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Phantom limb pain in young cancer-related amputees: Recent experience at St. Jude Children's Research Hospital

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Abstract

Objectives—This study in children and young adults having cancer-related amputation aimed to examine the incidence of phantom limb pain in the first year after amputation and also the proportion of patients who had pre-amputation pain.

Methods—A retrospective review of medical records was undertaken. The proportion of patients with phantom limb pain was reported. Fisher's exact test was used to examine the association between phantom limb pain and the presence of pre-amputation pain and between phantom limb pain and age (< 18 years vs. >18 years).

Results—26 amputations were performed on 25 patients. During the year following amputation, 76% of patients had experienced phantom limb pain at some time. After 1 year, though, only 10% still had phantom limb pain. Pre-amputation pain was present in 64% of patients. Although both of our patients with PLP at 1 year were young adults (< 18 years) and both had pre-amputation pain,

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we found no statistically significant associations between age or the presence of pre-amputation pain with phantom limb pain.

Discussion—Phantom limb pain following cancer related amputation in children and young adults appears to be common but generally short lived in most patients.

Introduction

Phantom limb pain (PLP) is pain experienced in a limb that is missing due to traumatic or surgical removal. It has been reported to occur in 60-80% of patients and to be less frequent in young children.¹ In Western countries, the most common reason for amputation is vascular disease¹ and consequently there is a paucity of data regarding our patient population of children and young adults having amputation for malignant disease.²

Previous studies that included children with malignancies were published 15 years ago and included data for patients dating back to the early 1980s.^{3, 4} In the last 30 years, drugs such as gabapentin and amitriptyline have been introduced into clinical pain practice and the use of perioperative epidural analgesia and peripheral nerve blocks have become more widespread. We were therefore interested in exploring the current incidence of phantom limb pain in patients having amputation for malignancy in a setting where the use of these agents and techniques is now commonplace.

Our hypothesis was that the incidence of phantom limb pain will have declined in the last few decades. The primary objective of this study was to determine the proportion of young patients who experienced PLP in the year following amputation. Our secondary objective was to determine if there was a relationship between pre-amputation pain and PLP in young patients.

Materials and Methods

This retrospective study was approved by the institutional review board of St. Jude Children's Research Hospital. Medical records for children and young adults who had undergone limb amputations between March 2000 and June 2007 were identified using an institutional database. Patients were included if they had above-knee amputation (AKA), below-knee amputation (BKA), below-elbow amputation (BEA), above-elbow amputation (AEA), hip disarticulation, or forequarter amputation (FQA). Excluded from the study were patients who had undergone non-major limb amputation or amputations that were not performed to treat malignancy.

Information obtained from the medical record included patient age, sex, diagnosis, and type of amputation. The pharmacological pain management (e.g., gabapentin, amitriptyline, NSAIDs, or opioids) of the patient before and after the amputation was identified, as well as any regional anesthetic technique used. The presence of pre-amputation pain was recorded. The presence of PLP was noted on post-operative day (POD) 1 through 7 and at 1 month, 6 months, and 1 year. PLP was considered present if it was documented in the medical record by a physician, nurse, or member of the pain management team. It was assumed to be absent if there was no mention of it in the medical record.

The pain standard of care required that nurses record pain scores for all inpatients every 4 hours while awake. Additionally, when a patient was seen as an outpatient the clinic nurse was required to document a pain score for each visit; if pain was present the nurse would ask the location, severity and quality of the pain. All patients remained in the hospital for at least 7 days after surgery. Additionally, each patient was followed by the pain service while inpatient after surgery and was seen every day by the pain service nurse and/or doctor.

Following discharge each patient was seen by the pain service for at least one month after surgery and was seen by the surgical and solid tumor services regularly for at least one year. In cases of problematic pain, the patient continued to be seen regularly by the pain service, or was referred back to the pain service if pain recurred. The pain service and surgery service shared the same clinic nurses, who were diligent in seeking pain scores and a history of PLP. After POD 3 the pain assessments were not always available at the precise time points, in which case the closest reasonable time point was used, and the deviation from this time point was recorded.

The proportion of patients with PLP was reported. Fisher's exact test was used to examine the association between PLP and the presence of pre-amputation pain and between PLP and age (≤ 18 years vs. >18 years). Logistic regression was used to examine whether age (as a continuous variable) was associated with PLP.

