Calcinosis Cutis: A Rare Complication Following Liver Transplantation

Wen-Chi Lin  Wan-Lung Lin  Jennifer C. Lee  Wei-Hsin Juan, Tseng-tong Kuo  Hong-Shang Hong

The clinical manifestations of calcinosis cutis vary from asymptomatic cutaneous papules to life-threatening calciphylaxis. We describe a 61-year-old female who was found to have extensive calcinosis cutis on her left forearm 4 days following liver transplantation. Large amount of calcium chloride solution was intravenously infused during the operation at the same site without gross extravasation. This uncommon complication may be attributed to local tissue hypercalcemia and concomitant impairment of renal function. Recognizing this phenomenon is important in managing patients with liver transplantation. (Dermatol Sinica 24: 131-134, 2006)

Key words: Calcinosis cutis, Liver transplantation, Calcium chloride solution, Blood transfusion

From the Departments of Dermatology and Pathology,1 Chang Gung Memorial Hospital, Taipei
Accepted for publication: November 24, 2005
Reprint requests: Wei-Hsin Juan, M.D., Department of Dermatology, Chang-Gung Memorial Hospital, No 199, Tung-Hwa North Road, Taipei 10507, Taiwan.
TEL: (02)27135211-3399  FAX: (02)27135211-3389
INTRODUCTION
Liver transplantation is performed more often nowadays because of improved surgical techniques and better immunosuppressive drugs. There have been a few reports of calcinosis cutis developing after liver transplantation. Intravenous calcium solution used to correct hypocalcemia secondary to large amounts of blood transfusion during surgery may be the cause when there is no tissue calcification of other organs besides the cutaneous tissue. We report a patient who developed extensive calcified skin lesions shortly after liver transplantation.

CASE REPORT
A 61-year-old woman underwent liver transplantation for hepatitis B virus-related cirrhosis and hepatocellular carcinoma. Hepatorenal syndrome developed 2 months prior to the operation, and serum creatinine fluctuated between 3.5 to 6.5 mg/dl (0.6-1.4). Serum calcium and phosphate levels were 9 mg/dl (8.6-10.3) and 5.9 mg/dl (2.5-4.5) preoperatively. During operation, 12 units of whole blood, 18 units of packed red blood cells, 32 units of fresh frozen plasma, 12 units of platelet and 12 units of cryoprecipitate were given through the central line on the neck. A total of 2,750 ml of 5% calcium chloride, which included approximately amount of 13.75g of calcium, were also administered slowly by intravenously drip through the peripheral catheter on the left forearm. There was no clinical evidence of extravasation such as local swelling, erythema nor signs of sluggishness of flow during or after surgery.

Four days after the operation, an indurated, yellow and asymptomatic plaque of 2-3 cm developed on the left forearm of this patient. In the subsequent four weeks, the plaque enlarged rapidly to 12 × 5cm with linear peripheral extensions and focal ulcerations that were extremely tender (Fig. 1). Serum calcium and phosphate levels were 7.6 mg/dl and 7.2 mg/dl, respectively, and the parathyroid hormone (PTH) level was 88 pg/ml (12-72) at that time. A skin biopsy taken from the lesion on the left forearm revealed diffuse basophilic calcium deposits in dermis without prominent inflammatory cell infiltrates (Fig. 2). Von Kossa stain confirmed the presence of calcium (Fig. 3) and radiographs also showed cutaneous calcification (Fig. 4). Such findings were consistent with calcinosis cutis. Gradual resolution was recorded 3 months later. Further investigations including computed tomography of abdomen, renal sonography, and chest radiograph disclosed no other soft tissue calcification.

DISCUSSION
Calcinosi cutis is classified into four subtypes: metastatic, dystrophic, idiopathic, and
Metastatic calcinosis cutis occurs in normal tissue when there is an underlying defect in calcium metabolism, and it occurs most commonly in chronic renal failure patients. Calciphylaxis is the life-threatening form of metastatic calcinosis cutis and is characterized by progressive vascular calcification, soft tissue necrosis, and ischemic necrosis of skin. Chronic renal failure along with secondary hyperparathyroidism is one of the risk factors for developing calciphylaxis. Iatrogenic calcinosis cutis due to extravasation of intravenous calcium solution and prolonged contact with electrode paste containing calcium salt when undergoing electroencephalography or electromyography have been reported. In our case, the existence of renal failure and the infusion of intravenous calcium solution are believed to be contributing to the calcium deposits.

During liver transplantation, patients often require transfusion of large amounts of blood products containing sodium citrate. Since sodium citrate can not be metabolized normally during the ahepatic phase of liver transplantation, it is likely to cause hypocalcemia and metabolic alkalosis by chelation of ionized calcium. Consequently, the routine use of intravenous calcium solution to correct hypocalcemia will result in transient and rapid elevation of local tissue concentration and local tissue damage, which is sufficient to form calcification. Metabolic alkalosis may also play a role in the pathogenesis because alkalinity favors the precipitation of calcium salts.

Munoz et al. first reported ectopic calcification in seven of twenty patients who underwent liver transplantation. The organs that were involved included lung, grafted liver, blood vessel walls, kidney, adrenal glands, and gastric mucosa. Five of these seven patients have had elevated serum PTH levels and chronic renal failure before liver transplantation.

Ectopic calcification solely confined to cutaneous tissue after liver transplantation had been reported in 6 patients. Juegla et al. reported four adults who developed calcinosis cutis after liver transplantation. All these patients had normal serum calcium, phosphate, and PTH and renal function, and all lesions were located near sites where intravenous calcium solution was given during surgery. Larralde et al. reported the occurrence of calcinosis cutis in a 3-year-old girl ten days after liver transplantation. The clinical presentation was multiple whitish papules on the trunk. Lateo et al. recently reported a case of calcinosis cutis in a 22-year-old woman on the upper arm where no intravenous calcium solution had been administered. Transient elevation of serum calcium and phosphate levels was noted on the first post-operation day. Intravenous calcium solution used to correct hypocalcemia secondary to large amounts of blood products transfusion during surgery.

![Fig. 3](image1)

Von-Kossa stain confirmed the extensive deposition of calcium. (100X)

![Fig. 4](image2)

The radiograph of left forearm revealed diffuse radio-opaque material in the subcutaneous tissue.
surgery may be the leading cause when there was no other organ involvement besides the cutaneous tissue. The pathogenesis was thought to be transient and rapid elevation in local tissue calcium concentration, local tissue damage, and metabolic alkalosis that facilitated the precipitation of calcium salts.1 Transient and undetected elevations of serum calcium and phosphate levels due to metabolic abnormalities during the post-operation period may also be implicated in this condition.

In our case, the pathogenesis of the skin lesion was considered multifactorial. The cutaneous calcification occurred near the intravenous calcium solution infusion site and the patient had also received large amounts of blood products transfusion during surgery. Histopathologic examination shows no marked inflammatory change. So, local transient elevation of calcium concentration with mild tissue injury may be the cause. At the same time, minor or sub-clinical extravasation of calcium chloride solution may also be the contributing factor, but the patient experienced no common symptoms of direct extravasation, such as pain, erythema, or swelling, immediately after infusion. Renal function impairment with secondary hyperparathyroidism also developed in our case. Therefore, metastatic calcinosis cutis could not be completely excluded, although there was only one cutaneous lesion where intravenous calcium chloride solution had been given and no evidence of involvement of other organs or vessels.

In conclusion, we report the seventh case of ectopic calcification occurred only in cutaneous tissue in patients following liver transplantation. Physicians should recognize the risk of this rare complication during the assessment of skin lesions in liver transplant recipients.

REFERENCES