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A qualitative study of the ramifications of rash from epidermal growth factor receptor (EGFR) inhibitors

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Abstract

Objective—Over 50% of cancer patients who are treated with epidermal growth factor receptor (EGFR) inhibitors develop a papulopustular rash that involves the face, neck, and upper torso. However, because relatively few previous reports have focused on the full ramifications of this drug-induced side effect, this qualitative study was undertaken.

Methods—Fifteen patients who had either an active or previous rash from these agents participated in scripted interviews. All interviews were transcribed and examined by means of a qualitative methodologic approach.

Results—Four major themes emerged: (1) actual physical discomfort was associated with the rash; (2) patients were concerned about their appearance; (3) despite initial denial, patients did suffer social isolation; and (4) high medical morbidity was associated with the rash. Patients voiced concerns such as: (1) ‘Especially when I try to sleep, I can feel the itch and burn all over...’; (2) ‘My face looks so bad that if I go to see my friends and they say, ‘What happened to you.’ I am self conscious about that’; (3) ‘I just told them they would be better off just calling me, don’t come visit...’; and (4) ‘I went to the hospital for my face...they made a bandage to put all over [my] face.... [I] just had a little nose hole, a mouth hole and holes for...eyes.’.

Conclusion—Rash from EGFR inhibitors can have a major negative impact upon cancer patients.

Keywords

rash; epidermal growth factor receptor inhibitors; social isolation; morbidity

Introduction

Over 50% of cancer patients who are treated with epidermal growth factor receptor (EGFR) inhibitors for their cancer develop a papulopustular rash that involves the face, neck, and

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upper torso [1]. Multiple studies have described this rash to be especially severe in 10% of patients, among whom the rash was more likely to occur with panitumumab and cetuximab as opposed to erlotinib, and in whom the occurrence of the rash was indicative of a better cancer prognosis [2]. Despite the fact that EGFR inhibitors are currently used in the treatment of cancers of lung, colorectum, pancreas, and head and neck, and despite several prospective palliative trials for rash, no known treatment provides highly effective rash palliation [3].

Relatively few previous reports have focused on the full ramifications of this drug-induced side effect. Wagner and Lacouture interviewed 20 patients with an EGFR inhibitor-induced rash in order to better understand the consequences of this drug-induced cutaneous toxicity [4]. For the first time, these investigators brought to light specific rash-related co-morbidities with a sharp focus on cutaneous burning, sleep disturbance, and patient self-consciousness. However, this study provided little focus on changes in social and family interactions, the possibility of rash fostering hope, other morbidity directly related to the rash, and patients' access to rash-related information resources. In effect, Wagner and Lacouture drew attention to the fact that cancer patients who are prescribed EGFR inhibitors suffer more rash-related distress than had been previously described, but they also underscored a need to further study such issues.

In view of the expanding indications for the EGFR inhibitors and in view of the paucity of previous studies that have attempted to assess the full ramifications of the rash, the current study was undertaken. This qualitative study sought to explore further the full impact of the EGFR inhibitor-induced rash.

Methods

The Mayo Clinic Institutional Review Board approved this study. All patients were enrolled from the Division of Medical Oncology in Rochester, Minnesota between October 2009 and February 2010.

Cancer patients who had developed a characteristic, drug-related rash while receiving an EGFR inhibitor were eligible to participate; patients did not have to have a rash at the time of their participation. In view of these circumstances, no attempt was made to glean information on rash grade or duration.

All patients were approached by an oncology healthcare provider and were informed of the goals of the study. If a patient expressed an initial willingness to participate, one of the study investigators (S.C.) met with the patient and further discussed the goals of the study. If willing to participate, patients then provided verbal study consent at the time of the interview.

The interviewer (S. C.) utilized a scripted list of general questions. These questions focused on the rash, were based on unanswered questions within the published medical literature, and reflected concerns derived from previous clinical interactions between healthcare providers on the study team and patients with EGFR-induced rashes. By design, most of these questions were not open-ended, but the interviewer followed each question with a

pause and an invitation to the patient to elaborate on the initial response. Follow up questions were asked, as appropriate, within the context of the ongoing interview, as long as such questions did not stray from the primary study goal of better understanding all the ramifications of the rash. All interviews were recorded and then professionally transcribed.

