

Breast pathology in complications associated with polyacrylamide hydrogel (PAAG) mammoplasty

KM Leung 梁啟文
Gary PS Yeoh 楊佩成
KW Chan 陳健慧

Objective To study the tissue pathology of breast lesions associated with hydrophilic polyacrylamide gel injection augmentation mammoplasty.

Design Retrospective study.

Setting Private anatomical pathology practice, Hong Kong.

Patients Eight patients who underwent lumpectomy of the breast due to complications of hydrophilic polyacrylamide gel injection for augmentation mammoplasty.

Main outcome measures Identification of hydrophilic polyacrylamide gel in breast tissue and associated pathological changes.

Results We reviewed the pathological changes in breast tissue associated with hydrophilic polyacrylamide gel injection in eight cases retrieved from our archive. Microscopically, the hydrophilic polyacrylamide gel appeared as pools of pale violet gelatinous material of variable size, between the interstices of connective tissue and fat cells. The larger pools were often surrounded by cellular reactions consisting of histiocytic cells and foreign body-type multinucleated giant cells. Inflammatory reaction featuring infiltration by lymphocytes and plasma cells in the adjacent breast tissue was observed in samples from four patients, and a sample from another patient showed acute inflammation with abscess formation. There was no evidence of abnormal cellular proliferation, atypia or malignant change in the stromal connective tissue or ductal-acinic epithelial components of the breast tissue.

Conclusions Hydrophilic polyacrylamide gel injection for augmentation mammoplasty can give rise to a breast lump and inflammation. Pathologically, this complication is associated with fibrosis, foreign body reaction, and inflammation.

Introduction

The complications of hydrophilic polyacrylamide gel (PAAG) augmentation mammoplasty have recently caught the attention of both the medical field and the general public in Hong Kong. Patients enduring complications typically complain of: pain, breast mass, and infection requiring surgical intervention, and rarely even mastectomy. Polyacrylamide gel is a combination of 2.5 to 5% polyacrylamide, a synthetic polymer, suspended in 95 to 97.5% apyrogenous water.¹⁻³ Contamination with the neurotoxic monomer acrylamide cannot be totally avoided in the manufacturing process, but as long as its content is below 0.0064 µg/mL, no toxic reactions (short- or long-term) were observed when administered orally to rats, fish, and dogs. Nor were complications encountered when it was inhaled by workers in the course of polyacrylamide production. Polyacrylamide gel is the only injectable implant that remains soft after it has been injected. Post-injection, the water content is absorbed by the body while the PAAG becomes encapsulated, remaining soft and pliable like the body's own tissue. At a tissue level, it is supposed to be non-absorbable and kept in place by fine fibrous capsules. The gel has been available for clinical use for more than 30 years; traditionally it was used to improve skin contour and reduce depressions due to scars, injury, or lines. It is used to correct facial lines and features that could have been amenable to collagen replacement or hyaluronic therapy, particularly if a more permanent solution is required. Since 1997, PAAG imported from the Ukraine has been used for augmentation mammoplasty in China.⁴ We report here the pathological changes in the breast tissue of eight patients who suffered complications of PAAG breast augmentation.

Key words

Acrylamides; Acrylic resins; Breast implants; Cosmetics; Injections

Hong Kong Med J 2007;13:137-40

Diagnostix Pathology Laboratories Ltd,
Canossa Hospital, 1 Old Peak Road,
Hong Kong

KM Leung, DABPath, FHKAM (Pathology)

GPS Yeoh, FRCPA, FHKAM (Pathology)

KW Chan, FRCPath, FHKAM (Pathology)

Correspondence to: Dr KM Leung
E-mail: kmleung@diagnostix.com.hk

與聚丙烯醯胺水凝膠乳房成形術相關的乳房 病理學併發症

- 目的** 研究因注射聚丙烯醯胺水凝膠 (PAAG) 乳房成形術引致乳房受損的病理學情況。
- 設計** 回顧式研究。
- 安排** 香港一所私家醫院的病理組織化驗所。
- 患者** 八名接受PAAG注射乳房成形術後產生併發症，而須進行乳房切除手術的病人。
- 主要結果測量** 在乳房組織發現的PAAG和有關的病理組織轉變。
- 結果** 我們從檔案得到八名病人的乳房組織，研究因注射PAAG有關的病理組織轉變。從顯微鏡觀察，PAAG形成不同大小的塊狀淡紫色明膠物體，位於結締組織和脂肪組織間的間隙。較大塊的PAAG經常被細胞的反應所圍繞，包括組織細胞和異物多核巨細胞。其中四名病人有乳房組織旁淋巴滲入和漿細胞滲入引致發炎，另一名病人的樣本則有急性發炎並形成膿腫。所有病人都沒有反常的細胞增生、畸形或在基質結締組織或乳房組織的管至腺泡上皮成份有惡性腫瘤病變。
- 結論** PAAG注射乳房成形術可以增加乳房成塊狀或發炎的風險。病理學上，這併發症與纖維化、異物反應和發炎有關。

Methods

Between January 2001 to July 2006, breast lumpectomy specimens from eight patients with a history of PAAG injection were retrieved from the surgical pathology archive of our laboratory. Relevant details pertaining to these patients are listed in Table 1. Information regarding their clinical presentations was recorded on the respective requisition forms. The specimens were processed in the routine fashion for breast lumpectomy and included a gross examination of the size, weight, and appearance of the tissue, marking for surgical margins and selection of tissue for paraffin sections and microscopic examination. The paraffin sections were stained with standard

haematoxylin and eosin (H&E) stains and examined under tungsten light microscopy.

