Management of Fat Necrosis after Autologous Fat Transplantation for Breast Augmentation

Jeng-Yee Lin, M.D., Ph.D.
Ping Song, M.D.
Lee L. Q. Pu, M.D., Ph.D.

Taipei, Taiwan; and Sacramento, Calif.

Background: Palpable lumps as sequelae of fat necrosis after fat grafting to the breast may not only cause physical or psychological symptoms to patients but also potentially complicate breast cancer screening. In this article, the authors present their experience in management of fat necrosis following fat grafting for breast augmentation.

Methods: Over a 5-year period, a total of 685 Asian women (age range, 20 to 58 years) underwent autologous fat transplantation to the breasts. The average volume of fat graft to each breast was 205 ± 45 cc. The preoperative and postoperative photographs and the breast volume were recorded. Detection of fat necrosis was based on clinical examinations and imaging studies. The mean follow-up was 208 ± 36 days.

Results: The mean volume increase was 135 ± 20 cc in a single breast, with a mean graft retention rate of 65 percent. Sixty-six patients (9.6 percent) were found to have fat necrosis in the form of solitary or multiple cysts, sclerotic nodules, or calcifications in either one or both breasts postoperatively. The average time before first detection of the breast lump was 108 ± 45 days. Management of fat necrosis included aspiration or excision based on the authors' treatment algorithm. The symptoms related to fat necrosis such as discomfort on palpation, pain, or possible skin reaction were significantly improved in 54 of 57 patients (94.7 percent).

Conclusions: Fat necrosis following autologous fat grafting for breast augmentation can be managed successfully and its related symptoms can be relieved in 94.7 percent of patients. It can be approached safely based on a sound algorithm developed by the authors. (*Plast. Reconstr. Surg.* 142: 665e, 2018.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

4
THERAPEUTIC

The history of autologous fat transplantation to the breasts can be dated back to 1895, but it was not until 1987 that Bircoll reported his experience with lipofilling to the breasts for breast augmentation.[1–3] However, controversy regarding whether consequences of fat necrosis associated with fat grafting could interfere with breast cancer screening concurrently arose. More recently, the American Society of Plastic Surgeons has relaxed its attitude toward fat grafting to the breasts following a report from the Fat Grafting Task Force in 2009.[4] Several authors have reported the safety and efficacy of fat grafting to the breasts,[5–10] and limited data on the radiologic impact of fat grafting to the breasts suggest that there is minimal interference with breast cancer screening. In addition, improved understanding and techniques of fat grafting have further contributed to the refinement and popularity of its application to breast augmentation.[8]

However, even with refined techniques and novel innovations, autologous fat transplantation still challenges surgeons with unpredictable graft survival and fat necrosis. Nonabsorbed necrotic fat may have a variety of presentations such as an oily cyst, sclerotic induration, and calcified solid tumor. It may also cause skin retraction, dermatitis, and postinflammatory hyperpigmentation

From the Division of Plastic Surgery, Department of Surgery, Taipei Medical University Hospital, Taipei Medical University; and the Division of Plastic Surgery, Department of Surgery, University of California, Davis Medical Center.
Received for publication June 12, 2017; accepted April 19, 2018.
Presented at the Third World Congress of the International Society of Plastic Regenerative Surgeons, in Beijing, People's Republic of China, December 4 through 6, 2015.

DOI: 10.1097/PRS.0000000000004898

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

when nonviable fat is close to the skin. The most worrisome consequence of fat necrosis revolves around the concern that scarring and calcification may potentially interfere with breast cancer surveillance. Therefore, complications of fat necrosis in the breast may cause discomfort physically or psychologically and should be managed promptly and properly. In this study, we present our clinical experience and an algorithm for management of fat necrosis in the breasts following autologous fat transplantation for breast augmentation.

PATIENTS AND METHODS

A total of 685 female Asian patients (age range, 20 to 58 years) who underwent autologous fat transplantation for primary or secondary breast augmentation from February of 2009 through March of 2014 were included in this study. The study was reviewed and approved by the Taipei Medical University Hospital Institutional Review Board. Autologous fat grafting was performed in 622 female patients for primary breast augmentation because of cosmetic concern and in 63 patients for secondary breast augmentation after removal of breast implants. All patients were advised to have at least one baseline breast imaging study to exclude any preexisting breast disease such as malignant breast tumors or highly suspicious lesions. Any patients at high risk for breast cancer were excluded from undergoing this procedure. All patients underwent bilateral breast augmentations. The mean follow-up was 208 ± 36 days. Detection of fat necrosis was based primarily on physical examination followed by imaging or histologic studies when necessary.