Results

Between March 2000 and June 2007, 30 amputations were identified, 26 of which were included in this analysis. One patient was excluded because he had received segmental mandibulectomy, and another was excluded because amputation was performed to treat bone marrow transplant complications rather than malignancy. Two young patients (one 5 months old at the time of amputation and another 2 years old) were excluded because they could not be expected to differentiate between PLP and nociceptive pain. Twenty-six amputations were performed in 25 patients; one patient had above knee amputation followed by a hip disarticulation. There were 13 males and 12 females. Patients' ages at the time of amputation ranged from 6 to 27 years (median, 15 years), with 9 patients aged 18 years or older. Most had primary bone tumors ($n=20$; 80%), and nearly all had lower limb amputations ($n=23$). Over half the patients ($n=16/25$; 64%) had pre-amputation pain.

Nineteen of 25 patients (76%) had PLP at some time during the year after amputation. Figure 1a shows the proportions of patients who experienced PLP at PODs 1, 2, 3, and 7 and after 1 month, 6 months, and 1 year for the patients who experienced pre-amputation pain. Of note, the 1 patient with 2 amputations is included as 2 separate cases in Figure 1a. Figure 1b displays the same data for the patients who did not have pre-amputation pain. PLP was more common within 7 days of amputation than after 6 months and 1 year. No statistically significant differences in the distributions of PLP according to the presence or absence of pre-amputation pain were observed at any time, although the numbers were small.

The proportion of patients with PLP 1 year after amputation was 10% (2/21). Three patients died and one patient was discharged from St. Jude within the year after amputation. One patient had another amputation less than one year after his first amputation. Although the two patients with PLP after 1 year both had pre-amputation pain, there was no evidence of a statistically significant difference in the proportions of patients with PLP after 1 year with respect to presence of pre-amputation pain ($p=0.50$), although once again the numbers were very small.

Of the 9 patients who were ≥ 18 years old at the time of amputation, 2 had PLP after 1 year (22%), compared with no patients who were younger than 18 years old. This difference was not statistically significant. When age was explored as a continuous variable there was no evidence of a significant association between age and presence of PLP at any of the assessment time points.

In our population, 5 patients had distal amputations (BKA or BEA) and none reported PLP after 1 year. Twenty patients had proximal amputations (AKA, AEA, FQA or hip

disarticulation); among 16 patients alive and evaluable after 1 year, only 2 (13%) reported PLP.

Pharmacological pain management and postoperative regional analgesia (i.e. epidural or continuous peripheral nerve block) is shown in Table 1. There were no statistically significant differences observed in the proportions of patients with PLP at any of the time points studied with respect to type of post-operative pain management.

There were 7 patients who had pain scores one or more days on either side of POD 7. Of these 7 patients the mean deviation was 2.5 days with a maximum of 7 days. There were 8 patients who had pain scores taken 4 or more days on either side of POD 1 month. Of these 8 patients the mean deviation was 7.5 days, with a maximum of 16 days. Likewise, 7 patients did not have pain scores within 7 days of POD 6 months. The mean deviation of these 7 patients was 27 days, with a maximum of 31 days.

Discussion

In this study of 25 young patients, 76% experienced PLP at some time during the first year after cancer-related amputation. This finding lies between those of two other studies of PLP in pediatric cancer-related amputation reported 15 years ago.^{3, 4} In their retrospective study of 67 patients, Smith et al³ reported that PLP was experienced at some point by 48% of pediatric patients with cancer-related amputation. In a similar pediatric study published in the same year in which only 10 patients had cancer-related amputations Krane et al⁴ reported a much higher rate of PLP (90%). The study design (a questionnaire in which patients self-reported pain), may have accounted for the higher rate of PLP.

Although 76% of the patients in our study experienced PLP during the first year after surgery, resolution of symptoms was the norm, with only 10% still experiencing PLP after 1 year. This is a much lower rate than was found in two earlier studies of pediatric cancer patients, both of which reported that 70% of patients still had PLP at long-term follow-up.^{4, 5} A further study of pediatric patients, not specifically cancer-related, found that 42% had PLP in long term follow-up.⁶

There are several possible explanations for the marked difference in the rates of PLP between the studies. The preventive or therapeutic treatments offered to the patients were almost certainly different, as there have been many major changes in practice over the last 3 decades. For example, in the study by Krane et al,⁴ in which 90% of cancer-related amputees experienced PLP persisting over months to years, pre-amputation therapies were not administered. In our study, all patients received treatment with gabapentin before or within 24 hours of amputation, and 21 of 26 cases received epidural analgesia or continuous peripheral nerve block.

Many studies in both adult and pediatric populations have found that PLP is more common in patients who experienced limb pain prior to amputation.^{4, 7, 8, 9, 10, 11} In this study we were not able to detect a statistically significant difference between patients who did or did not have pre-amputation pain. However, both of our patients who had PLP at 1 year had pre-amputation pain, and our sample size may have been too small to detect a difference.

