Exploring management of acrodermatitis

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Running title: Acrodermatitis management insights

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ABSTRACT

Background and Objectives: Acquired acrodermatitis enteropathica (AE), a rare dermatological condition, often stems from nutritional zinc deficiency linked to prolonged total parenteral nutrition (TPN). This study aims to explore the pathogenesis, clinical characteristics, and treatment approaches for AE, emphasizing the importance of early recognition and intervention. **Methods and Study Design:** A 51-year-old female patient with acquired AE presented with widespread erythema, pustules, and itching. A comprehensive diagnostic approach, including various tests and skin biopsy pathology, confirmed the diagnosis. Treatment involved zinc gluconate supplementation, topical applications, and symptomatic TPN support. **Results:** One week post-treatment initiation, significant improvement was noted, with reduced erythema, pustules, and skin lesions, alongside improved hair loss. Erosive and ulcerative surfaces healed substantially, indicating positive treatment outcomes. **Conclusions:** The successful management of adult-onset AE in this case underscores the significance of recognizing clinical features and implementing effective treatment strategies. These findings provide valuable insights for diagnosing and managing AE.

Key Words: acrodermatitis enteropathica, acquired zinc deficiency; zinc gluconate, skin biopsy, total parenteral nutrition

INTRODUCTION

In contemporary medical practice, total parenteral nutrition (TPN) has become an essential treatment for sustaining the lives of patients with severe illnesses, with its application increasingly widespread.[1-3] TPN involves administering nutrients to patients unable to obtain sufficient nutrition orally or via the gastrointestinal tract.[4, 5] This method provides essential energy, amino acids, fats, vitamins, and minerals necessary for maintaining bodily functions.[6, 7] However, patients reliant on TPN over the long term may face risks of trace elements deficiencies, notably zinc deficiency.[8-10] Zinc, a crucial trace element, is vital in various physiological processes, including immune response, cell division, and wound healing. A zinc deficiency can lead to various health issues, such as compromised immune function, delayed growth and development, and dermatological and mucosal lesions.[11, 12]

Acrodermatitis enteropathica (AE) is a rare condition closely associated with zinc deficiency, characterized by dermatitis, alopecia, and mucosal inflammation. While AE is typically linked to genetic malabsorption of zinc, acquired nutritional zinc deficiency due to

prolonged TPN in adults can also precipitate AE. Cases of AE in adults are relatively rare and present clinical challenges in diagnosis and treatment. Zinc deficiency not only leads to dermatological damage but can also compromise overall health, exacerbate the progression of existing conditions, and potentially be life-threatening.[13-15] Therefore, timely identification and treatment of zinc deficiency in patients reliant on TPN is crucial.

Although the link between zinc deficiency and AE is recognized to some extent, literature on AE in adults remains sparse. [16, 17] Current research primarily focuses on the genetic basis, clinical manifestations, and treatment approaches of AE in children, with relatively limited findings on AE in adults, particularly those cases resulting from zinc deficiency due to prolonged TPN.[18-20] Moreover, there is significant scope for further discussion within the academic community regarding effective prevention and management strategies for TPN-related zinc deficiency and optimizing diagnostic and treatment strategies for AE. Consequently, in-depth investigation into adult cases of AE, especially those associated with zinc deficiency from TPN, is crucial for enriching existing clinical practices and theoretical knowledge.

Against this backdrop, this study aims to delve into the pathogenesis, clinical characteristics, and treatment strategies of AE triggered by zinc deficiency due to TPN in an adult case. By conducting a comprehensive case analysis, this research offers fresh insights and strategies for identifying and treating adult AE, especially those caused by prolonged TPN-induced zinc deficiency. Additionally, this study aims to heighten healthcare practitioners' awareness of potential trace element deficiencies in TPN patients and enhance their understanding of the diagnostic and therapeutic approaches for adult AE. Through an integrated analysis of this case, the research promises to contribute valuable clinical experience and provide a scientific basis for future preventative strategies and management measures, thereby improving the quality of life and treatment outcomes for TPN patients. In summary, this study's purpose and clinical significance lie in bolstering medical practitioners' awareness of the nutritional deficiencies that TPN may provoke, facilitating timely diagnosis and effective treatment of adult AE, and offering new perspectives and data support for research in related fields.

ETHICAL STATEMENT

This study adhered strictly to medical ethical principles and local laws and regulations, ensuring the rights and privacy of the patient were protected. All clinical practices and experimental procedures received approval from the hospital's ethics committee (2024-34)

and complied with the Declaration of Helsinki. Informed consent was fully obtained from the patient before any diagnostic and therapeutic procedures commenced. The patient understood and agreed to participate in the study, including disclosing case details and treatment plans. Patient privacy and data protection were prioritized, with all personally identifiable information anonymized to prevent disclosure of patient identity. Furthermore, the treatment methods used in this study were based on the latest medical evidence and clinical guidelines aimed at providing the most effective treatment for the patient while minimizing potential risks and discomfort. All treatment decisions were made following thorough discussion and agreement with the patient, ensuring patient autonomy and welfare were upheld.