Results

Patient age ranged from 29 to 45 (mean, 33) years. Seven of them presented with a lump in the breast. In one patient, the lump was only detectable by ultrasound and mammogram. One presented with repeated episodes of inflammation with abscess formation and had been treated surgically erstwhile. The size of the lesions ranged from 1 to 10.5 cm (mean, 4.4 cm). In three patients, the lesions were removed piecemeal, so the size could not be accurately measured. Cut surfaces of the specimens showed a gelatinous appearance. Examined microscopically, the consistent features seen in all lesions were pools of pale purple gel of various sizes and shapes. The gelatinous substance was neither refractile nor birefringent under polarised light. Most of the pools were oval to round shaped, but some were irregularly shaped with sharp pointed edges, probably as a result of retraction due to dehydration during tissue processing (Fig 1). The size of these gel pools varied from microscopic (30-40 μ m) to macroscopic (1-1.5 cm). No special stains were known to illustrate the gelatinous substance any better than the regular H&E stain. When there was no foreign body reaction or inflammation, the larger gel pools appeared surrounded by a thin fibrous capsule, about 30 to 50 μ m thick. The larger pools appeared to have been formed by coalescence of smaller pools. Hypocellular collagenous fibrous tissue was seen between and surrounding the gel pools. Unlike silicon implants, no crystalline substances were seen in any of the lesions. The second commonest feature was foreign body reaction, noted in the specimens from six of the eight patients. The cellular reaction was composed of histiocytic and multinucleated foreign body-type giant cells, intimately surrounding the gel pools (Fig 2). This reaction was more commonly associated with larger than smaller gel pools. Inflammation was only noted in specimens with foreign body reactions. Non-specific chronic inflammation was noted in specimens from three patients and one showed both acute and

TABLE 1. Clinical characteristics of eight patients suffering complications from polyacrylamide gel augmentation mammoplasty

Case No.	Age (years)	Presentation	Size of tissue removed (cm)
1	34	Mass*	1.1 x 1 x 0.9
2	29	Mass	4.5 x 3 x 2
3	45	Abscess	1.6 x 0.6 x 1.2
4	31	Mass	2 x 1.5 x 0.6 to 5 x 4 x 0.7
5	32	Mass	Up to 4.5 x 3 x 2
6	32	Mass	3.7 x 2 x 1.1 to 10.5 x 7 x 2
7	Unknown	Mass	7 x 4 x 1 and 1.5 x 1 x 0.6
8	29	Mass	1 x 1 x 0.8

* Detected by ultrasound and mammogram only

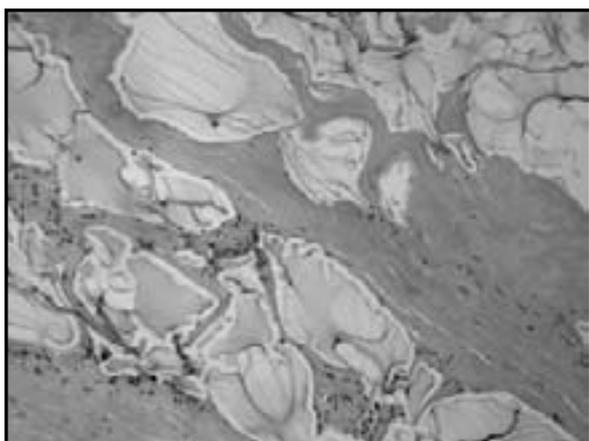


FIG 1. Pools of gelatinous material, some retracted (presumably due to dehydration during tissue processing)

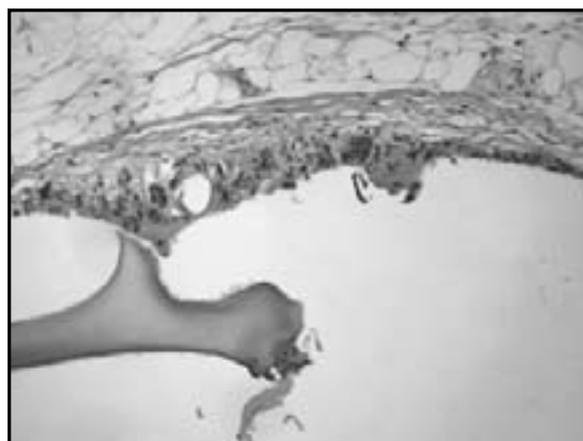


FIG 2. Cellular membrane surrounding a gel pool

TABLE 2. Summary of pathological findings in complications of polyacrylamide gel mammoplasty

Case No.	Pools of gelatinous material	Foreign body reaction	Chronic inflammation	Acute inflammation
1	✓	✓		
2	✓	✓		
3	✓	✓	✓	✓
4	✓			
5	✓	✓	✓	
6	✓			
7	✓	✓	✓	
8	✓	✓	✓	

chronic inflammation. The chronic inflammation was characterised by infiltration with lymphocytes, plasma cells, and a small number of eosinophils between and surrounding the gel pools. Periductal lymphoid follicles with germinal centres were seen in one specimen. An acute inflammatory component with neutrophilic infiltration was only noted in the specimen from the patient presenting with repeated abscesses (Table 2). Microcalcifications, a long-term side-effect of silicone-covered implants,⁵ were not seen. There was no evidence of malignancy or atypical cellular change in the stromal tissue or in the ductal epithelial components.