Two investigators (S. C. and A. J.) reviewed transcripts of the interviews on an ongoing basis. Patient enrollment ceased once it appeared that no new content themes were emerging.

Then, these same two investigators (S. C. and A. J.) independently reviewed each transcript, utilizing the principles inherent in an inductive qualitative approach, to identify and categorize themes [5]. These investigators met multiple times to discuss and reconcile any differences of opinions relevant to theme identification and to extract phrases that illustrated each theme.

Results

Demographics

Fifteen patients participated in this study. Most were men who were no longer working, and the most common cancer type was colon cancer. Demographics, including type of EGFR inhibitor prescribed, appear in Table 1.

Patient-reported factual rash information

All patients except three had a rash at the time of the interview (Table 1). The face and especially the nose were the most problematic areas, and nearly all patients (93%) also described cutaneous discomfort. Most (86%) had been warned about rash development prior to starting the EGFR inhibitor, and most (80%) relied exclusively on their healthcare provider for rash information.

Moreover, the interviews revealed morbidities that included hospitalization, the need for a morphine drip for pain control, and bleeding from the rash. Despite the foregoing, 60% of patients reported the rash made them feel hopeful (Table 1).

Qualitative themes

Four themes emerged as a result of using qualitative methodology: (1) actual physical discomfort was associated with the rash; (2) patients were concerned about their appearance; (3) despite initial denial, patients did feel social isolation; and (4) high medical morbidity was associated with the rash. Illustrative quotes are provided in Table 2.

Discussion

The purpose of this study was to probe further into the impact of EGFR inhibitor-induced rash on cancer patients. We identified four major themes, as outlined above, all of which demonstrate this rash has far-reaching ramifications. Although nine patients (60%) described that the rash spawned some degree of hope with regard to cancer outcome, in general, the rash otherwise appeared to have only a negative impact.

Ironically, although initially all patients denied social isolation, their subsequent comments suggested that the rash was having a negative impact on communal interactions, an observation that suggests uncovering this issue requires time and probing on the part of the healthcare provider. Based on the comments gleaned from our interviews, there is no question that, despite what patients initially stated, social isolation is a major consequence of EGFR inhibitor-induced rash.

This study appears to be the first to identify and focus on other medical morbidity associated with the rash. To our knowledge, hospitalization, the use of a morphine drip to control pain, and bleeding from the rash have not previously gained attention in rash studies. Although these morbidities might be rare, healthcare providers may choose to discuss these possibilities as they prescribe EGFR inhibitors to cancer patients.

Along these same lines, it is noteworthy that healthcare providers appear to play a pivotal role in educating patients about the EGFR inhibitor-induced rash. Although this study focused on a small group of only 15 patients, it is nonetheless remarkable that only 3 patients utilized resources other than their healthcare provider to learn about the rash. Curiously, there were also 2 patients who were never told about their high risk for developing a rash. These findings should underscore to healthcare providers the importance of providing a comprehensive discussion of rash risk and its ramifications when prescribing EGFR inhibitors.

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Table 1Patient demographics^a and rash-related information^b

Age, median in years (range) ^c	58 (36, 81)
Gender	
Male	10 (67)
Female	5 (33)
Cancer type	
Colon	7 (47)
Head and neck	5 (33)
Lung	2 (13)
Pancreas	1 (7)
Type of EGFR inhibitor	
Cetuximab	8 (53)
Erlotinib	3 (20)
Panitumumab	1 (7)
Unknown	3 (20)
Rash at time of interview	
Yes	12 (80)
No	3 (20)
Time to rash development	
Greater than 1 week after starting the EGFR inhibitor	8 (53)
One week or less after starting most problematic area with rash	6 (40)
Nose	6 (40)
Entire face	5 (33)
Eyes	1 (7)
No specific area	2 (13)
Pain/burning/itching from the rash?	
Yes	14 (93)
No	1 (7)
Social isolation from the rash?	
No	15 (100)
Yes	0
Rash spawned hope	
Yes	9 (60)
No	5 (33)
Do not know	1 (7)
Healthcare provider gave rash warning	
Yes	13 (86)
No	2 (14)
Sources of rash information	
Only healthcare provider	12 (80)
Internet	3 (20)

^a Numbers in parentheses indicate percentages unless otherwise specified.