CASE

A 51-year-old female presented to our hospital with "widespread erythema and pustules accompanied by itching across her body for three months, with symptoms worsening over the last month." One year prior, she underwent adhesiolysis, small bowel detorsion, abdominal lavage and drainage for small bowel volvulus, adhesive intestinal obstruction, and an enterocutaneous fistula at our gastroenterology surgery department. Postoperative care included debridement, suture, drainage tube placement, and an external ostomy bag, with long-term reliance on TPN. The components of the TPN used for this patient included: Compound Amino Acid Injection (18AA-I) 750 ml, Medium/Long Chain Fat Emulsion Injection (C6~24) 20% 250 ml, 50% Glucose Injection 300 ml, Magnesium Sulfate Injection 2 ml, Calcium Gluconate Injection 2 ml, One vial of water-soluble vitamins for injection, One vial of fat-soluble vitamins (Ⅱ) lyophilized powder, 10% Sodium Chloride Injection 20 ml, Potassium Chloride Injection 20 ml, Trace Elements Injection 10 ml, Sodium Glycerophosphate Injection 10 ml, Alanyl-Glutamine Injection 50 ml, and Insulin Injection 12 IU. The patient received TPN treatment for a total of 12 months. Three months ago, without any apparent triggers, symmetric erythema and pustules appeared on the extensor sides of both lower limbs, accompanied by mild itching, which was not adequately addressed. Subsequently, the rash increased in number and spread to the face, extremities, and perioral, perinasal, periocular, and perianal regions, with some pustules rupturing to form ulcerative surfaces with exudation, especially prominent at the limbs' extremities. The patient reported intense itching and pain, which worsened with movements such as stretching and walking. In the past two months, she experienced significant hair loss but denied joint pain, photosensitivity, chills, fever, abdominal bloating, or diarrhea. Over the last six months, she

lost 10 kilograms in weight. The patient denied consanguinity in her parents and any familial history of genetic diseases.

Physical examination revealed the patient's temperature at 36.4°C, pulse at 95 beats per minute, respiratory rate at 19 breaths per minute, and blood pressure at 120/74mmHg. Her height was 150 cm, and her weight was 40 kg. The patient appeared chronically ill, and no palpable lymphadenopathy was detected. Lung auscultation revealed clear breath sounds without any dry or wet rales. The abdomen was soft and non-tender without rebound tenderness. Specialized examinations showed symmetric erythema, erosion, and crusting around the mouth, nose, and eyes, with minor serous fluid exudation (Figure 1 A1). On the buttocks, well-defined purplish-red patches were observed, with maceration, erosion, and fissures in the gluteal cleft surrounded by dark brown crusts (Figure 1 A6). The extensor sides of the lower legs and the hands and feet displayed dark erythema with variably sized thick-walled pustules, negative Nikolsky's sign, with some of the vesicular walls ruptured, leading to eroded surfaces on an erythematous base, interspersed with dark red crusts (Figure 1 A4-A5). Hair was sparse, with scattered soybean-sized erythematous papules on the scalp (Figure 1 A2). Cheek and tongue mucosae exhibited cottage cheese-like white adhesions (Figure 1 A3).

Laboratory and auxiliary examinations revealed that the patient's complete blood count showed a white blood cell count of 3.12×109/L, a red blood cell count of 2.73×1012/L, and a hemoglobin level of 78g/L, all below the normal range. Electrolyte panel results indicated a potassium level of 3.2mmol/L, below average. Liver function tests showed an albumin level of 31.20g/L and a globulin ratio of 1.35ng/mL, suggesting impaired liver function. Trace element analysis revealed a serum zinc level of 55.68μmol/L, below the normal range of 76.5-150μmol/L, and an iron level of 6.59mmol/L, indicating deficiency. Urinalysis, stool tests, and lupus erythematosus full panel were within normal limits. Secretion culture identified Staphylococcus epidermidis. Fluorescence microscopy of oral and tongue swabs for fungi was positive (Figure 2). Skin biopsy pathology of the erythema on the left lower leg showed pustule formation, localized rupture, and erosion in the epidermis, with acantholysis in the spinous layer (Figure 3). Genetic testing of the patient's peripheral blood for the entire coding sequence and splice regions of the SLC39A4 gene (Solute Carrier Family 39 Member A4) found no pathogenic mutations. Therefore, treatment, including oral zinc gluconate, topical application of recombinant human epidermal growth factor, and Mupirocin ointment to promote healing of lesions, along with TPN for symptomatic support, was initiated. One week after treatment began, the lesions around the patient's mouth had healed mainly, the erythema

across her body had lightened in color and reduced in number, most of the dark red crusts covering the erythema had fallen off, pustules had subsided, erosive and ulcerative surfaces had primarily healed, and there was a significant reduction in hair loss (Figure 1 B1-6).