Discussion

Hydrophilic PAAG is considered atoxic, non-immunogenic, and can be injected directly into human tissue as a permanent tissue expander for cosmetic surgery. In one study involving 228 patients undergoing facial reconstruction by PAAG injection followed up for 1 year, 37 presented with complications, including swelling, haematoma, redness, pain, or itching.⁶ No severe adverse events were related to the gel. The reactions observed were attributable to the injection procedure rather than the gel's chemical properties.

During the first year after treatment, no permanent soft-tissue reactions were observed. Arguably the follow-up period was short, but the evidence seemed to suggest that the use of PAAG in facial reconstructive surgery is reasonably safe.

Reactions to silicone also tend to present as breast masses. A previous study⁷ and ours found that in general, the thick fibrous capsules described following silicone implants were not detected with PAAG. Instead, individual gel pools were surrounded by delicate fibrous tissue. Extravasated silicone is readily visualised as refractile translucent particles with the microscope condenser lowered, while this property was not evident with PAAG. When silicone leaks and comes into contact with breast tissue, it causes a tissue response involving histiocytes, foreign body-type multinucleated giant cells and lymphocytes,⁵ similar to the tissue response to PAAG. Synovial-like metaplasia and calcifications, features associated with silicone implants, were not seen with PAAG in this study, nor are they reported in the literature. Also unlike silicone, PAAG tends to stay at the injection site without being degraded or displaced.

However, the true incidence of complications associated with the injection of PAAG in augmentation

mammoplasty is difficult to ascertain, owing to the lack of well-designed follow-up studies. In one series reporting 30 patients from China, complications were encountered between 3 and 36 months following surgery.⁴ However there was no information on the numbers who had undergone the procedure in the first place. As in our series, nearly all the patients presented with breast lumps; other common complications included breast pain, disfigurement, and infection. Ultrasound examination showed diffuse, irregular, anechoic zones of mammary tissue. Pathological examination revealed inflammatory cell infiltration and fibrous capsule formation. The symptoms of most of their patients were relieved after removal of the PAAG. The largest series has been reported from the Kiev City Hospital, Ukraine.⁷

Of the approximately 300 women per year treated for breast augmentation using PAAG (manufactured in Switzerland), only 27 returned for re-operation. However, the rate of minor complications not requiring surgical treatment was not reported. According to the hospital pathology reports they cited, PAAG appeared to be well-tolerated in the subcutaneous compartment and in glandular breast tissue for up to 10 years. When not producing a mass, the gel was seen as thin elongated deposits splitting the connective tissue fibres or fat cells. We searched the literature and found no reports of carcinogenesis associated with PAAG use. We believe that carefully planned prospective studies are needed to determine the true incidence of complications associated with injection PAAG mammoplasty.

References

1. Amended final report on the safety assessment of polyacrylamide and acrylamide residues in cosmetics. *Int J Toxicol* 2005;24(Suppl 2):21S-50S.
2. Smith EA, Oehme FW. Acrylamide and polyacrylamide: a review of production, use, environmental fate and neurotoxicity. *Rev Environ Health* 1991;9:215-28.
3. King DJ, Noss RR. Toxicity of polyacrylamide and acrylamide monomer. *Rev Environ Health* 1989;8:3-16.
4. Cheng NX, Wang YL, Wang JH, Zhang XM, Zhong H. Complications of breast augmentation with injected hydrophilic polyacrylamide gel. *Aesthetic Plast Surg* 2002;26:375-82.
5. Yeoh G, Russell P, Jenkins E. Spectrum of histological changes reactive to prosthetic breast implants: a clinicopathological study of 84 patients. *Pathology* 1996;28:232-5.
6. von Buelow S, von Heimburg D, Pallua N. Efficacy and safety of polyacrylamide hydrogel for facial soft-tissue augmentation. *Plast Reconstr Surg* 2005;116:1137-48.
7. Christensen LH, Breiting VB, Aasted A, Jørgensen A, Kebuladze I. Long-term effects of polyacrylamide hydrogel on human breast tissue. *Plast Reconstr Surg* 2003;111:1883-90.

Coming in the June 2007 issue of the *Hong Kong Medical Journal*

- Patients' attitudes towards epidural analgesia in labour
- Delayed presentation and treatment of newly diagnosed pulmonary tuberculosis patients in Hong Kong
- Diagnostic utility and safety of long-term video-EEG monitoring