^b Numbers in parentheses refer to the percentage of patients and do not always sum to 100% because of missing data.

^c Two patients did not state their age during the interview.

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Table 2

Direct quotes

Theme	Relevant quotes
Rash-related discomfort	<p>‘...[the burning] is a little disruptive.’</p> <p>‘One area versus another was not any worse, it was all a nuisance.’</p> <p>‘It was like it was on fire whenever you take a bath....’</p> <p>‘... on my face and head it is very hot and it itches... yes, very very hot.’</p> <p>‘Especially when I try to sleep, I can feel the itch and burn all over...’</p> <p>‘It itches like in the evening.’</p> <p>‘I got real red eyes, the whites were just like bloodshot, real red itchy.’</p> <p>‘Itchy, burning, painful.’</p> <p>‘I take a hot wash cloth, as hot as I can, and lay it over my face.... It brings out the rash a little bit more but it soothes the pain...’</p> <p>‘The scalp is probably the worst, the scalp and my back is where it itches the most...’</p>
Concerns over appearance	<p>‘My sister laughing at me because I never had acne when I was younger.’</p> <p>‘When I look in the mirror, yeah it bothers me, but I try to ignore...’</p> <p>‘I feel a little self conscious.’</p> <p>‘Well, I think that my face looks so bad that if I go to see my friends and they say, ‘What happened to you.’ I am self conscious about that.’</p>
Social isolation	<p>‘There was one social event [I] did not want to go to; ‘looked like hell’...’</p> <p>‘[do] very little outside of the home....basically only come to Mayo or stay home...’</p> <p>‘I like to stay away from them [children, husband, mom]... I feel more comfortable that way... to me it looks so dirty on my face and I don’t want them to kiss me on the forehead.’</p> <p>‘... if there is a pool, I am self-conscious...’</p> <p>‘I feel like I don’t want to be gross to her [wife].... I feel self-conscious even in front of her...’</p> <p>‘...I could have went, but I had to be home every three hours to change my [dressings].’</p> <p>‘I... was just... feeling I lived in a motel room and that was it... I was just isolated and I just sat there and waited it out.’</p> <p>‘... he was downstairs playing X-box so I reached around and gave him a hug and he turned around and went, ‘Whoa.’ ...he didn’t say anything else, but the ‘whoa’ kind of said it all... he was 9.’</p> <p>‘The people I couldn’t give two hoots about I wasn’t going to worry about their reaction anyway.’</p> <p>‘When the rash was the worst I generally stayed at home... my colleague also just feels... to see that kind of rash.’</p> <p>‘I didn’t want to go anywhere...’</p> <p>‘I just told them they would be better off just calling me, don’t come visit...’</p> <p>‘You are who you are and that is the way it is. If they come up to me and ask me I tell them what is going on and like I said it is an inconvenience that we have to work a little bit more on.’</p> <p>‘My boys make fun of me... I have my boys living at home and they are 20... so they like to throw jabs at me and we laugh.’</p>
Rash-related medical morbidity	<p>‘...he then had an open wound from scratching’</p> <p>‘I went to the hospital for my face...they made a bandage to put all over [my] face.... [I] just had a little nose hole, a mouth hole and holes for...eyes.’</p> <p>‘...on medication for that [the rash].... Morphine drip.’</p> <p>‘...it split your skin open at the end of my fingernails.’</p> <p>‘It actually started to bleed...’</p> <p>‘I am on a blood thinner, so if you itch for a few seconds, they bleed.’</p>

Theme	Relevant quotes
	Wife speaking, 'It was hard on both of us; he couldn't take care of himself anymore.'

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