DISCUSSION

AE is a disorder closely associated with zinc absorption anomalies, categorized into genetic and acquired forms characterized by dermatitis, alopecia, and diarrhea. The genetic form of AE is caused by mutations in the SLC39A4 gene located at chromosome 8q24.3, which encodes a zinc transporter protein crucial for zinc absorption in the intestine.[21, 22] Mutations in this gene impair zinc absorption, particularly in areas such as the duodenum and jejunum, closely associated with zinc uptake, leading to reduced plasma and intracellular zinc levels.[22-25] Recently, identifying new mutation sites in the SLC39A4 gene has provided fresh insights into the genetic heterogeneity of AE.[26] Unlike genetic AE, acquired AE, also known as acquired zinc deficiency, primarily results from inadequate zinc intake, absorption disorders, or excessive excretion. This condition is commonly observed in individuals post-gastrointestinal surgery, on TPN, with anorexia nervosa, inflammatory bowel disease, renal diseases, or malignancies.[27-31] For example, patients reliant on intravenous nutrition without adequate zinc supplementation may directly develop zinc deficiency. Clinically, distinguishing genetic and acquired AE is challenging due to their similar manifestations, including characteristic rashes and reduced serum zinc levels. Therefore, testing for the SLC39A4 gene mutation becomes crucial in differentiating between genetic and acquired AE, aiding in establishing an accurate diagnosis.

Zinc, an essential trace element for human health, plays multiple crucial roles, including serving as a cofactor for alkaline phosphatase, alcohol dehydrogenase, RNA polymerase, and various digestive enzymes.[32, 33] It is vital in maintaining immunity, enhancing antioxidant actions, regulating apoptosis, supporting cellular proliferation and differentiation, and promoting growth.[34-36] Zinc's role is particularly significant in skin health, where it participates in the differentiation and proliferation of keratinocytes, demonstrating notable anti-inflammatory properties and wound healing capabilities.[37-39] In the immune system, zinc's importance cannot be overlooked.[40-42] It is essential for innate immunity, enhancing the activity of neutrophils, natural killer cells, and macrophages, increasing Toll-like receptor expression, and regulating cytokine production post-inflammation.[41, 43] Zinc also plays a critical role in adaptive immunity, involving T and B cell proliferation, differentiation, and function maintenance, thereby central to regulating immune responses.[44, 45] Consequently,

zinc deficiency can not only diminish immune function but also increase the risk of infections, such as the formation of cottage cheese-like white adhesions and Candida infections.[46-48]

Advancements in the treatment of AE, for both its genetic and acquired forms, have validated the significant effectiveness of zinc supplementation. The study conducted a comprehensive review of literature published between 2010 and 2024 in the PubMed database using "zinc deficiency" and "total parenteral nutrition" as search keywords. This review, as summarized in Table 1, encompasses case reports detailing symptoms of zinc deficiency and their treatment outcomes across a diverse age range, from infants to adults. These patients exhibited clinical symptoms such as dermatological lesions, diarrhea, and alopecia due to zinc transport issues caused by mutations in the SLC39A4 gene. Treatment primarily involved zinc supplementation, with the duration of therapeutic response varying from days to months, yet most cases demonstrated considerable clinical improvement. This underscores the pivotal role of zinc supplementation in managing symptoms related to zinc deficiency. For instance, literature reports highlighted the complete resolution of AE-related skin lesions within one and six months post-zinc treatment in a two-month-old female infant and a ten-year-old boy, respectively.[49, 50] These case studies highlight the critical role of zinc supplementation in managing AE, emphasizing the necessity of monitoring and supplementing zinc levels in specific populations, such as patients reliant on long-term TPN. While healthy individuals typically acquire sufficient zinc through their diet, those on prolonged TPN face a significant risk of zinc deficiency, which can lead to severe health complications, including AE. Various case studies underscore the urgency of zinc supplementation for this group. For instance, one study described AE developing in a patient after long-term TPN treatment following small intestine resection due to an enterocutaneous fistula. Another case reported AE symptoms in a patient post-bariatric surgery. In these instances, timely zinc supplementation markedly improved skin lesions (Danielle[51]; Kurt BÖ[52]). Furthermore, a report by Lauren et al. detailed severe skin lesions in a 9-year-old child within two weeks of starting TPN, with significant lesion improvement and normalization of zinc levels within 13 days of zinc supplementation (reference range 60-120 μg/dL). These cases demonstrate the significant effectiveness of zinc supplementation for AE patients, highlighting the importance of monitoring and supplementing trace elements, especially zinc, in populations such as TPN patients.