Operative Technique

Potential donor sites for fat grafting include the medial and lateral thighs, upper and lower abdomen, and the flanks where excess fat can be harvested. Suction-assisted harvest technique was used to obtain the fat graft in the following sequence: infiltration of tumescent fluid (2% lidocaine, 10 ml; adrenalin, 0.5 mg; and sodium bicarbonate, 35 mg in 500 ml normal saline solution), followed by low-pressure liposuction, and final purification of lipoaspirates with centrifugation. Vacuum-assisted liposuction was set to a pressure of −70 cmH_2O. Lipoaspirates were collected into a 2-liter canister before they were transferred into multiple 10-cc Luer-lock syringes, which were subsequently centrifuged at 3000 rpm (1200 *g*) for 3 minutes.[11] The fluid layer at the bottom of the syringe was discarded after opening the syringe plug and the supernatant oil layer in the upper part was decanted. The middle layer containing the adipose cells was preserved for injection. A 15-cm 12-gauge cannula was attached to each syringe containing the fat graft, which was then slowly injected into the breast in a radial fashion through tiny incisions at the 3-, 6-, and 9-o'clock positions to achieve even distribution of fat graft into the breast mound. The fat grafts were placed above and beneath the breast tissue. Specifically, fat graft was injected into the subcutaneous layer, behind the breast parenchyma, intramuscularly, and beneath the pectoralis muscle (referring to the proximal thicker part of the muscle). Fat graft was injected in small amounts as the cannula was withdrawn; we used multiple passes, with multiple tunnels, and within multiple tissue planes. Breast ultrasonography can be used as guidance for more precise fat graft placement. The endpoint of fat injection is based on the tension across the skin pocket caused by filling of the fat graft as judged by the operating surgeon. The average injection volume was 205 ± 45 cc in each breast.

Fat grafting to the breasts was performed as secondary breast augmentation in 63 patients who had breast implants previously for primary breast augmentation and requested implant removal because of capsular contracture (Baker grade III to IV) in 18 patients or because of a nonspecific reason of discomfort either psychologically or physically in 45 patients. No implants were replaced and augmentation to the breast was performed with only fat grafts for all secondary cases. Removal of breast implants was performed through the incisions of previous implant breast augmentation. The fat grafting procedure was performed immediately after implant removal with the method as described. Immediate fat grafting after implant removal was also reported to be an effective and successful strategy for breast augmentation.[12] Capsulotomy was performed for grade I to II capsular contracture and partial capsulectomy on the anterior wall for grade III to IV capsular contracture to ensure an adequate expansion of subcutaneous skin pocket for maximum lipofilling, especially in the lower pole of the breast. Fat grafts were injected to the areas above the anterior wall of the capsule to avoid fat grafts being placed into the cavity following implant removal.

Postoperative Assessment

Preoperative and postoperative photographs were taken in each patient. Breast volumes were

measured using the Vectra XT 3D imaging system (Canfield Scientific, Parsippany, N.J.) before the operation and at 6 months postoperatively. The difference between preoperative and postoperative breast volume was recorded. Fat necrosis was detected primarily by manual palpation during regular follow-up visits by the primary surgeon. All palpable masses were evaluated and diagnosed by breast ultrasound. The results of ultrasound then serve as the basis for the subsequent management of fat necrosis.

Specific Types of Fat Necrosis and Related Management

In this study, the classification of fat necrosis in its variable form is based on clinical examination that can be used by the authors to guide their management of fat necrosis in this series. Therefore, the definition of each type can be subjective, and different types of fat necrosis can be found in one breast of the same patient.

Cysts

Oil cysts are soft and mobile on palpation. This category represents the majority of fat necrosis and requires only simple aspiration using a syringe and an 18-gauge needle. The cohesive oil content may appear yellowish or white in color (Fig. 1) and usually cannot be aspirated with smaller needles. A gentle squeeze on the palpated nodule may assist in aspiration.

Calcification

The calcified fat nodule appears firm and hard on palpation and can be either mobile or fixed (Fig. 2). A small 2- to 3-mm stab incision is usually enough for direct excision of the nodule. A hemostat or Allis clamp can be applied to the mass for traction and ease of excision. Larger calcified nodules (>3 cm) should be approached with a larger incision. Using digital sensation as guidance or visual confirmation for excision of the calcified nodule through the smaller stab incision is the key to success for complete removal. Sometimes, repeated excisions may be necessary if residual lumps remain after the initial swelling subsides. Discomfort related to fat necrosis such as pain or paresthesia associated with these calcified nodules can be satisfactorily relieved after complete or even partial removal.

Sclerosing Nodules

These nodules usually appear as firm, fixed, and flat coin-like lesions (Fig. 3), which can be felt on palpation if located superficially underneath the skin. The margins are usually ill-defined and feel more like a sheet than a nodule on palpation. The sclerotic masses were excised directly through one or two stab incisions. The endpoint of excision is achieved when no further nodularity can be palpated.

