which, when excised, was found to have positive lymph nodes as well as metastasis to the bone. Over a year later, the patient developed pain in the donor site (latissimus dorsi flap), and pathologically similar cancer was found. The authors noted the inevitability of contact between the cancer and the graft site due to the "extensive axillary involvement with infiltration into the surrounding tissue," and stated that this case should serve as a reminder for "standardized operative safety measures (eg, the obligatory change of gloves and instruments after tumor excision)."[9]

Hussain, et al, published a case report with convincing evidence of iatrogenic implantation with SCC in 2011. Despite adhering to glove and instrument changes, they noted the most likely cause was the use of the same hollow needle to give anesthetic in the tumor area (right hand) as the donor site (right thigh). Other possibilities given included contamination of the graft harvesting equipment with tumor cells, a new primary lesion, or systemic spread.[10] In 2012, Morritt and Khandwala also had a case of possible iatrogenic SCC implantation. However, they believed the most likely cause to be primary. This reasoning was supported by primary SCC in the cases of grafts used for burns, describing the increased risk as due to the donor site being an "area of inflammation with fibroblast and vascular proliferation. The dividing cells are more susceptible to carcinogenesis."[11]

Also in 2012, Wright, et al, reported a case with haematogenous spread of tumor cells as the most likely cause for metastasis. The patient underwent facial reconstruction for right post-auricular SCC with a right anterolateral thigh free flap, which required a split thickness skin graft from the left thigh. Approximately 6 months later, the patient demonstrated SCC nodules on the left thigh donor site. The authors believed they maintained sterile technique between all fields, and cited a case report of haematogenous spread of tumor cells to the contralateral thigh donor site in melanoma (the skin graft was delayed versus the excision thus excluding implantation) as evidence of the most likely mode in their case. However, they did not rule out "iatrogenic mechanical spread at time of surgery," but only due to the unlikely risk of airborne spread, as detected via "viable melanoma cells [sic] in electrocautery plume in mice."[12]

In 2015, Pai, et al, described a case of soft tissue sarcoma in which iatrogenic implantation was also the most likely mechanism. The patient was found to have a sarcoma on the skin graft of his left leg. On further investigation, it was ascertained 8 years ago he underwent excision and radiation for sarcoma on the right leg, and workup for metastasis was negative. This led the authors to conclude there were 3 possible mechanisms: implantation, a second primary tumor, or haematogenous spread. They believed implantation was the most likely cause given that there were no other sites of metastasis. Pai, et al, went on to recommend the following measures when using grafts in oncologic reconstructions: "A common draping for the primary tumor and flap donor site should be avoided. Ulcerated or fungating tumors should be sealed with impermeable skin barriers to avoid tumor spillage in the operative field. Harvesting of the flap should be started only after resection of the primary is complete to avoid cross contamination. Change of gloves is mandatory for all the surgeons and nurses after resection of the primary and before reconstruction begins. Separate surgical trolley with a separate set of instruments including cautery tip should be used for both the procedures. Hollow needles if used for infiltration during primary surgery should not be reused at flap donor sites. Proper irrigation of the operative field at the end of resection decreases chances of implantation of the tumor cells. Gentle handling of the tissues so that tumor cell dissemination can be minimized particularly in the case of necrotic tumors."[13]

Discussion

Despite the case reports described above and listed in Table 1, there is no general consensus for recommendation of instrument/glove changes following cancer excision.[5] In addition, some authors made reference to specific gown and draping practices for maintaining separation between tumor and graft sites, while others did not.[4,9,13] These are supplementary to standard surgical protocols such as excision into negative margins, en-bloc resection to avoid local recurrence, and avoidance of tumor spillage as recommended, for example, in colon cancer removal.[14] The case reports, as summarized in Table 1, communicate the potential of iatrogenic spread via gloves and instruments. If this is possible to carry over to a distant site, via eg, gloves, there is no reason to believe this low risk of seeding is not also present at the excision site. However, Table 1 also demonstrates the various potential mechanisms of cancer spread, and that often the reason for recurrence is unclear. Perhaps due to this uncertainty, Berger-Richardson, et al, called for more research to ascertain whether viable cancer cells are detectable on gloves and instruments.[5] However, as cited by Berger-Richardson, et al, Curran, et al, in 1993 had already demonstrated "squamous epithelial debris, consistent with squamous cell carcinoma" was found in both glove and instrument washings following

Table 1. Summary of Published Case Reports in Chronological Order Documenting Possible Iatrogenic Implantation of Cancer Cells in Graft Donor Sites, with 10 of 15 Papers Listing Iatrogenic Implantation as One of the Most Likely Proposed Mechanisms.

Year	Authors	Cancer Site	Cancer Type	Donor Site	Proposed Most Likely Mechanism
1986	Carr, et al.	Right retromolar fossa	SCC	Right temporalis muscle flap	Iatrogenic implantation
1988	Neilson, et al.	Right finger	SCC	Right thigh	*De novo*
1995	Cole Jr and Sindelar	Right tibia	Osteosarcoma	Left iliac crest	Iatrogenic implantation
1996	Yip, et al.	Left iliac crest	Osteosarcoma	Left fibula	Haematogenous spread
2000	Hughes, et al.	Right popliteal artery	Soft tissue sarcoma	Left saphenous vein	Iatrogenic implantation
2000	Dias, et al.	Left distal femur	Malignant fibrous histiocytoma	Left iliac crest	Iatrogenic implantation or haematogenous spread
2001	Sadahira, et al.	Right orbit	Meningioma	Abdominal wall	Iatrogenic implantation
2003	Singh, et al.	Right humerus	Osteosarcoma	Left iliac crest	Iatrogenic implantation or haematogenous spread
2003	Hoopmann, et al.	Left breast	Adenocarcinoma	Left latissimus dorsi	Iatrogenic inoculation
2010	May, et al.	Periorbital	Keratoacanthoma	Thigh (unspecified)	*De novo*
2011	Hussain, et al.	Right hand	SCC	Right thigh	Iatrogenic implantation
2012	Wright, et al.	Right post-auricular region	SCC	Left thigh	Haematogenous spread
2012	Morritt, et al.	Left lower leg	SCC	Left thigh	Systemic spread
2015	Pai, et al.	Right leg	Soft tissue Sarcoma	Left leg	Iatrogenic implantation
2017	Aloraifi, et al.	Left cheek	Merkel cell carcinoma	Right supraclavicular area	Iatrogenic implantation or viral recurrence

surgeries for SCC in the head and neck.[15] This review demonstrates conclusive evidence that while changing gloves and instruments following cancer excision may not fully protect versus the risk of tumor implantation, it should be considered as the standard of care.

Conclusion

Although consensus does not exist, based on multiple case reports and observations, it is strongly advisable to change gloves and instruments following resection of any suspicious or established cancerous tumors.[9,13]

Conflict of Interest

None of the authors identify any conflicts of interest.

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