In addition, long-term use of TPN may not only lead to zinc deficiency but also other serious adverse events, such as refeeding syndrome, parenteral nutrition-associated liver disease (PNALD), and catheter-related bloodstream infections (CRBSIs). We conducted a

comprehensive review of related literature published between 2010 and 2024 by searching the PubMed database using "clinical case" and "total parenteral nutrition" as keywords, with "Clinical Trial" as a filter. Ultimately, we identified 15 relevant papers, which are summarized in Table 2.

In the clinical application of TPN, it is widely used for patients unable to intake nutrients through normal routes, particularly in special populations such as cancer patients, postoperative recovery cases, and premature infants. For cancer patients, TPN not only maintains nutritional balance but also effectively manages blood glucose fluctuations, with significant effects observed in liver and colorectal cancer patients.[53] In postoperative gastrointestinal cancer patients, supplementation with antioxidants and vitamins significantly improved oxidative stress and antioxidant enzyme activity, especially in small intestine cancer patients.[54] For preterm infants, the addition of phosphorus to TPN effectively increased bone density and prevented osteoporosis.[55] In patients who rely on home TPN for long-term nutrition, studies suggest that using taurolidine lock can reduce catheter-related bloodstream infections, but its clinical benefit is not significant in cases with low infection rates.[56]

For patients with severe Crohn’s disease, preoperative TPN significantly reduced postoperative complications.[57] In acute pancreatitis patients, the combination of TPN with glutamine helped lower the risk of infections and mortality, while shortening hospital stay.[58] Additionally, some studies highlight the important role of TPN in addressing specific complications. For instance, in high-risk neuroblastoma patients, vitamin B-1 deficiency in TPN can lead to Wernicke encephalopathy, but timely supplementation can quickly reverse the symptoms.[59]

In liver transplant patients, the combination of TPN with omega-3 fatty acids improved liver function and reduced postoperative hospital stay.[60] Meanwhile, fish oil lipid emulsions showed positive effects in preventing parenteral nutrition-associated cholestasis (PNAC) in infants.[61] Another study demonstrated that combining EPA and DHA with TPN reduced tumor-promoting fatty acid levels in metastatic liver cancer.[62] Furthermore, vitamin monitoring in TPN is critical during stem cell transplantation, as prolonged TPN treatment may lead to severe micronutrient deficiencies.[59]

For low-birth-weight infants, studies show that the timing of enteral nutrition can impact the effectiveness of TPN in overall nutritional management, supporting full recovery in these infants.[61] The efficacy of fish oil lipid emulsions in preventing TPN-associated cholestasis has also been confirmed, particularly in preterm infants.[60] TPN has demonstrated benefits in adult

acute myeloid leukemia patients, reducing gastrointestinal discomfort and shortening the duration of treatment-related hospitalization.[63]

Overall, TPN serves as a critical nutritional support method widely applied in various diseases and postoperative patients. When properly administered, TPN can improve patient prognosis, reduce complications, and enhance survival quality. However, close monitoring of patients' nutritional status, micronutrient balance, and potential complications is essential to ensure the safety and efficacy of TPN.[55, 62]

This case report describes a 51-year-old female patient who developed a rare case of acquired AE due to nutritional zinc deficiency caused by long-term reliance on TPN (Figure 4). The patient presented with erythema and pustules, accompanied by itching and a gradual worsening of symptoms, marking an acute phase of dermatological lesion development. Clinical examination revealed significant hair loss, skin lesions, and oral mucosal changes. Laboratory tests highlighted characteristic findings of low white blood cell count, low hemoglobin, and low serum zinc levels, with no pathogenic mutations in the SLC39A4 gene identified, confirming the diagnosis of nutritional deficiency. Despite notable improvement in dermatological symptoms following zinc supplementation, the underlying issue of the enterocutaneous fistula remained unresolved, necessitating further gastroenterological surgical intervention. This case underscores the importance of meticulous nutritional monitoring and assessment in patients dependent on TPN long-term, with a particular focus on essential trace elements like zinc. Although AE is exceedingly rare in adults, this case demonstrates that it is not exclusive to infants and children; adults can also develop the condition under specific circumstances, such as prolonged TPN. The possibility of nutritional zinc deficiency should be considered for adults presenting with clinical features of AE, with prompt testing and supplementation of zinc levels. This case emphasizes the necessity of comprehensive nutritional evaluation and monitoring for long-term TPN patients to prevent complex diseases caused by trace element deficiencies. Furthermore, it suggests the need for further research into the precise mechanisms linking nutritional zinc deficiency and AE, as well as exploring more effective prevention and treatment strategies. Additionally, for patients requiring long-term TPN support due to reasons such as enterocutaneous fistulas, actively seeking definitive solutions, such as surgical interventions, is critical to addressing the root cause.