Large Lumps

Large palpable lumps greater than 5 cm in size following fat grafting to the breasts are rare if the procedure is performed with expertise. It is the result of an inappropriately large bolus of fat graft being injected into one fixed area or space. Treatment involves aspiration with a large-bore cannula and repeated cycles of suction-irrigation using normal saline solution if the mass is soft and cystic in nature. The outermost shell that encapsulates the cystic mass can be left intact without the need for excision because it is usually thin and pliable. If the mass is calcified, fibrotic, and hard in consistency, it is best managed with direct excision. For optimal cosmesis, either aspiration or excision can be performed using a traditional breast augmentation incision such as an inframammary, periareolar, or transaxillary approach. If the transaxillary approach is used, assistance with

Fig. 1. Oil content aspirated from an oil cyst following fat necrosis.

Fig. 2. The excised fibrotic and calcified necrotic fat.

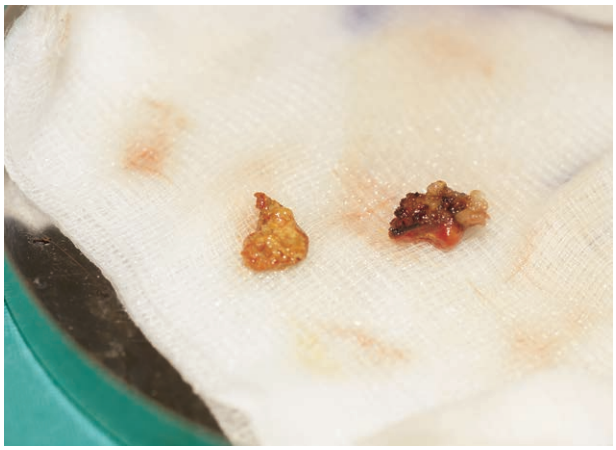

Fig. 3. The flat coin-like sclerosing tumor of fat necrosis.

endoscopic instruments may be necessary to facilitate excision.

In general, soft masses are often cystic in nature and can be aspirated, whereas hard or firm masses require excision. However, smaller, asymptomatic, and deep-seated (nonpalpable) solid masses found incidentally by imaging may not require any surgical intervention. In these scenarios, the possible risks of surgery, including poor cosmesis, outweigh any clinically significant benefits. When excision is considered as an option for management, the surgeon should look for any evidence of keloids or hypertrophic scars in the patient. If the patient has keloids or hypertrophic scars, the surgeon should have a discussion with the patient about potential problems, such as whether excision is worth the risk of having unsightly scars. Ultimately, surgical approaches to fat necrosis are individualized depending upon the depth, consistency, and size of each nodule.

RESULTS

No patients had reported breast cancer or interference with cancer screening during the follow-up period. The average increase in breast volume was 135 ± 20 cc on each side after one session of autologous fat transplantation. Combination of clinical examination and breast ultrasound revealed that 66 patients (9.6 percent) were found to have fat necrosis in the form of solitary or multiple cysts, sclerosing nodules, or calcifications in either one or both breasts postoperatively. Oil cysts were noticed in 63 patients, sclerosing nodules in 13 patients, calcified nodules in 25 patients, and a large lump/mass in two patients who had implant removal followed by immediate fat grafting for breast enhancement. The symptoms of different forms of fat necrosis in the superficial location of the breast could easily be differentiated from one another just by palpation of the mass size and consistency and could be further confirmed by breast ultrasound. The average time before first detection of any breast lump was 128 ± 45 days.

Among the 66 patients with some form of fat necrosis, 57 received treatment and nine refused any intervention because of the small size of the solitary lesion and absence of symptoms. Of the 57 patients treated, 32 required only simple aspiration, whereas 25 received at least one session of excision or a combination of more than one type of treatment modality. Pathologic evaluation of the excised masses showed necrotic fat cells surrounded by macrophages and multinucleated giant cells, chronic fibrosis, and calcification (Fig. 4). All nodules or lumps were successfully removed and incisional scars healed unremarkably. Three of 25 patients who required excision of the necrotic fat nodule had a repeated excision using the previous stab incision because of incomplete excision. After the second excision, the palpability of the nodule was successfully resolved. One patient was left with a depression at the site where the lump was removed previously and underwent subsequent fat grafting for correction of the contour deformity. Three patients complained of hypertrophic scar sitting at the stab incision site. The physical discomfort related to mass effect exerted by the oil cyst or calcified nodule found in all 11 patients was completely relieved after treatment. Overall, fat necrosis was satisfactorily managed in 54 of the 57 patients (94.7 percent symptom relief rate).

