Cutaneous skin changes are common in patients undergoing treatment for cancer. However, changes in central line care, maintenance practices, and chemotherapy protocols in the early 2000s may have led to the development of a common problem of irritant contact dermatitis (ICD) at peripherally inserted central catheter (PICC) insertion sites. Repeated exposure to chlorhexidine gluconate topical antiseptic solution, used in the general dressing care and maintenance with PICCs, may be leading contributor to the development of ICD at the insertion site. A number of additional factors theoretically contribute to the development of ICD at the PICC insertion site in patients receiving chemotherapy. In this article, ICD will be defined, incidence and potential risk factors will be identified, and a diagnostic framework will be explored; in addition, pathophysiology, onset, presentation, evaluation, and differential diagnosis of ICD at PICC sites will be analyzed. Finally, a synopsis of three different treatment approaches from healthcare facilities in Canada as well as implications for nursing practice and research will be presented.