Despite this study offering valuable insights into adult cases of AE, it has limitations. Primarily, being based on a single case report restricts our ability to generalize findings across all patients on TPN. Individual patient conditions, including underlying health status,

nutritional needs, and potential genetic predispositions, could affect AE's incidence and treatment response. Hence, while this case contributes significant clinical insights, its applicability to all similar scenarios may be limited. Additionally, the study's design limitations, particularly the need for long-term follow-up data, preclude a comprehensive assessment of the long-term health impacts of treatment interventions, including risks of relapse and the durability of treatment effects. These factors limit our understanding of the comprehensiveness and sustainability of AE treatment outcomes.

Given the findings and limitations of the current study, future research needs to focus on several key areas. Broader studies, including multiple case studies or clinical trials, are necessary to validate the generalizability of these findings and the efficacy of treatment approaches. Such studies should encompass patients of diverse ethnicities, ages, and health backgrounds to understand AE's clinical manifestations and treatment responses comprehensively. Future research should also explore more effective treatment combinations, especially for those patients who respond poorly to conventional treatments. Optimizing treatment strategies can enhance therapeutic outcomes and improve patient quality of life. Lastly, emphasizing the importance of preventive strategies, particularly implementing regular nutritional assessments and monitoring plans in TPN patients, is crucial for reducing the incidence of AE and other nutritional deficiencies. Through these efforts, more significant progress can be anticipated in preventing, diagnosing, and treating adult AE.

Conclusion

In summary, by detailing a case of adult-acquired AE, this study underscores the critical role of zinc deficiency induced by prolonged TPN in the pathogenesis of AE. While it is a single case study, it provides invaluable clinical observations that serve as essential references for understanding AE's clinical features, diagnostic processes, and treatment approaches. Facing this complex clinical issue, future research requires broader data collection and deeper scientific exploration to enhance diagnostic accuracy, optimize treatment plans, and improve patient outcomes and quality of life.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no conflict of interest.

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Table 1. Summary table of literature on zinc deficiency-related acrodermatitis enteropathica in patients on long-term TPN

Journal	Authors	PMID	Year	Case Presentation	Diagnosis	Treatment	Outcome
StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan.	Not provided	28722865	2023	Inherited form of zinc deficiency due to mutations in SLC39A4.	Inherited zinc deficiency.	Not specified.	Not specified.
Oman Med J.	Not provided	33274070	2020	Two-month-old girl with skin lesions, diarrhea, and alopecia.	Acrodermatitis enteropathica.	Zinc therapy.	Resolved after one month.
Cureus.	Not provided	37214014	2023	10-year-old male with diarrhea, abdominal pain, and skin lesions.	Acrodermatitis enteropathica confirmed by low serum zinc levels.	Oral zinc sulfate supplementation.	Resolved after six months.
Acta Biomed.	Not provided	37486600	2023	5-year-old with diarrhea, alopecia, and skin lesions during parenteral nutrition.	Acquired zinc deficiency.	Oral zinc supplementation.	Rapid clinical improvement.
BMC Pediatr.	Not provided	31987033	2020	16-month-old twin boys with skin lesions and normal plasma zinc levels.	Compound heterozygous for two unreported SLC39A4 mutations.	Not specified.	Not specified.
Indian J Dermatol.	Not provided	36386094	2022	6-year-old boy with hard plaques over both palm and sole, and periorificial areas.	Zinc deficiency dermatoses.	Zinc supplementation	Improvement of serum alkaline phosphatase level within 3 months.
J Ayub Med Coll Abbottabad.	Not provided	36566420	2022	12-year-old boy with cutaneous manifestations, diarrhoea, and sparse hairs.	Low level of plasma zinc, and alkaline phosphatase level.	Zinc supplements	Significantly improved in a few days.
Case Rep Dermatol Med.	Not provided	34123436	2021	28-year-old male with type 1 diabetes presenting with signs and symptoms of AE.	Inherited or acquired zinc deficiency.	Not specified	Not specified
Front Pediatr.	Not provided	36479285	2022	9 years and 4 months old girl with a repeated skin rash and low blood zinc level.	Compound heterozygous for two SLC39A4 mutations.	Continuous zinc supplementation.	Significant improvement after continuous supplementation.
Not provided	Not provided	33837739	Not specified	Analysis of AE-causing missense mutations in hZIP4-ECD showing abolished zinc transport activity.	Loss-of-function mutations of hZIP4 causing AE.	Not specified	Not specified