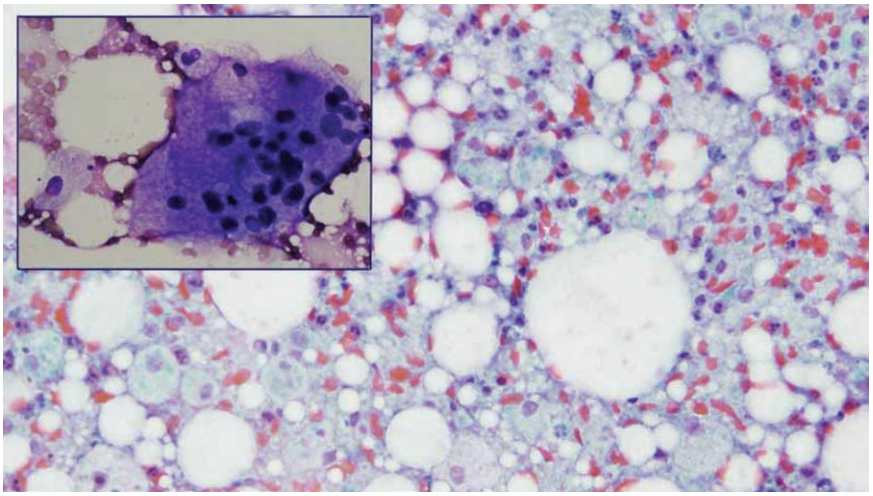

Fig. 4. Histology of necrotic fat typically show vacuoles with remnants of necrotic adipocytes surrounded by acute inflammatory cells, lipid-laden macrophages, and multinucleated giant cells.

CASE REPORTS

Case 1

A 22-year-old woman initially underwent 220-cc fat injection bilaterally for cosmetic breast augmentation. Approximately 4 months after her primary operation, three to four soft, tender breast lumps were palpated bilaterally. Sonography showed several well-defined 7- to 10-mm cysts. Using an 18-gauge needle and a 3-cc syringe, aspiration was performed on the painful, superficial cysts. Aspirated content appeared as an oily, yellow-tinged, semiliquid substance. Pain was relieved and the cysts were no longer palpable after aspiration. The puncture site for aspiration healed well (Fig. 5).

Case 2

A 25-year-old woman had received a 180-cc fat injection bilaterally for cosmetic breast augmentation and had an uneventful recovery. Two hard, 0.5-cm, flat, coin-like breast nodules were palpated 6 months postoperatively. Results of breast ultrasonography were negative. A stab incision was made directly above the lesions. Excision of the nodules was performed using careful finger palpation as guidance. Excised nodules appeared as yellowish white, fibrotic lesions. Final pathologic evaluation demonstrated necrotic fat cells surrounded by multinucleated giant cells with calcification and fibrosis. No further nodules were palpated after excision, and the incision healed well (Fig. 6).

Case 3

A 31-year-old woman who had previously undergone breast augmentation with saline implants presented for explantation because of Baker grade II to III capsular contracture and immediate breast augmentation with autologous fat transplantation. The 275-cc implants were removed through previous bilateral inframammary fold incisions, and 250 cc of fat was injected into each breast. Six months after surgery, breast asymmetry was noticed with the left breast larger than the right side, which was not observed before surgery. A sizable mass over the left breast and a smaller one on the right side was palpated. Breast echography showed solid heterogenous tumors inside the capsules from the previous saline implants on both sides. A 4-cm incision over the bilateral inframammary folds was made to approach the lumps. The mass appeared as a cluster of yellowish white, pearl-like cysts and firm calcified or fibrotic balls; each one measured 3 to 5 mm. Pathologic evaluation showed necrotic adipocytes with numerous inflammatory cells. After aggressive irrigation of the capsular space, the incisions were closed primarily. The breasts were asymmetric after débridement and the shape of the breasts became symmetric after management (Fig. 7).

DISCUSSION

It is believed that both survival and replacement are responsible for long-term retention of fat grafts.[13,14] Different approaches and techniques at each step could influence graft survival in this multistep procedure.[15] We also noticed that patients can respond very differently after fat grafting, even under the same strict protocol by the same surgeon. This may contribute to the wide range of reported fat necrosis rates; anywhere from 2 to 20 percent has been published in the literature.[6,16–18] According to the survival theory of fat grafting, fat necrosis is volume dependent. The more volume injected, the higher chances of fat necrosis, because it is technically more difficult to achieve an even distribution of graft placement during injection. In our series, we injected on average 200 cc of centrifuged fat with an observed rate of fat necrosis of approximately 9.6 percent.