This study was limited by its retrospective nature and the sample size. The small number of patients, as well as the small number of patients with PLP, limits our ability to draw definitive conclusions. Although both of our patients with PLP at 1 year after amputation were 18 years and both had pre-amputation pain, we were unable to detect significant associations between age and pre-amputation pain with PLP in our study. These may be foci for further investigation, as the lack of statistically significant findings in our study may be a

result of a type II error. The lack of prospective patient interviews lessens the ability to effectively report the occurrence of PLP. We assumed that the lack of mention of PLP in patient records meant that PLP was not present, but it is likely that this underestimates the incidence of PLP. Even documented pain scores of zero may have missed intermittent pain that was not present when a pain score was recorded. We also assumed that the documentation of PLP actually signified PLP and not phantom limb sensation or stump pain. The pharmacological management of the patients, including the use of epidural analgesia and peripheral nerve blocks, was not randomized and was provided as background only.

In conclusion, the key finding of this study was that although 76% of pediatric and young adult patients experienced PLP in the year following amputation it was generally short lived in most patients, with only 10% still experiencing PLP at 1 year. While this is reassuring, the challenge still remains to identify why PLP persists in some patients and to reduce the incidence even further. Larger studies as well as prospective studies are needed to identify which children are at risk of having PLP and also to investigate the association between pre-emptive therapies and the incidence and severity of PLP.

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Figure 1a.
Numbers of patients with PLP by time point in the subset of patients with pre-amputation pain

Figure 1b.
Numbers of patients with PLP by time point in the subset of patients without pre-amputation pain

Table. Listing of cases (n=26) with patient age, type of amputation and pharmacological pain management pre- and post-amputation

Case #	Age	Type of Amputation	PAP	GBP Pre	AMIT Pre	GBP Post	AMIT Post	CEI	CPNB
1	6	R HIP DISARTICULATION		y		y		y	
2	11	L BKA				y		y	y
3	16	L AKA	y	y		y			
4	18	R AKA	y	y		y	y	y	
5	22	L AEA	y			y			
6	14	R BKA	y			y		y	
7	13	L AKA	y	y	y	y	y		
8	18	L AKA	y	y		y		y	
9	20	L AKA	y			y		y	
10	9	R BKA				y		y	
11	16	R BKA		y		y		y	
12	15	L HIP DISARTICULATION		y		y		y	
13	18	L AKA	y	y		y		y	
14	27	L HIP DISARTICULATION	y	y		y		y	
15	14	R AKA	y	y	y	y	y	y	
16a	22	R AKA	y	y		y		y	
16b	22	R HIP DISARTICULATION	y	y		y		y	
17	7	R BEA	y	y		y	y		y
18	9	L FQA	y	y		y			y
19	14	L HIP DISARTICULATION	y	y	y	y	y	y	
20	6	L AKA		y		y		y	
21	16	L AKA		y		y		y	
22	23	R AKA	y	y		y		y	
23	7	R AKA				y			
24	8	R AKA				y		y	
25	18	R AKA	y	y		y			

Abbreviations: PAP = pre-amputation pain, Pre = pre-amputation, Post = postamputation, GBP = gabapentin, AMIT = amitriptyline, CEI = continuous epidural infusion post-amputation, CPNB = continuous peripheral nerve block post-amputation.

Case #	Age	Type of Amputation	PAP	GBP Pre	AMIT Pre	GBP Post	AMIT Post	CEI	CPNB
1	6	R Hip Disarticulation		y		y		y	
2	11	L BKA				y		y	y
3	16	L AKA	y	y		y			
4	18	R AKA	y	y		y	y	y	
5	22	L AEA	y			y			
6	14	R BKA	y			y		y	
7	13	L AKA	y	y	y	y	y		
8	18	L AKA	y	y		y		y	
9	20	L AKA	y			y		y	
10	9	R BKA				y		y	
11	16	R BKA		y		y		y	
12	15	L Hip Disarticulation		y		y		y	
13	18	L AKA	y	y		y		y	
14	27	L Hip Disarticulation	y	y		y		y	
15	14	R AKA	y	y	y	y	y	y	
16a	22	R AKA	y	y		y		y	
16b	22	R Hip Disarticulation	y	y		y		y	
17	7	R BEA	y	y		y	y		y
18	9	L FQA	y	y		y			y
19	14	L Hip Disarticulation	y	y	y	y	y	y	
20	6	L AKA		y		y		y	
21	16	L AKA		y		y		y	
22	23	R AKA	y	y		y		y	
23	7	R AKA				y			
24	8	R AKA				y		y	
25	18	R AKA	y	y		y			