Table 2. Cases of adverse events associated with long-term use of TPN

Journal	Authors	PMID	Year	Case Presentation
Scand J Gastroenterol	Jacobson S	22242614	2012	Crohn's disease, Preoperative TPN
Chin Med J (Engl)	Yang JC, Dai YY, Wang LM, Xie YB, Zhou HY, Li GH	26228214	2015	Glycemic variation in tumor patients receiving TPN
JPEN J Parenter Enteral Nutr	Klek S, Szczepanek K, Hermanowicz A, Galas A	24604029	2015	Home parenteral nutrition, catheter-related bloodstream infections
Pediatr Blood Cancer	Darlington WS, Pinto N, Hecktman HM, Cohn SL, LaBelle JL	26174546	2015	Wernicke encephalopathy during stem cell transplantation
Acta Med Iran	Mazouri A, Khosravi N, Bordbar A, Khalesi N, Saboute M, Taherifard P, Mirzababaee M, Ebrahimi M	28843241	2017	Premature neonates, phosphorus supplementation in TPN
Chin Med J (Engl)	Yang JC, Dai YY, Wang LM, Xie YB, Zhou HY, Li GH	26228214	2015	Glycemic variation in tumor patients receiving TPN
Cell Biochem Funct	Szpetnar M, Matras P, Kiełczykowska M, Horecka A	22125185	2012	Antioxidant depletion post gastrointestinal cancer surgery with TPN
Acta Med Iran	Mazouri A, Khosravi N, Bordbar A, Khalesi N	28843241	2017	Phosphorus supplementation with TPN in preterm neonates
JPEN J Parenter Enteral Nutr	Klek S, Szczepanek K, Hermanowicz A, Galas A	24604029	2015	Taurolidine lock use in home parenteral nutrition
Scand J Gastroenterol	Jacobson S	22242614	2012	Preoperative TPN in Crohn's disease patients
JPEN J Parenter Enteral Nutr	Hajdú N, Belágyi T, Issekutz A, Bartek P	22740219	2012	Glutamine with TPN in acute pancreatitis
Pediatr Blood Cancer	Darlington WS, Pinto N, Hecktman HM	26174546	2015	Wernicke encephalopathy in neuroblastoma with TPN

Journal	Diagnosis	Treatment	Outcome
Scand J Gastroenterol	Crohn's disease	Total parenteral nutrition (TPN)	Reduced postoperative complications
Chin Med J (Engl)	Cancer with TPN	TPN with blood glucose monitoring	Glycemic control varies with tumor type
JPEN J Parenter Enteral Nutr	Home parenteral nutrition	Taurolidine lock, home parenteral nutrition	No significant reduction in infection rates with taurolidine lock
Pediatr Blood Cancer	High-risk neuroblastoma	Total parenteral nutrition with vitamin B1	Wernicke's symptoms resolved with Vitamin B1
Acta Med Iran	Premature neonates with low bone density	TPN with intravenous Glycophos (sodium glycerophosphate)	Increased bone mineral density, lower ALP levels
Chin Med J (Engl)	Cancer with TPN	TPN with blood glucose monitoring	Significant glycemic variation among tumor types
Cell Biochem Funct	Gastrointestinal cancer surgery	TPN with antioxidants and vitamins	Antioxidant enzyme activity decreased in small intestine cancer patients
Acta Med Iran	Preterm neonates with low bone density	TPN with sodium glycerophosphate	Increased bone mineral density in neonates
JPEN J Parenter Enteral Nutr	Home parenteral nutrition	Taurolidine lock in TPN	Low infection rates, no added value of taurolidine lock
Scand J Gastroenterol	Crohn's disease	Preoperative TPN for 18-90 days	Reduced postoperative complications
JPEN J Parenter Enteral Nutr	Severe acute pancreatitis	TPN with intravenous glutamine	Reduction of mortality with glutamine
Pediatr Blood Cancer	High-risk neuroblastoma	TPN with vitamin B1 supplementation	Wernicke's symptoms resolved with Vitamin B1

Table 2. Cases of adverse events associated with long-term use of TPN (cont.)

Journal	Authors	PMID	Year	Case Presentation
Pediatr Blood Cancer	Darlington WS, Pinto N, Hecktman HM	26174546	2015	Wernicke encephalopathy in neuroblastoma with TPN
World J Gastroenterol	Zhu XH, Wu YF, Qiu YD, Jiang CP	24576844	2012	Liver protection with omega-3 fatty acids in TPN
Neonatology	Lam HS, Tam YH, Poon TC	31994953	2020	PNAC prevention with fish oil lipid in infants
Prostaglandins Leukot Essent Fatty Acids	Stephenson JA, Al-Taan O, Arshad A	24342144	2014	Eicosapentaenoic and docosahexaenoic acid impact in TPN

Journal	Diagnosis	Treatment	Outcome
Pediatr Blood Cancer	High-risk Neuroblastoma	TPN with vitamin B1 supplementation	Wernicke's symptoms resolved with Vitamin B1
World J Gastroenterol	End-stage liver disease	TPN with omega-3 fatty acids	Liver function improved with omega-3s
Neonatology	Parenteral Nutrition Associated Cholestasis	TPN with fish oil lipid emulsion	PNAC progression halted
Prostaglandins Leukot Essent Fatty Acids	Liver Cancer Metastases	TPN with EPA and DHA	Lower liver tumor-promoting fatty acids in metastases