A landmark study reported by Eto et al. demonstrates that adipocytes within 300 μm from the outermost surface of the transplanted adipose tissue survive and remain viable.[19] However, the fat graft located within the inner most part of the sphere eventually dies because of insufficient oxygen and nutrient support from the recipient

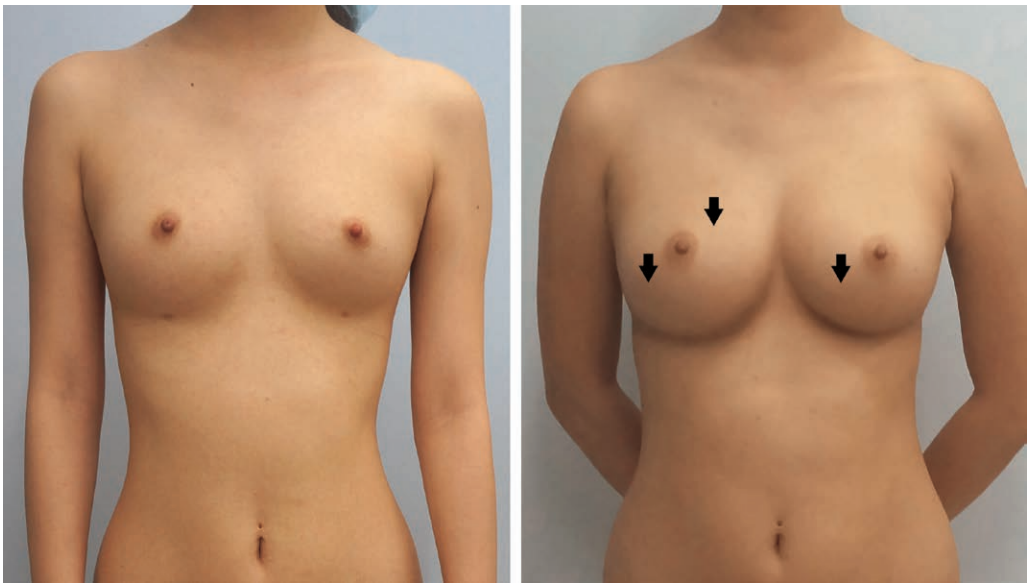

Fig. 5. The patient underwent breast augmentation with fat grafting (220 cc for each side) and developed several palpable oil cysts subsequently. Photographs of the patient before (*left*) and after (*right*) receiving aspiration of the oil cyst. Barely any surgical marks can be seen at the puncture sites (*arrows*).

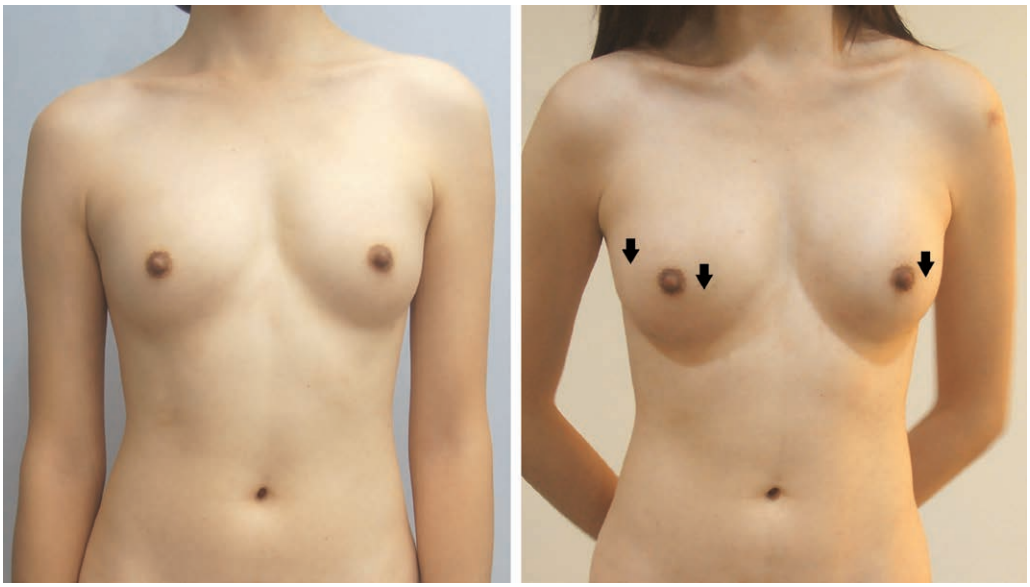

Fig. 6. The patient received 180 cc of fat grafts to each side of her breast for breast augmentation and developed several hard nodules caused by fat necrosis subsequently. Photographs obtained before (*left*) and after (*right*) stab incisions (*arrows*) for excision of calcified tumors caused by fat necrosis are shown. The scars healed inconspicuously.

tissue. In between these two zones lies the transitional zone, where part of the graft can be retained because of regeneration, likely through the help of adipose-derived stem cells. Three pathologic stages of retained necrotic fat after autologous fat transplantation have been identified.[20] Continued fibrosis and calcification can be seen in the histology of retained necrotic fat.[20,21] If fat necrosis takes place superficially or close to the skin, it tends to induce more inflammatory responses and can cause dermatitis and skin rashes because of the inherently higher immunogenicity of skin. Postinflammatory hyperpigmentation on breast skin can also develop.

Fat necrosis should be removed as early as possible once identified clinically. The palpable

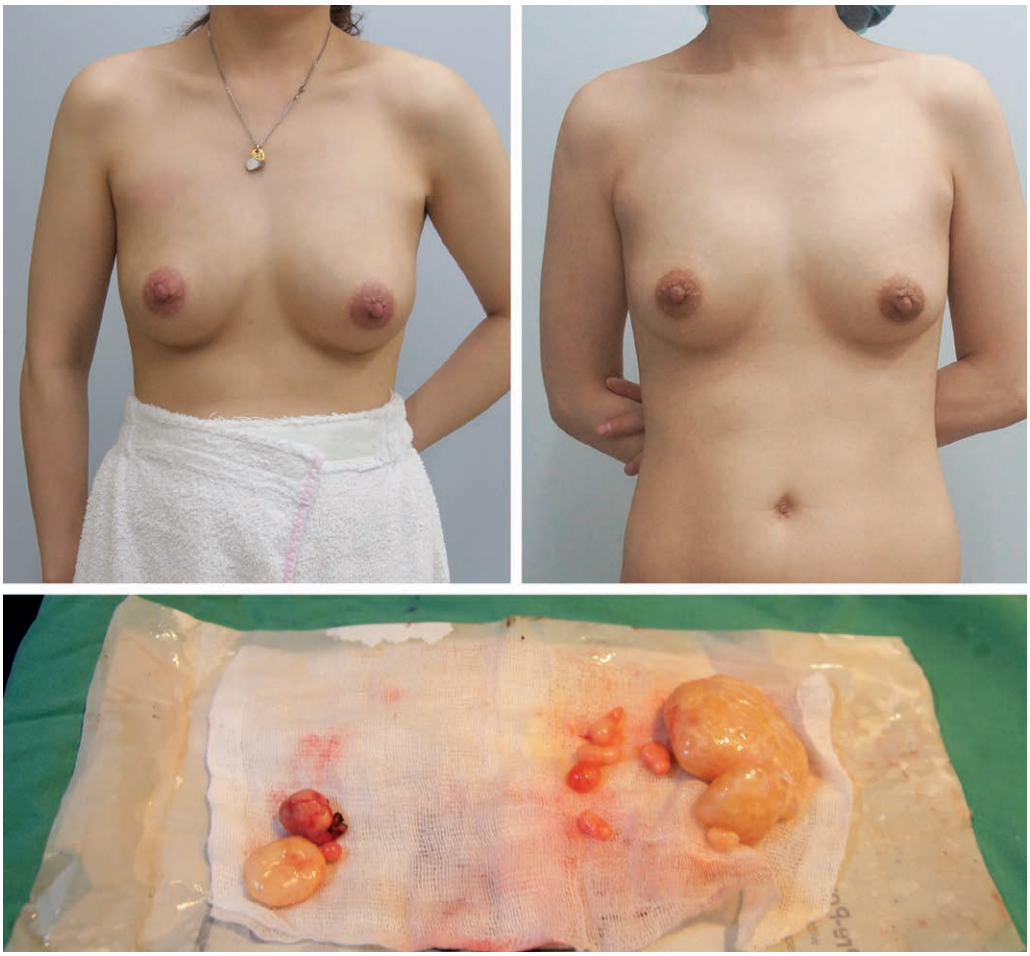

Fig. 7. The patient had undergone fat grafting to the breasts for augmentation immediately after removal of saline implants. Six months later, asymmetry of her breasts was noticed (*left*). A larger lump and a smaller lump (*center*) were removed from both breast capsules left behind from previous saline implants through a 4-cm incision in both inframammary folds. Symmetry was achieved and the incisions are well hidden (*right*).

lesions are generally easier to manage at an earlier stage. As the necrotic fat continues to mature, it becomes fixed to the surrounding tissue because of a continued fibrotic and inflammatory process, which may result in more difficultly in removal and usually requires excision. In our experience, multiple aspirations with a large-bore needle or liposuction technique to remove these fibrotic or sclerotic nodules is neither adequate nor completely successful once a firm and hard lesion is detected. In our series, the time needed to detect fat necrosis ranged from 3 months to 1 year postoperatively, which coincides with the time needed for encapsulation around necrotic fat to take place, leading to a palpable lesion. We believe that any lump or mass that develops more than 1 year after fat grafting to the breasts is less likely related to fat necrosis and requires a further comprehensive workup to rule out malignancy. We find it reasonable and adequate that we follow our patients by clinical palpation/examination only because palpability and its associated complications such as pain and skin reaction are the only complaints and symptoms we have found in all cases of fat necrosis. In addition, because of its benign nature, we believe that it may not be necessary to treat nonpalpable and asymptomatic fat necrosis. Therefore, we have only performed breast ultrasound for patients with positive clinical symptoms (i.e., palpability) because only those are of enough clinical significance and interest to the surgeon for diagnosis.