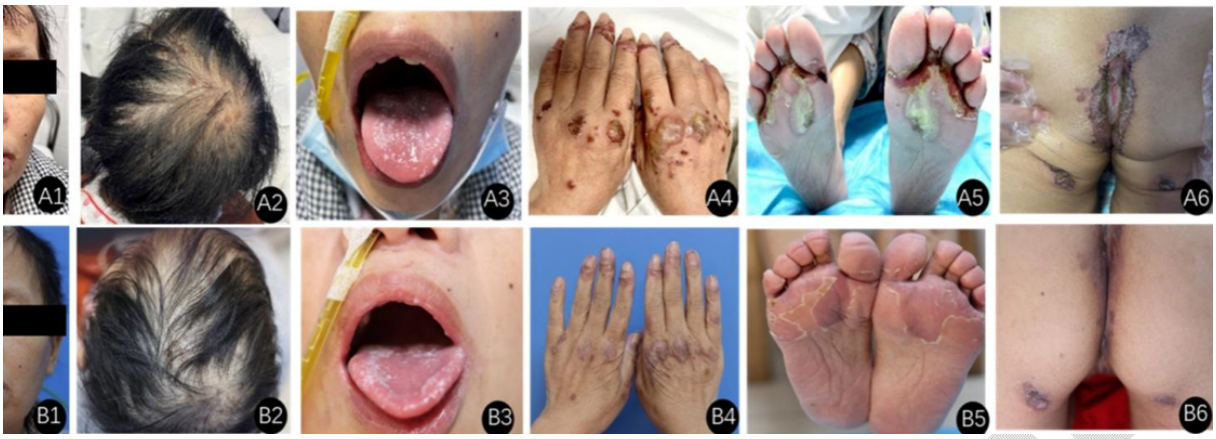

Figure 1. Clinical manifestations of acquired zinc deficiency dermatitis in adults and comparison before and after treatment. This series of images originates from a case of adult-onset dermatitis due to acquired zinc deficiency following TPN. Comparing clinical manifestations before treatment (A1-A6) and one week after treatment (B1-B6) illustrates significant improvement in clinical symptoms through a comprehensive treatment regimen, including oral zinc gluconate, topical application of recombinant human epidermal growth factor, and Mupirocin ointment.

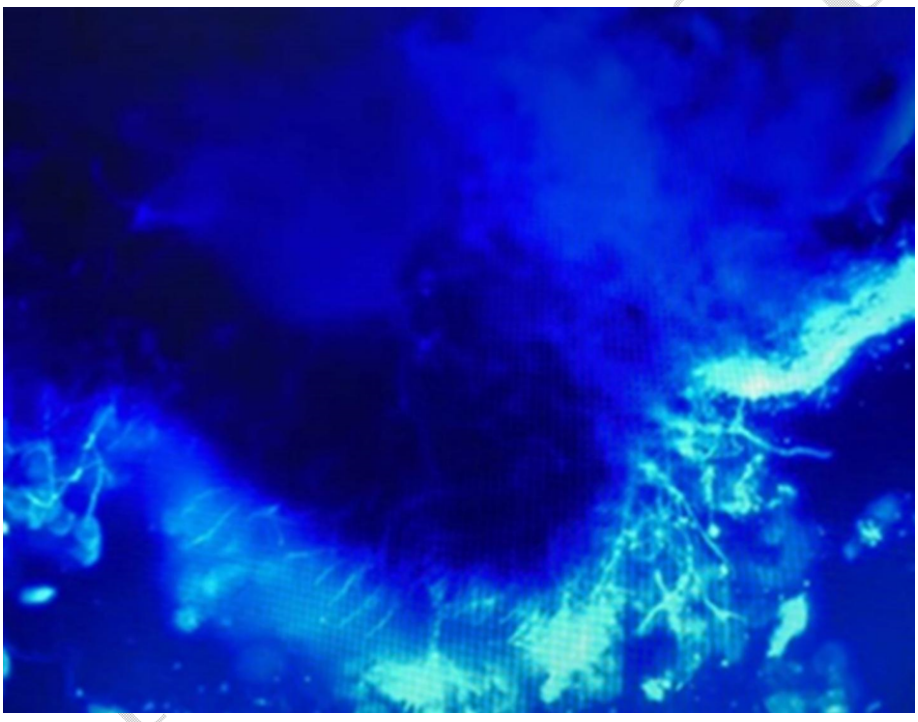

Figure 2. Fluorescence microscopy illustration of oral fungal infection. This image employs fluorescence microscopy to demonstrate fungal infection in a swab sample from the patient's oral mucosa. Under specific excitation wavelengths, fungal cell wall components emit fluorescence, making the fungi visible under the fluorescence microscope. The fluorescent areas in the image indicate the presence of fungi