We propose an algorithm (Fig. 8) to serve as a guide for approaching fat necrosis after fat grafting to the breasts. The strategy and technique were developed based on our previous

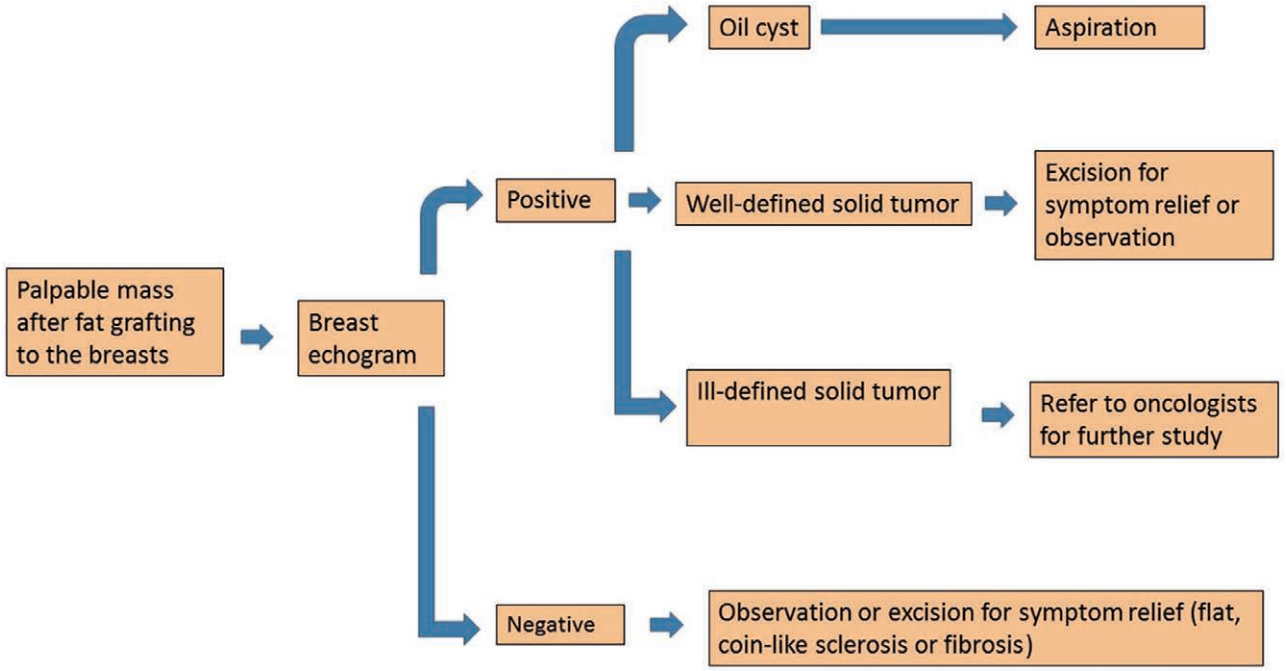

Fig. 8. Algorithm proposed for managing fat necrosis following autologous fat transplantation to breasts.

experience in managing fat necrosis after fat grafting to breasts in approximately 200 patients before 2009. Breast echography is performed whenever one or multiple nodules are palpable clinically. If a positive finding is confirmed under sonography, it can be identified by well-defined or ill-defined characteristics. An oil cyst appears as a well-defined hypoechoic halo and can be easily aspirated by a syringe mounted with an 18-gauge needle. Calcification or well-encapsulated fibrosis may appear as a well-defined hyperechoic mass and can be excised through stab incisions if located superficially. Any newly formed solid tumor with ill-defined borders or suspicious shape should be referred to an oncologist for further studies to rule out malignancy. In contrast, a palpable hard nodule that has benign and reassuring findings under sonography and contains a sclerosing or fibrotic component should be excised for symptom relief (pain or anxiety) or observed in asymptomatic cases. Asymptomatic fat necrosis in the deep layer may not be palpable and may be discovered only incidentally during routine breast imaging. These masses can be left untreated if they are relatively small or asymptomatic. On rare occasions, a large lump of necrotic fat can be developed in the deep breast tissue (especially when a large volume of fat graft is mistakenly placed into the capsule following breast implant removal). In these cases, the mass should be excised or aspirated because it will likely result in breast deformity or asymmetry.

There are limitations in this study in calculating the true incidence of fat necrosis because the true incidence of fat necrosis could be higher than reported in our series. In addition to clinical examination, breast ultrasound should have been performed routinely for all patients after fat grafting so that the incidence of fat necrosis could be determined more accurately. In addition, selected imaging studies with more specificity and sensitivity to fat necrosis, such as combination of ultrasound, mammographic, and three-dimensional magnetic resonance imaging studies, would demonstrate the true incidence of fat necrosis in all patients with follow-up to at least 1 year.

Ultimately, plastic surgeons must aim to primarily avoid fat necrosis. The effort must be made to pay close attention to precise fat grafting technique, as it is the expert consensus that this is still the best way to prevent fat necrosis and reduce its extent and severity following autologous fat transplantation to the breast.

CONCLUSIONS

Fat necrosis, as one of the major complications following autologous fat grafting for cosmetic breast augmentation, can be properly and safely managed as demonstrated by our large case series. The related symptoms of fat necrosis can

be satisfactorily relieved with few complications through the sound approach and practical guidelines as proposed by the authors.

Lee L. Q. Pu, M.D., Ph.D.
Division of Plastic Surgery
University of California, Davis
2221 Stockton Boulevard, Suite 2123
Sacramento, Calif. 95817
llpu@ucdavis.edu

REFERENCES

1. Czerny V. Plastischer Ersatz der Brustdruse durch ein Lipom. *Chir Kongr Verhandl.* 1895;2:216–217.
2. Bircoll M. Cosmetic breast augmentation utilizing autologous fat and liposuction techniques. *Plast Reconstr Surg.* 1987;79:267–271.
3. Bircoll M, Novack BH. Autologous fat transplantation employing liposuction techniques. *Ann Plast Surg.* 1987;18:327–329.
4. Gutowski KA. Current applications and safety of autologous fat grafts: A report of the ASPS Fat Graft Task Force. *Plast Reconstr Surg.* 2009;124:272–280.
5. Coleman S, Saboeiro AP. Fat grafting to the breast revisited: Safety and efficacy. *Plast Reconstr Surg.* 2007;119:775–785.
6. Zheng DN, Li QF, Lei H, et al. Autologous fat grafting to the breast for cosmetic enhancement: Experience in 66 patients with long-term follow up *J Plast Reconstr Aesth Surg.* 2008;61:792–798.
7. Illouz YG, Sterodimas A. Autologous fat transplantation to the breast: A personal technique with 25 years of experience. *Aesthetic Plast Surg.* 2009;33:706–715.
8. Voglimacci M, Garrido I, Mojallal A, et al. Autologous fat grafting for cosmetic breast augmentation: A systematic review. *Aesthet Surg J.* 2015;35:378–393.
9. Veber M, Tourasse C, Toussoun G, Moutran M, Mojallal A, Delay E. Radiographic findings after breast augmentation by autologous fat transfer. *Plast Reconstr Surg.* 2011;127:1289–1299.
10. Coleman SR, Saboeiro AP. Primary breast augmentation with fat grafting. *Clin Plast Surg.* 2015;42:301–306, vii.
11. Coleman SR. Structural fat grafting: More than a permanent filler. *Plast Reconstr Surg.* 2006;118(Suppl):108S–120S.
12. Abboud MH, Dibo SA. Immediate large-volume grafting of autologous fat to the breast following implant removal. *Aesthet Surg J.* 2015;35:819–829.
13. Pu LL. Mechanism of fat graft survival. *Ann Plast Surg.* 2016;77(Suppl):S49–S52.
14. Pu LL. Towards more rationalized approach to autologous fat grafting. *J Plast Reconstr Aesthet Surg.* 2012;65:413–419.
15. Lin JY, Wang CM, Pu LL. Can we standardize the techniques for fat grafting? *Clin Plast Surg.* 2015;42:389–394.
16. Mu DL, Luan J, Mu L, Xin MQ. Breast augmentation by autologous fat injection grafting: Management and clinical analysis of complications. *Ann Plast Surg.* 2009;63:124–127.
17. Hyakusoku H, Ogawa R, Ono S, Ishii N, Hirakawa K. Complications after autologous fat injection to the breast. *Plast Reconstr Surg.* 2009;123:360–370; discussion 371–372.
18. Petit JY, Lohsiriwat V, Clough KB, et al. The oncologic outcome and immediate surgical complications of lipofilling in breast cancer patients: A multicenter study—Milan-Paris-Lyon experience of 646 lipofilling procedures. *Plast Reconstr Surg.* 2011;128:341–346.
19. Eto H, Kato H, Suga H, et al. The fate of adipocytes after nonvascularized fat grafting: Evidence of early death and replacement of adipocytes. *Plast Reconstr Surg.* 2012;129:1081–1092.
20. Kato H, Mineda K, Eto H, et al. Degeneration, regeneration, and cicatrization after fat grafting: Dynamic total tissue remodeling during the first 3 months. *Plast Reconstr Surg.* 2014;133:303e–313e.
21. Mineda K, Kuno S, Kato H, et al. Chronic inflammation and progressive calcification as a result of fat necrosis: The worst outcome in fat grafting. *Plast Reconstr Surg.* 2014;133:1064–1072.