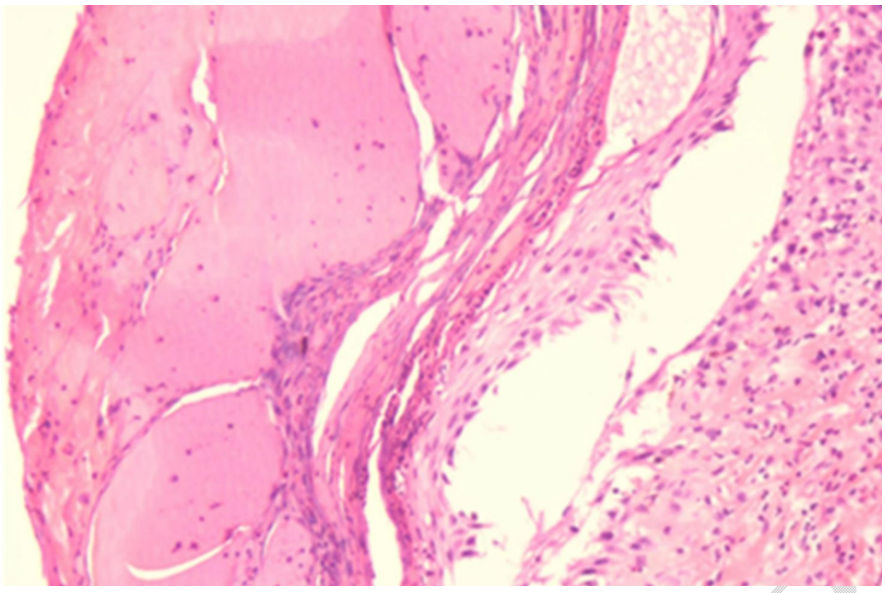

Figure 3. Histopathological evidence of epidermal pustule formation and rupture (HE stain, 20× magnification)

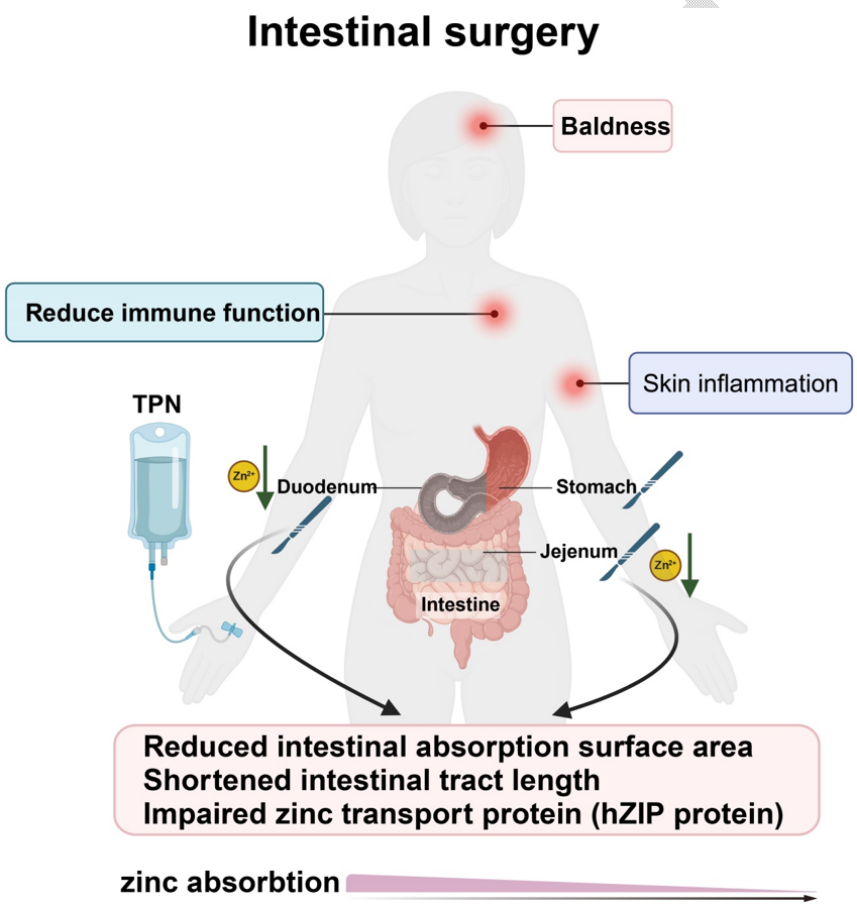

Figure 4. Potential causes of adult acquired AE following intestinal surgery